Efficacy of Guselkumab in Moderately to Severely Active Crohn's Disease According to Induction Clinical Response Status: Week 48 Results from the GALAXI 2 & 3 Phase 3 Trials

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Key Takeaways

- Among the subset of participants with moderate to severely active Crohn's disease who achieved clinical response to GUS induction at Week 12, most went on to achieve clinical remission, PRO-2 remission, or endoscopic response at Week 48, across both GUS SC maintenance dose cohorts.
- Efficacy at Week 48 with both GUS SC maintenance doses was also observed among participants who were not in clinical response at Week 12, suggesting a potential benefit of continued treatment with GUS even if clinical response is not achieved at Week 12 after IV induction.

Background

- Guselkumab (GUS) is a dual-acting IL-23p19 subunit inhibitor that potently neutralizes IL-23 and binds to CD64, a receptor on cells that produce IL-23[1]
- GALAXI 2 & 3 (NCT03466411) are identical 48-week, randomized, double-blind, double-dummy, placebo (PBO)- and active comparator (ustekinumab)–controlled registrational trials assessing the efficacy and safety of GUS in participants with moderately to severely active Crohn's disease
- As reported previously, composite co-primary efficacy endpoints were met for both GUS dose cohorts versus PBO in both studies[2]
  - Clinical response at Week 12 **and** clinical remission at Week 48
  - Clinical response at Week 12 **and** endoscopic response at Week 48
  - **Both GUS dose regimens also demonstrated statistical superiority to ustekinumab in pre-specified and multiplicity controlled analyses of pooled data at Week 48**

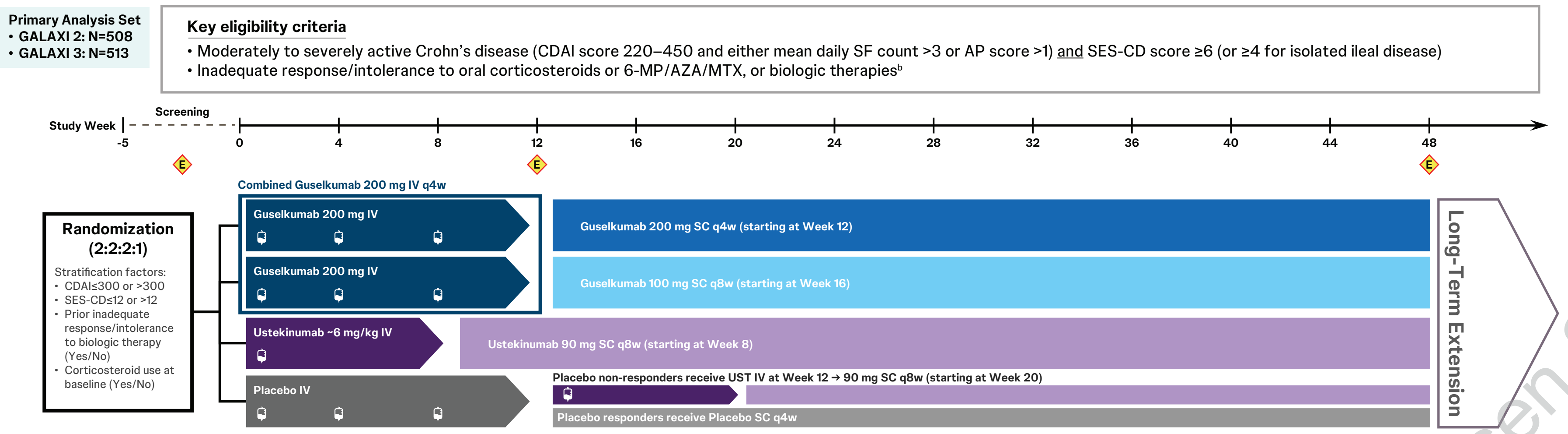
Objective

These exploratory analyses evaluated clinical and endoscopic endpoints at Week 48 among pooled GALAXI 2 & 3 participants with and without a clinical response to GUS induction therapy at Week 12

Methods

GALAXI 2 & 3 used a treat-through design, where participants were randomized to a treatment regimen at Week 0 and remained on that regimen through Week 48 of each study regardless of their clinical response status at Week 12 (**Figure 1**)[a]

Figure 1. Identical, Double-Blind, Treat-Through Studies: GALAXI 2 & 3


Primary Analysis Set
• GALAXI 2: N=508
• GALAXI 3: N=513
Key eligibility criteria
• Moderately to severely active Crohn's disease (CDAI score 220–450 and either 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[b]
Study Week
Screening
-5
0
4
8
12
16
20
24
28
32
36
40
44
48
E
Combined Guselkumab 200 mg IV q4w
Randomization (2:2:2:1)
Stratification factors:
• CDAI≤300 or >300
• SES-CD≤12 or >12
• Prior inadequate response/intolerance to biologic therapy (Yes/No)
• Corticosteroid use at baseline (Yes/No)
Guselkumab 200 mg IV
Guselkumab 200 mg IV
Guselkumab 200 mg SC q4w (starting at Week 12)
Guselkumab 100 mg SC q8w (starting at Week 16)
Ustekinumab ~6 mg/kg IV
Ustekinumab 90 mg SC q8w (starting at Week 8)
Placebo IV
Placebo non-responders receive UST IV at Week 12 → 90 mg SC q8w (starting at Week 20)
Placebo responders receive Placebo SC q4w
Long-Term Extension

[a]With the exception of participants randomized to placebo at Week 0 who did not achieve clinical response at Week 12; these participants crossed over to treatment with the active comparator, ustekinumab. [b]Biologic therapies: TNF antagonists or vedolizumab. 6-MP=6-mercaptopurine; AP=abdominal pain; AZA=azathioprine; CDAI=Crohn's disease activity index; E=endoscopy; IV=intravenous; MTX=methotrexate; q4w=every 4 weeks; q8w=every 8 weeks; SC=subcutaneous; SES-CD=Simple Endoscopic Score for Crohn's Disease; SF=stool frequency; UST, ustekinumab. 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.

Week 48 efficacy outcomes were evaluated according to Week 12 clinical response status (**Table 1**)

Table 1. Clinical and Endoscopic Outcome Definitions

Outcome	Definition
GUS induction clinical responders at Week 12	
Clinical response	≥100-point reduction from baseline in CDAI score or CDAI score <150
Efficacy outcomes at Week 48	
Clinical remission	CDAI score <150
PRO-2 remission	Participant-reported CDAI components of AP and SF mean daily scores ≤1 and ≤3, respectively, with no worsening from baseline
Endoscopic response	≥50% improvement in SES-CD score or SES-CD score ≤2

AP=abdominal pain; CDAI=Crohn's disease activity index; GUS=guselkumab; PRO-2=participant-reported CDAI components of abdominal pain and stool frequency; SES-CD=Simple Endoscopic Score for Crohn's Disease; SF=stool frequency.

Analysis methods

- These post-hoc analyses used pooled GALAXI 2 & 3 data
  - The analysis included GUS SC maintenance dose cohort participants from the primary analysis set of each study who were treated at Week 12
  - The same analyses of the individual trials were prespecified

Results

Population

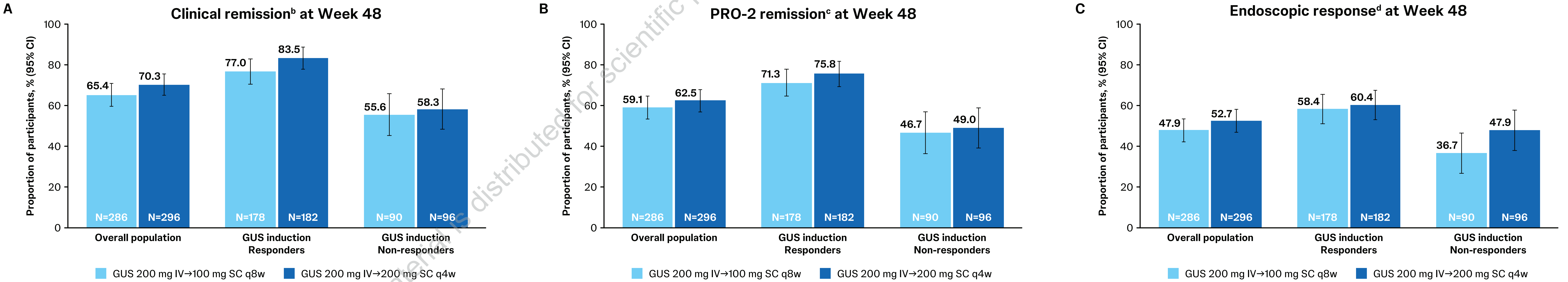
- 546 participants were included in this analysis of the pooled GALAXI 2 & 3 datasets
- 65.9% (360/546) achieved a clinical response to GUS 200 mg IV induction therapy at Week 12

Efficacy Outcomes

Among the subset of participants who achieved clinical response at Week 12, most achieved clinical remission (77.0–83.5%, **Figure 2A**) or PRO-2 remission (71.3–75.8%, **Figure 2B**) at Week 48 in both GUS SC maintenance dose cohorts. Likewise, the majority of GUS recipients who achieved clinical response at Week 12 achieved endoscopic response at Week 48 (58.4–60.4%, **Figure 2C**)

More than half of the participants who did not achieve clinical response at Week 12 achieved clinical remission at Week 48 (55.6–58.3%, **Figure 2A**). Many participants achieved PRO-2 remission at Week 48 (46.7–49.0%, **Figure 2B**) along with endoscopic response at Week 48 (36.7–47.9%, **Figure 2C**)

Figure 2. Efficacy Outcomes at Week 48 in GALAXI 2 & 3 Participants with and without a Clinical Response to 12-Week Induction Treatment with Guselkumab (Week 12 Treated Primary Analysis Set)[a]


A
Clinical remission[b] at Week 48
Proportion of participants, % (95% CI)
100
80
60
40
20
0
65.4
70.3
77.0
83.5
55.6
58.3
N=286
N=296
N=178
N=182
N=90
N=96
Overall population
GUS induction Responders
GUS induction Non-responders
GUS 200 mg IV→100 mg SC q8w
GUS 200 mg IV→200 mg SC q4w
B
PRO-2 remission[c] at Week 48
Proportion of participants, % (95% CI)
59.1
62.5
71.3
75.8
46.7
49.0
N=286
N=296
N=178
N=182
N=90
N=96
Overall population
GUS induction Responders
GUS induction Non-responders
GUS 200 mg IV→100 mg SC q8w
GUS 200 mg IV→200 mg SC q4w
C
Endoscopic response[d] at Week 48
Proportion of participants, % (95% CI)
47.9
52.7
58.4
60.4
36.7
47.9
N=286
N=296
N=178
N=182
N=90
N=96
Overall population
GUS induction Responders
GUS induction Non-responders
GUS 200 mg IV→100 mg SC q8w
GUS 200 mg IV→200 mg SC q4w

[a]Includes participants from the primary analysis set, defined as all randomized participants who received ≥1 (partial or complete) dose of study intervention and had a screening SES-CD score ≥6 (or ≥4 for pts with isolated ileal disease), who were treated at Week 12 and did not have a CD-related surgery; prohibited change in concomitant CD medication; or discontinue study agent due to lack of efficacy, an AE of worsening CD, or for any other reason other than COVID-19-related reasons or regional crisis in Ukraine and Russia prior to Week 12. Overall population data are for the primary analysis set. Responder and non-responder to GUS induction treatment defined as achieving a clinical response at Week 12 (≥100-point reduction from baseline in CDAI score or CDAI score <150) or not, respectively. 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 non-response, 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 onward. Missing data imputation: 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. [b]CDAI remission defined as CDAI score <150. [c]PRO-2 remission defined as AP mean daily score ≤1 and SF mean daily score ≤3, and no worsening of AP or SF from baseline. [d]Endoscopic response defined as ≥50% improvement from baseline in SES-CD score or SES-CD score ≤2. AE=adverse event; AP=abdominal pain; CD=Crohn's disease; CDAI=Crohn's disease activity index; CI=confidence interval; GUS=guselkumab; IV=intravenous; PRO-2=participant-reported CDAI components of abdominal pain and stool frequency; q4w=every 4 weeks; q8w=every 8 weeks; SC=subcutaneous; SES-CD=Simple Endoscopic Score for Crohn's Disease; SF=stool frequency.

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REFERENCES: 1. Atreya R, et al. *J Crohns Colitis.* 2024;18(suppl):S470. 2. Panaccione R, et al. *Gastroenterology.* 2024;166(5 suppl):1057b–1057b2.

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