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

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Background

Guselkumab 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]

Clinical trials of guselkumab in Crohn's disease (CD) excluded individuals who had inadequate response or intolerance to ustekinumab; therefore, the efficacy of guselkumab after ustekinumab treatment has not been previously evaluated

GALAXI 1 (NCT03466411) is a phase 2b study that evaluated guselkumab in participants with moderately to severely active CD

- Participants treated with ustekinumab who met inadequate response criteria during long term extension (LTE) could switch to guselkumab

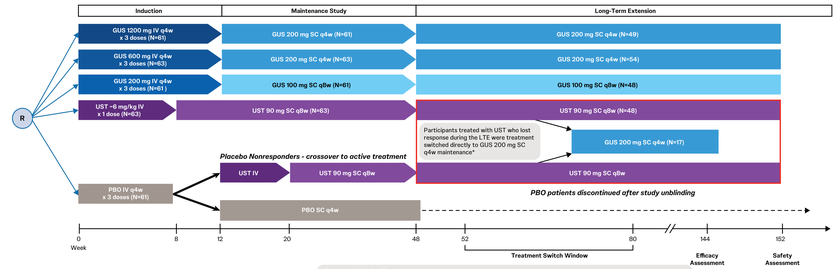
The results of the GALAXI 2/3 studies have been previously reported[2]

Objective

Here, we present efficacy and safety results in participants who received guselkumab after experiencing an inadequate response to ustekinumab in the GALAXI 1 LTE

Methods

GALAXI-1 Long-Term Extension Study Design



*Treatment Switch 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.

Endpoints

Assessed 16 weeks after treatment adjustment:
- Clinical response
- Clinical remission

Assessed at LTE Weeks 96 and 144 (approximately 1 and 2 years after treatment adjustment, respectively)
- Endoscopic response
- Endoscopic remission

Outcome Definitions
- **Clinical response:** ≥100-point reduction from baseline in CDAI score or CDAI score <150
- **Clinical remission:** CDAI score <150
- **Endoscopic response:** ≥50% improvement from baseline in SES-CD score or SES-CD ≤2
- **Endoscopic remission:** SES-CD ≤4 and at least a 2-point reduction from baseline and no subscore greater than 1 in any individual component

Data Handling
- Efficacy and safety analyses include data starting from the time of dose-adjustment
- Participants who had a CD-related surgery or discontinued study intervention due to lack of efficacy or an AE of worsening CD prior to the timepoint were considered not to have met the endpoint at the timepoint. Participants who had discontinued study intervention due to the reasons other than COVID-19 restrictions/issues, lack of efficacy or AE of worsening Crohn's disease prior to the timepoint had their observed data used, if available. Participants who had discontinued study intervention due to COVID-19 restrictions/issues prior to the timepoint did not have their data used at the timepoint.
- After applying the above treatment failure rules, participants who had missing outcome data at the designated analysis timepoint were considered not to have achieved the endpoint at that timepoint.

Key Takeaways

- **Among participants who experienced inadequate response to ustekinumab and switched to guselkumab in the GALAXI 1 LTE:**
  - **The majority achieved clinical remission 16 weeks after treatment switch**
  - **The majority were in endoscopic response approximately 1 year after treatment switch**
- **These data suggest that patients with moderately to severely active CD who experienced an inadequate response to ustekinumab may benefit from guselkumab treatment**
- **Results are limited by small sample size and direct treatment switch to guselkumab SC maintenance dosing without IV induction.**

Results

Table 1. Demographics and Disease Characteristics at Induction Baseline

Participants treatment-switched in LTE	Ustekinumab 90 mg SC q8w → Guselkumab 200 mg SC q4w (N=17)
Demographics	
Age in years, mean (SD)	35.4 (10.95)
Male, n (%)	12 (70.6%)
Characteristics	
CD duration in years, mean (SD)	10.0 (7.40)
CDAI score, mean (SD)	293.0 (41.09)
SES-CD score, mean (SD)	13.2 (6.64)
Endoscopic disease severity (SES-CD score), n (%)	
Moderate (7–16)	9 (52.9%)
Severe (>16)	6 (35.3%)
Involved GI areas by central reader, n (%)	
Ileum only	3 (17.6%)
Colon only	5 (29.4%)
Ileum and Colon	9 (52.9%)
CRP in mg/L, median (IQR)	2.6 (0.8; 6.4)
Fecal calprotectin in µg/g, median (IQR)	369.0 (179.0; 512.0)
History of inadequate response/intolerance[a] to biologic therapy (BIO-IR), n (%)	12 (70.6%)

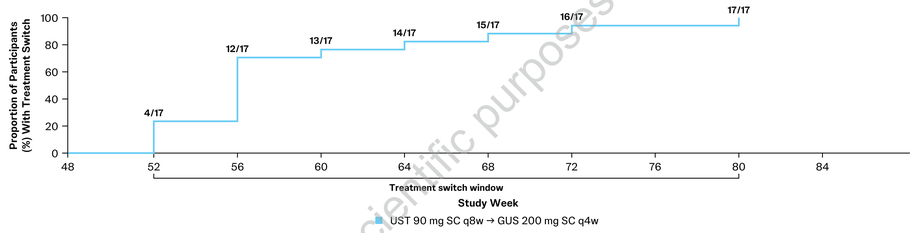
[a]Primary nonresponse, secondary nonresponse, or intolerance. **CD**=Crohn's disease; **CDAI**=Crohn's disease activity index; **CRP**=C-reactive protein; **IQR**=interquartile range; **LTE**=long-term extension; **SC**=subcutaneous; **SD**=standard deviation; **SES-CD**=simple endoscopic score for Crohn's disease.

Safety Summary

- 1 injection-site reaction occurred (participant recovered and continued in the study)
- 1 serious adverse event occurred (irritable bowel syndrome; participant recovered and continued in the study)
- There were no adverse events that led to discontinuation in the subgroup

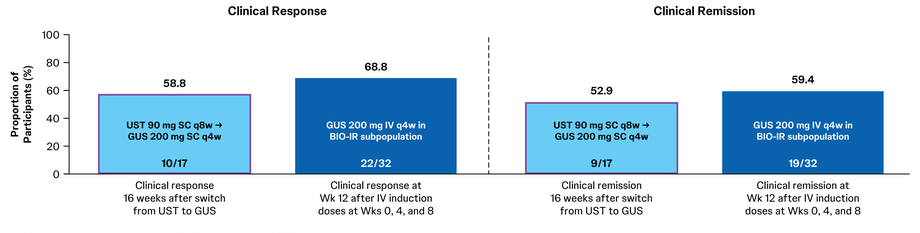
A total of 17 participants treated with ustekinumab during the LTE had inadequate response and switched to guselkumab 200 mg SC q4w without IV induction
- The majority of these participants switched to guselkumab within the first 8 weeks of the treatment switch window

Figure 1. Time to Inadequate Response and Treatment Switch: Participants Treatment-switched to Guselkumab 200 mg SC q4w From Ustekinumab 90 mg SC q8w



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

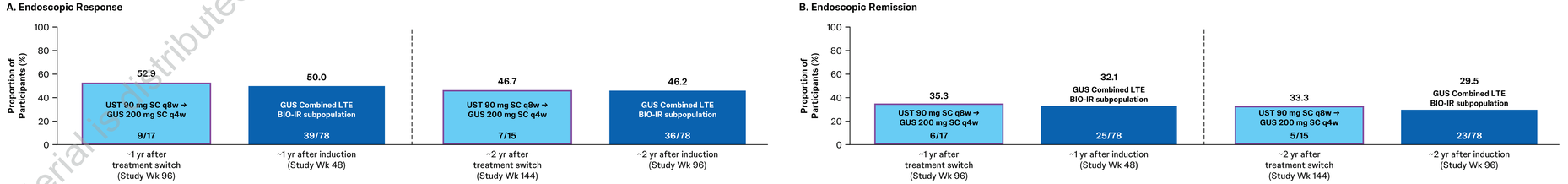
Figure 2. Clinical Outcomes 16 Weeks After Treatment Switch



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.

Endoscopic response and remission approximately one and two years after treatment switch (study weeks 96 and 144, respectively) were consistent with the one- and two-year endoscopic response and remission results (study weeks 48 and 96, respectively) in BIO-IR patients who received guselkumab throughout the LTE

Figure 3. Endoscopic Outcomes by Years Treated With Guselkumab



BIO-IR=history of inadequate response/intolerance to biologic therapy.

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