MP582

# Guselkumab maintenance dose regimens in patients with high disease activity and severity: subgroup analysis of participants with moderately to severely active Crohn's disease in the GALAXI Phase 3 Studies


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## Key Takeaways

- Both subcutaneous guselkumab maintenance doses (200 mg q4w and 100 mg q8w) were safe and effective
- Clinical and endoscopic outcomes at Week 48 were greater with the higher guselkumab maintenance dose (200 mg q4w) for the following subgroups of participants:
  - High clinical or endoscopic disease severity at baseline
  - High inflammatory burden after induction
  - Not in endoscopic response after induction
- For the higher disease severity subgroups, outcomes in the BIO-IR subpopulation were generally consistent with those in the overall population
- Outcomes in participants with lower disease severity were generally similar between the two maintenance doses

## Background

- Guselkumab is a dual-acting IL-23p19 subunit inhibitor that potently blocks IL-23 and binds to CD64, a receptor on cells that produce IL-23
- Guselkumab 200 mg IV induction followed by 100 mg SC q8w or 200 mg SC q4w maintenance were evaluated in the GALAXI 2 & 3 phase 3 studies of participants with moderately to severely active Crohn's disease (CD)
- Both SC maintenance doses were highly effective in the overall study population compared with placebo and ustekinumab

## Objectives

**To evaluate guselkumab maintenance dose efficacy in subgroups based on baseline disease activity and post-induction inflammatory burden and endoscopic response**

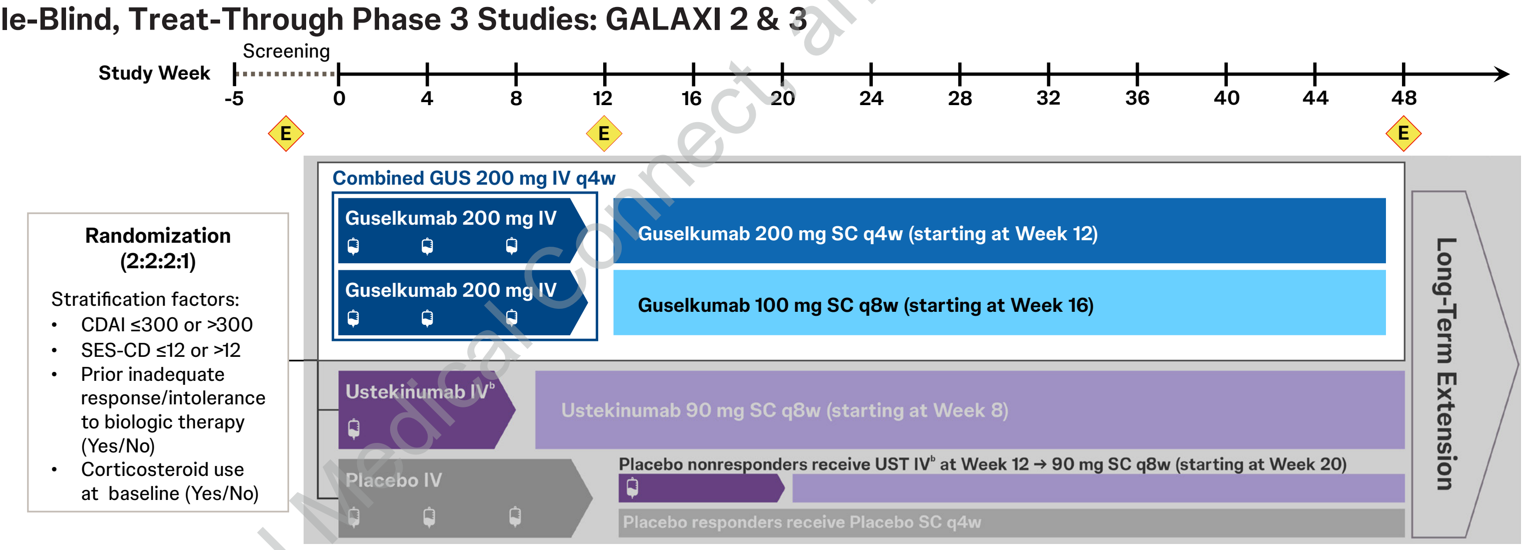
## Methods

- Prespecified subgroup analyses were conducted on randomization stratification factors and clinically relevant prespecified outcomes at Week 12
  - Baseline clinical disease activity: CDAI ≤300 or CDAI >300
  - Baseline endoscopic disease activity: SES-CD ≤12 or SES-CD >12
  - Inflammatory burden at Week 12: CRP ≤5 or CRP >5
  - Endoscopic response at Week 12
- Results were deemed clinically relevant if the findings were replicated in the individual GALAXI-2 and GALAXI-3 studies

**Identically Designed, Double-Blind, Treat-Through Phase 3 Studies: GALAXI 2 & 3**

**Key eligibility criteria**

- Moderately to severely active CD: CDAI score 220–450 + 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[a]




a. Biologic therapies: TNF antagonists or vedolizumab (participants with a history of inadequate response or intolerance to ustekinumab were excluded)
b. Ustekinumab IV ~6 mg/kg
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

## Results

### *Baseline demographics and disease characteristics*

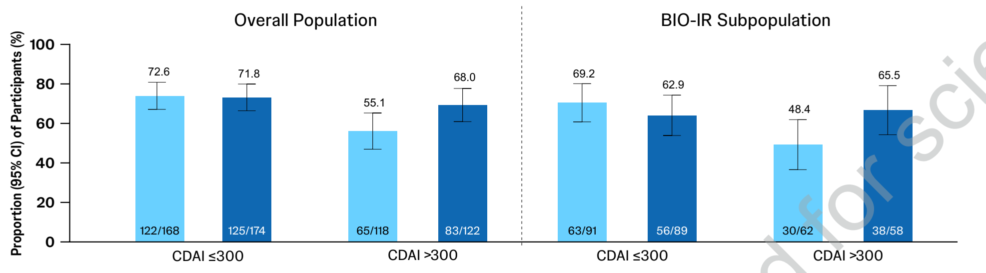
| Primary analysis set[a] | GUS 200 mg IV q4w → 100 mg SC q8w (N=286) | GUS 200 mg IV q4w → 200 mg SC q4w (N=296) |
|---|---|---|
| **Demographics** | | |
| **Age in years,** mean (SD) | 36.0 (12.24) | 36.9 (13.27) |
| **Male,** n (%) | 154 (53.8%) | 178 (60.1%) |
| **Characteristics** | | |
| **CD duration in years,** mean (SD) | 7.12 (6.717) | 7.07 (7.240) |
| **CDAI score,** mean (SD) | 296.3 (54.27) | 295.9 (52.74) |
| **CDAI score ≤300,** n (%) | 168 (58.7%) | 174 (58.8%) |
| **CDAI score >300,** n (%) | 118 (41.3%) | 122 (41.2%) |
| **SES-CD score,** mean SD | 13.2 (7.43) | 12.5 (7.24) |
| **SES-CD score ≤12,** n (%) | 160 (55.9%) | 174 (58.8%) |
| **SES-CD score >12,** n (%) | 126 (44.1%) | 122 (41.2%) |
| **Concomitant CD medications at baseline** | | |
| **No history of inadequate response/intolerance[b] to biologic therapy,** n (%) | 133 (46.5%) | 149 (50.3%) |
| **Biologic naïve,** n (%) | 116 (40.6%) | 128 (43.2%) |
| **Biologic experienced, but no documented nonresponse/ intolerance,** n (%) | 17 (5.9%) | 21 (7.1%) |
| **History of inadequate response/intolerance[b] to biologic therapy (BIO-IR),** n (%) | 153 (53.5%) | 147 (49.7%) |

a. All randomized participants who received at least 1 (partial or complete) dose of study intervention and had a screening SES-CD score ≥6 (or ≥4 for participants with isolated ileal disease).
b. Primary nonresponse, secondary nonresponse, or intolerance.
Note: Participants with a history of inadequate response or intolerance to ustekinumab were excluded.

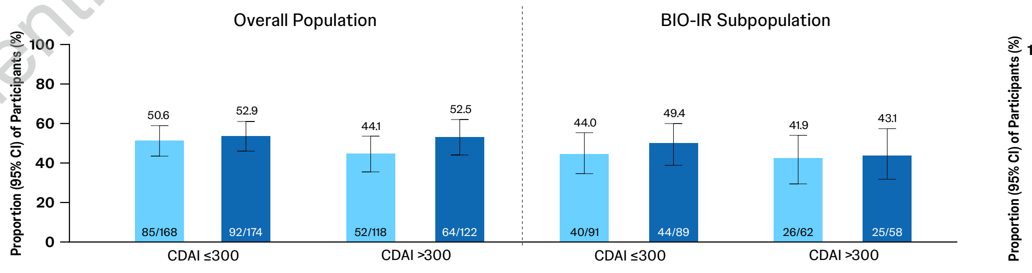
***For participants with higher clinical disease severity (CDAI >300) at baseline, higher endoscopic disease severity (SES-CD >12) at baseline, higher inflammatory burden at the end of induction (CRP >5), or who were not in endoscopic response at the end of induction, clinical remission at Week 48 and endoscopic response at Week 48 were greater for those who received GUS 200 mg q4w compared with GUS 100 mg q8w. For participants with lower disease severity or inflammatory burden, Week-48 outcomes were similar between the doses***

### *By CDAI Score at Baseline*

#### Clinical Remission at Week 48

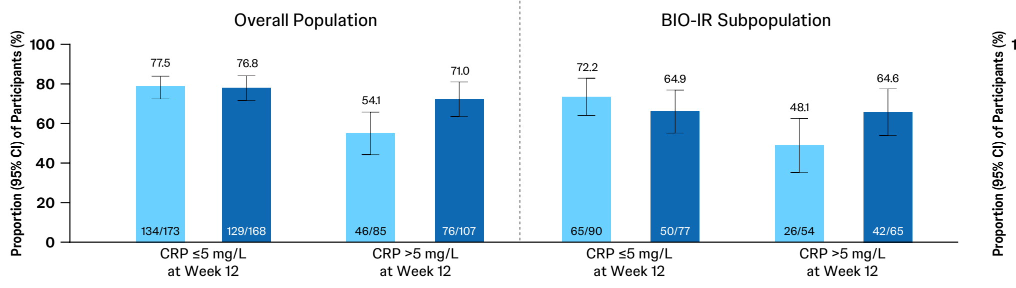



#### Endoscopic Response at Week 48

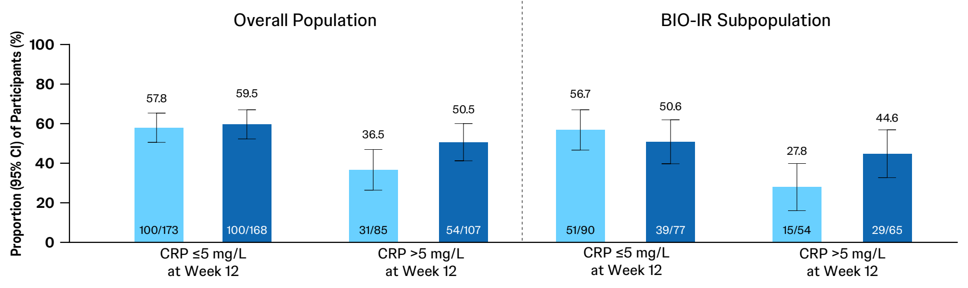



### *By CRP Level at the End of Induction*

#### Clinical Remission at Week 48

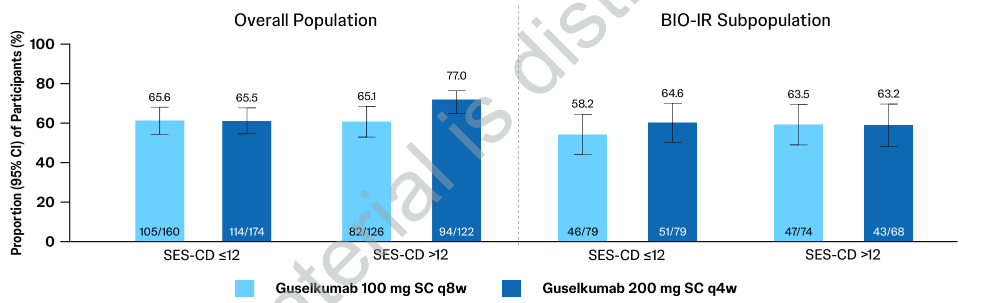



#### Endoscopic Response at Week 48



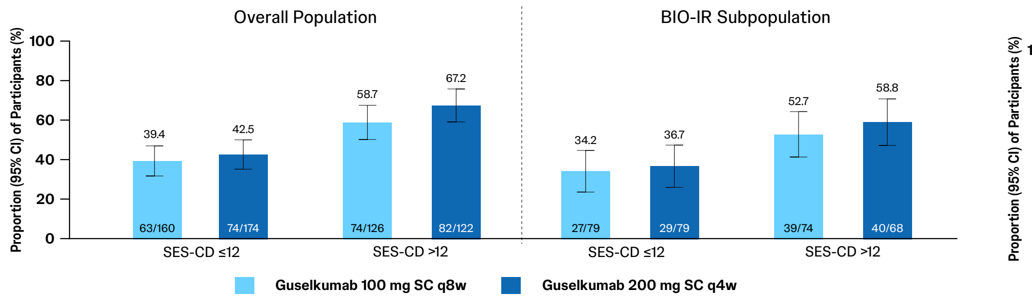

### *By SES-CD Score at Baseline*

#### Clinical Remission at Week 48




Clinical remission: CDAI <150

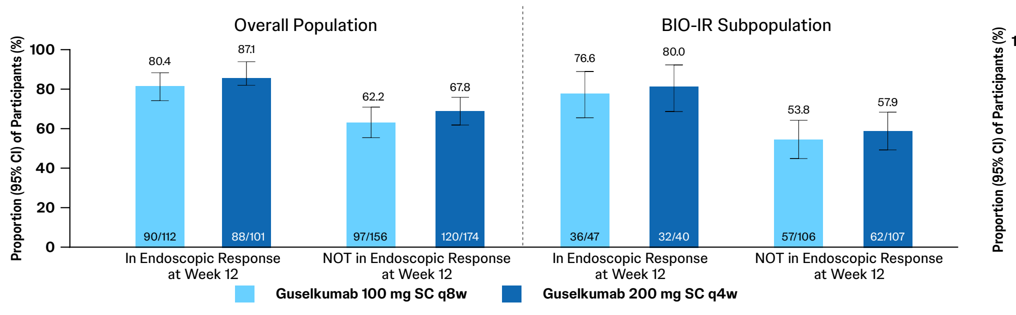
#### Endoscopic Response at Week 48




Endoscopic response: ≥50% improvement from baseline in SES-CD or SES-CD ≤2

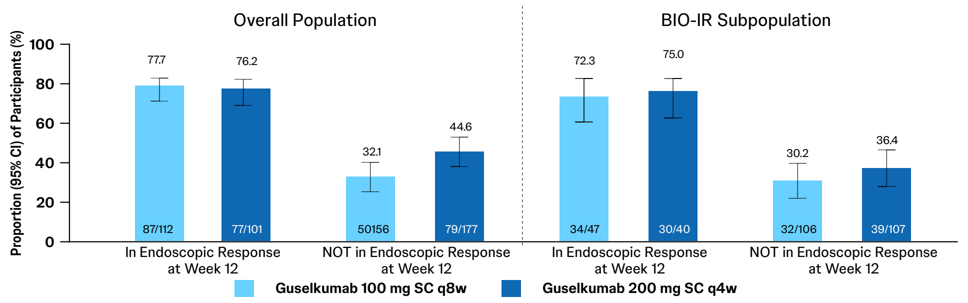
### *By Endoscopic Response Status at the End of Induction*

#### Clinical Remission at Week 48




Clinical remission: CDAI <150

#### Endoscopic Response at Week 48




Endoscopic response: ≥50% improvement from baseline in SES-CD or SES-CD ≤2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