Guselkumab Efficacy in Subgroups of Adults With a History of Inadequate Response or Intolerance to Anti-Tumor Necrosis Factor-α Therapy and Moderately to Severely Active Crohn's Disease: Results From the GALAXI 2 & 3 Studies

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Background

Crohn's disease (CD) is a chronic inflammatory bowel disease associated with swelling, full-thickness lesions and ulcers within the gastrointestinal tract[1]

Guselkumab (GUS) is a fully human, dual-acting monoclonal antibody that selectively inhibits interleukin (IL)-23 by targeting its p19 subunit and binding to CD64 on IL-23 producing inflammatory monocytes[2]

- GUS previously showed superior efficacy vs placebo (PBO) and ustekinumab (UST) at Week (W) 48 in participants pooled from the GALAXI 2 & 3 trials with moderately to severely active CD; no new safety signals were identified with GUS treatment[3]

Anti-Tumor Necrosis Factor-α (anti-TNF) agents are widely used as first line-therapy for CD, but loss of response is often experienced in patients over time

Objective

These post hoc analyses of pooled GALAXI 2 & 3 data evaluated efficacy outcomes at W12 and W48 in participants with CD who had an inadequate response or intolerance (IR) to anti-TNF therapies

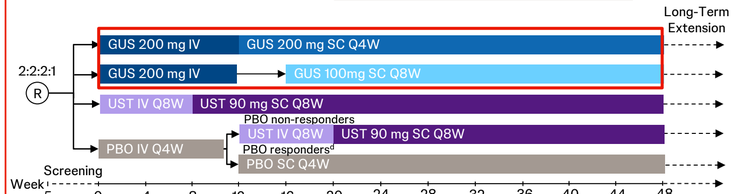
Analysis Cohort

Key inclusion criteria

- ≥18 years of age
- Moderately to severely active CD (based on CDAI[a] and SES-CD[b] scoring)
- Inadequate response or intolerant to conventional or biologic therapies

Post hoc analysis cohort

- The analysis cohort was pooled participants from the Phase 3 GALAXI 2 & 3[c] trials who had moderately to severely active CD and IR to anti-TNF therapies



*[a]Cutoff score of 220-450 (inclusive). [b]Cutoff score of ≥6 (or ≥4 for participants with isolated ileal disease). [c]NCT03466411. [d]≥100-point decrease in CDAI score from baseline or a CDAI score <150. **CDAI**=Crohn's disease activity index, **E**=endoscopy, **IV**=intravenous, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks, **R**=randomization, **SC**=subcutaneous, **SES-CD**=Simple Endoscopic Score for Crohn's disease.*

Outcomes and Analyses

Definitions	
Anti-TNF-IR subgroups[a]	
1 anti-TNF-IR	Participants with only 1 prior anti-TNF-IR; may have failed other non-anti-TNF therapies[b]
≥2 anti-TNF-IR	Participants with ≥2 prior anti-TNF-IR; may have failed other non-anti-TNF therapies[b]
Anti-TNF-IR only	Participants who had failed only anti-TNF agents prior

Outcomes	Analyses
Clinical Response[c]	Proportion of participants achieving clinical response, clinical remission, and endoscopic response at W12 with GUS induction vs PBO
Clinical Remission[d]	
Endoscopic Response[e]	Proportion of participants achieving clinical remission, endoscopic response, and endoscopic remission at W48 with both GUS maintenance dose regimen and UST
Endoscopic Remission[f]	

- Participants with missing data after applying intercurrent event rules were considered as non-responders

[a]Prior exposure to IL-12/IL-23 inhibitors was not allowed. [b]Including conventional (oral corticosteroid, immunomodulators) and biologics (vedolizumab). [c]Assessed only at W12; ≥100-point decrease from W0 in CDAI or CDAI<150. [d]CDAI score <150. [e]≥50% improvement from W0 in SES-CD or SES-CD≥2. [f]Assessed only at W48; SES-CD≤4, ≥2-point reduction from W0 in SES-CD, and no sub-score >1.

Key Takeaways

- **In the Phase 3 GALAXI 2 & 3 trials of participants with moderate to severe active CD with prior inadequate response or intolerance to anti-TNF therapies:**
  - ✓ **GUS showed numerically greater clinical and endoscopic outcomes vs PBO at W12 and vs UST at W48**
- **Both GUS maintenance dosing regimens provided comparable efficacy at W48 in the 1 anti-TNF-IR and anti-TNF-IR only subgroups**
  - ✓ **In participants with ≥2 prior anti-TNF-IR, GUS 200mg SC Q4W appeared more efficacious than GUS 100mg SC Q8W and UST**
- **These findings suggest that treatment with GUS SC 200 mg Q4W may provide additional benefit over UST and GUS SC 100mg Q8W in participants with CD and extensive prior anti-TNF treatment failure (≥2 anti-TNF-IR)**

Results

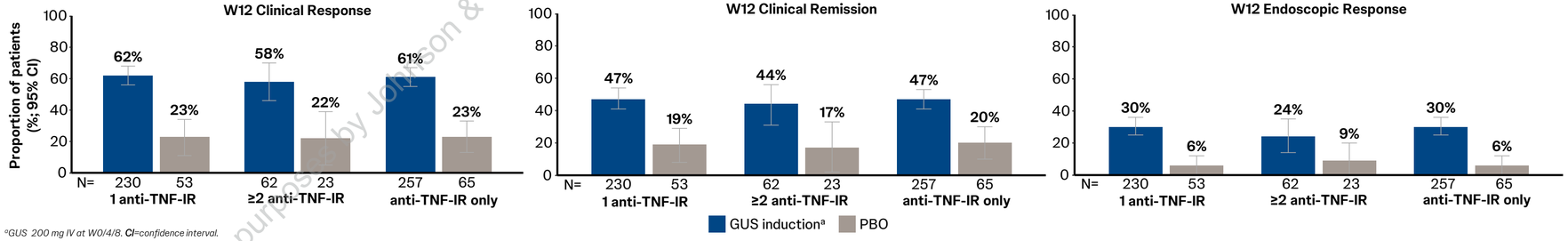
Baseline participant and disease characteristics were generally balanced across treatment groups in the TNF-IR population

- 50% of the randomized participants in the GALAXI 2 & 3 studies were eligible for this post hoc analysis

Baseline Participant and Disease Characteristics	GUS 200mg SC (N=143)	GUS 100mg SC (N=149)	UST 90mg SC (N=147)	PBO (N=76)
Demographics				
Age, years	37.0 (13.5)	35.3 (11.7)	38.9 (13.4)	35.7 (11.5)
Male	57%	56%	56%	63%
BMI, kg/m^2	23.3 (5.1)	23.2 (5.0)	23.5 (5.6)	22.7 (6.1)
Disease Characteristics				
Disease duration, years	8.2 (7.4)	8.5 (6.8)	8.9 (8.0)	8.7 (8.7)
CDAI, 0-600	295.2 (53.4)	293.5 (52.8)	294.8 (51.1)	296.3 (55.7)
SES-CD, 0-56	13.2 (7.7)	14.1 (7.7)	13.3 (6.8)	14.8 (8.2)
CRP, mg/L	17.3 (22.5)	19.9 (24.7)	15.7 (19.6)	19.6 (26.4)
Involved GI Areas[a]				
Ileum only	26%	17%	22%	18%
Colon only	22%	23%	19%	24%
Ileum and colon	52%	58%	56%	58%
Previous Crohn's Disease Medication				
1 anti-TNF agent	78%	79%	69%	70%
≥2 anti-TNF agents	22%	21%	31%	30%
Anti-TNF agent only	90%	86%	85%	86%

*Data shown are mean (SD) unless otherwise noted. [a]Assessed by central reader. **BMI**=body mass index, **CRP**=c-reactive protein, **GI**=gastrointestinal, **SD**=standard deviation.*

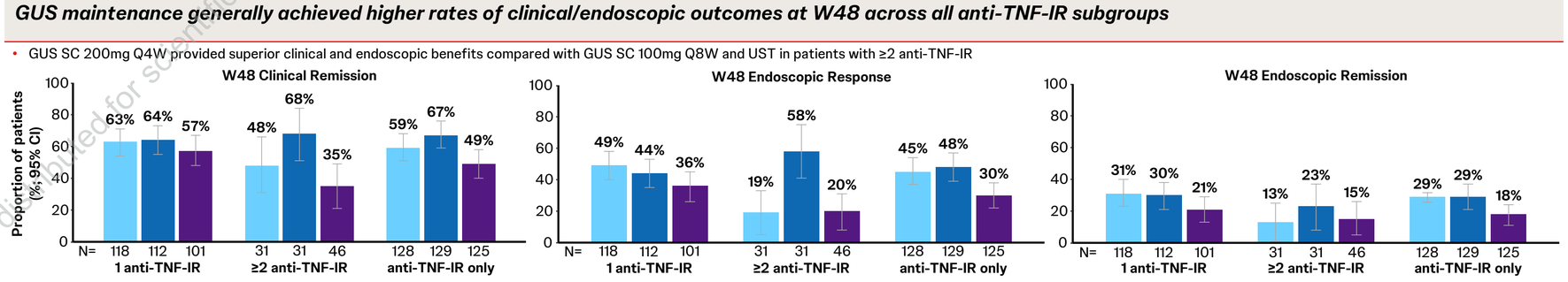
GUS induction achieved higher rates of clinical/endoscopic outcomes vs PBO at W12 across all anti-TNF-IR subgroups



*[a]GUS 200 mg IV at W0/4/8. **CI**=confidence interval.*

GUS maintenance generally achieved higher rates of clinical/endoscopic outcomes at W48 across all anti-TNF-IR subgroups

- GUS SC 200mg Q4W provided superior clinical and endoscopic benefits compared with GUS SC 100mg Q8W and UST in patients with ≥2 anti-TNF-IR



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PRESENTED AT: United European Gastroenterology Week (UEGW); October 17-20, 2026; Barcelona, Spain. **REFERENCES:** 1.Cushing K. *JAMA.* 2021; 69-80. 2. Sanchen. K. *Front Immunol.* 2025; 1532852. 3. Panaccione R. *Lancet.* 2025; 358-375. Medical writing support was provided by JSS Medical Research under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;175:1298-1304). This presentation was sponsored by Johnson & Johnson. **DISCLOSURES: WR:** Speaker: AbbVie, Celltrion, Ferring, Johnson & Johnson, Galapagos Medice. 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