Endoscopic Patient Clustering to Investigate Differential Treatment Effects of Guselkumab and Ustekinumab in Crohn's Disease: Post-hoc Analysis of GALAXI and GRAVITI Trials

Dylan Richards[1], Loqmane Seridi[1], Klebea Sohn[1], Brad Mcrae[1], Nat A. Terry[1], Marion Vetter[1], Daniel Cua[1], Patrick Branigan[1], Walter Reinisch[2], Raja Atreya[3]

[1]Janssen Research & Development, LLC, Spring House, PA, USA; [2]Division Gastroenterology & Hepatology, Medical University of Vienna, Vienna, Austria; [3]Department of Medicine I, Gastroenterology, Endocrinology and Pneumology, University Hospital Erlangen, Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany

Su1861

Key Takeaways

- **Data-driven endoscopic patient clustering in Crohn's disease can lead to stratified understanding of differential treatment effects between guselkumab (GUS) and ustekinumab (UST)**
- **In addition to overall WK48 endoscopic superiority, endoscopic clustering indicated higher WK12 endoscopic remission with GUS than UST in ~40% of patients**
- **Improved narrowing characterized a subset of GUS responders at WK12, and not UST, highlighting potential role of GUS in affecting stricture biology for future mechanistic research**

Background

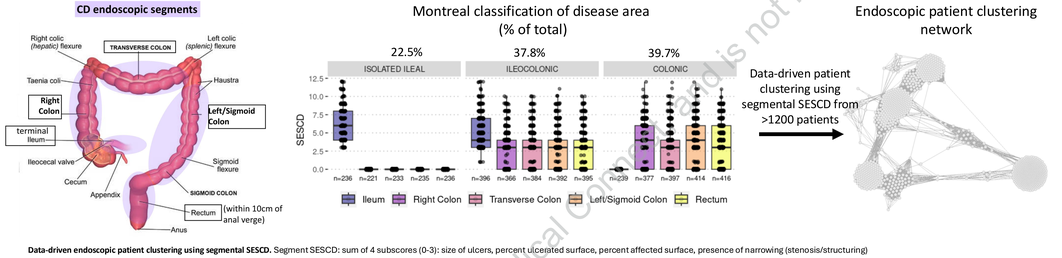
- Guselkumab (GUS), a selective IL-23p19 subunit inhibitor, demonstrated statistical superiority in endoscopic endpoints to ustekinumab (UST), an IL-23/IL-12p40 subunit inhibitor, by end of maintenance treatment in patients with moderately to severely active Crohn's disease (CD) in the Phase 2/3 GALAXI studies.[1]
- Differences in endoscopic response and biological features across ileum- and colon-involved Crohn's disease (CD) suggest distinct mechanisms for healing.[2]

Objectives

Understanding endoscopic heterogeneity (i.e., degree of involvement in each segment) across patients may help to delineate treatment effect differences between GUS and UST

Methods

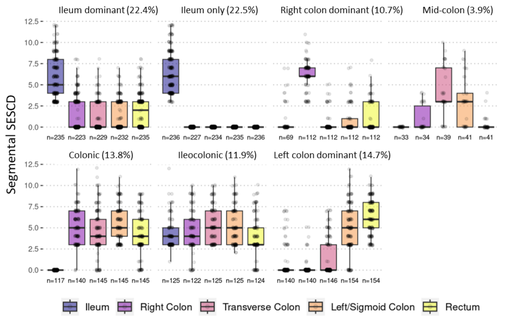
- Endoscopic clustering was established using baseline segment Simple Endoscopic Score for CD (SES-CD) values from terminal ileum, right colon, transverse colon, left/sigmoid colon, and rectum from cohort 1 (1233 patients, GALAXI 1, GALAXI 2, GRAVITI trials) and cohort 2 (525 patients, GALAXI 3).
- Patient clusters were identified using consensus hierarchical clustering, and a machine learning classification model was developed for patient cluster assignment of cohort 2.
- GALAXI 2 and GALAXI 3 patients were combined to evaluate Week (WK) 12 and WK48 endoscopic outcomes between PBO, GUS, and UST.

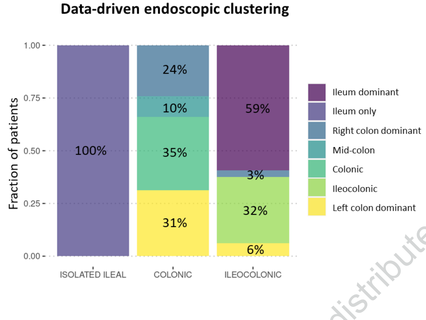


Data-driven endoscopic patient clustering using segmental SESCD. Segment SESCD: sum of 4 subscores (0-3): size of ulcers, percent ulcerated surface, percent affected surface, presence of narrowing (stenosis/structuring)

Results

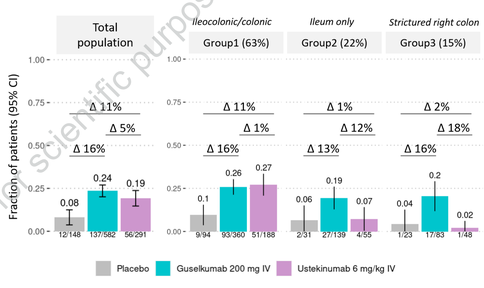
Data-driven endoscopic clustering identified 7 CD subtypes, highlighting heterogeneity within ileocolonic and colonic standard classifications

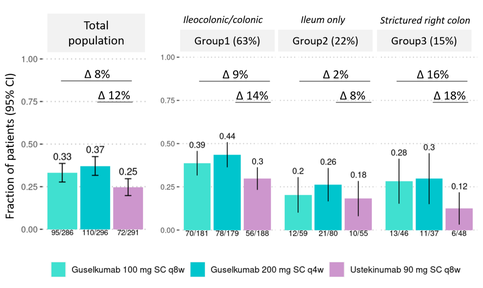




- The identified subtypes were used to stratify endoscopic remission rates along with additional clinical features, such as segmental narrowing scores, to identify consolidated groups with differential treatment effects

Guselkumab showed higher WK12 endoscopic remission rates than ustekinumab in 38% of patients followed by higher rates overall by WK48

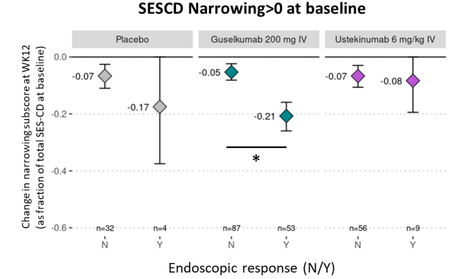




- GUS shows early WK12 endoscopic remission for all patients
  - Endoscopic characterization indicates UST having placebo-like efficacy at WK12 in 38% of patients, including Group 2, characterized by the "Ileum only" subtype and Group 3, consisting largely of "Right colon dominant" and "Colonic" subtypes with impassable right colon narrowing scoress
- GUS shows higher endoscopic remission than UST in all patients at WK48

Endoscopic remission: SES-CD ≤ 4 and a ≥2-point reduction from baseline and no subscore greater than 1 in any individual component

Improved narrowing at WK12 contributes to endoscopic response with guselkumab, but not with ustekinumab, in patients with stricturing CD



- For other endoscopic subscores, endoscopic response at WK12 for GUS and UST was also characterized by greater decreases in percent affected, ulcer size, and percent ulcerated surface compared to non-responders *(data not shown)*

Endoscopic Response: ≥50% improvement from baseline in SES-CD or SES-CD ≤ 2
** p < 0.05*

PRESENTED AT: Digestive Disease Week (DDW), May 3-6, 2025, San Diego, CA. **REFERENCES: 1.** Panaccione, R et al. Efficacy and safety of guselkumab therapy in patients with moderately to severely active Crohn's disease: results of the GALAXI 2 & 3 phase 3 studies. Oral presentation (Abstract #10576) at Digestive Disease Week (DDW) 2024. May 2024. **2.** Atreya, R., Siegmund, B. Location is important: differentiation between ileal and colonic Crohn's disease. Nat Rev Gastroenterol Hepatol 18, 544–558 (2021). https://doi.org/10.1038/s41575-021-00424-6.

DISCLOSURES: Dylan Richards, Loqmane Seridi, Klebea Sohn, Brad Mcrae, Natalie A. Terry, Marion Vetter, Daniel Cua, Patrick Branigan are employees of Janssen and may hold stock in Johnson & Johnson. **Walter Reinisch** reports serving as a speaker for AbbVie, Celltrion, Ferring, Janssen, Galapagos Medice, MSD, Roche, Pfizer, Sobi, Takeda; serving as a consultant for AbbVie, Amgen, AOP Orphan, Boehringer Ingelheim, Bristol Myers Squibb, Calyx, Celltrion, Eli Lilly, Galapagos, Gilead, Index Pharma, Janssen, Medahead, Microbiotica, Pfizer, and Takeda; serving as an advisory board member for AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Galapagos, Janssen, and Pfizer; and receiving research funding from AbbVie, Janssen, Sandoz, Sanofi, and Takeda. **Raja Atreya** has served as a speaker or consultant, or received research grants from AbbVie, Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion Healthcare, Dr Falk Pharma, Galapagos, Gilead, InDex Pharmaceuticals, Janssen-Cilag, Lilly, Merck Sharp & Dohme, Novartis, Pandion Therapeutics, Pfizer, Roche, Samsung Bioepis, Takeda, and Viatris.