

# Comparison of pharmacodynamic serum IL-22 and mechanistic tissue molecular changes between guselkumab subcutaneous and intravenous induction dosing in moderately to severely active Crohn's disease: Post-hoc analysis of the GRAVITI and GALAXI Phase 3 studies

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## Key Takeaways

- ✓ GUS reduced serum levels of IL-22 protein at WK12 relative to baseline in both SC and IV induction treatments.
- ✓ Following GUS SC induction, tissue changes observed at WK12 in GRAVITI were highly correlated with those observed with GUS IV induction from GALAXI Ph3 in both ileum and rectum segments.
- ✓ These data demonstrate similar molecular effects of GUS SC and IV induction doses aligned with previously reported comparable efficacy, supporting the flexible choice for patients and healthcare professionals between GUS SC and IV to treat patients with CD.

## Background

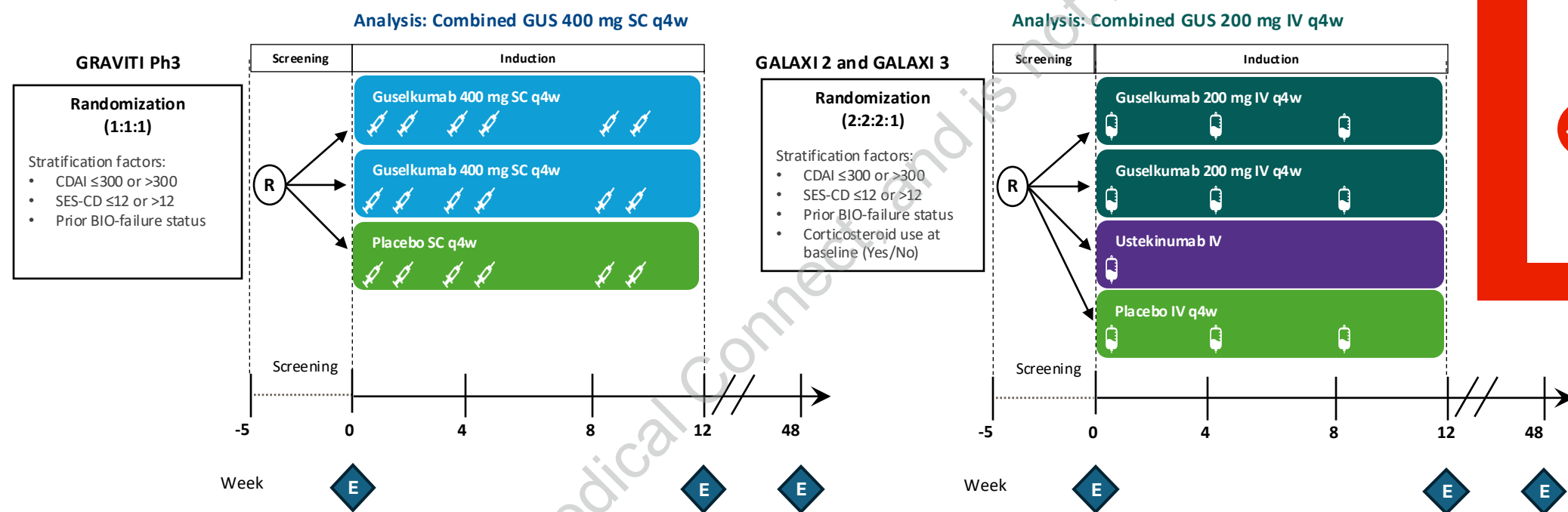
- Guselkumab (GUS) is a selective dual-acting IL-23p19 subunit inhibitor that potentially blocks IL-23 and binds to CD64, a receptor on cells that produce IL-23.<sup>1</sup>
- GUS demonstrated short- and long-term efficacy in patients (pts) with intravenous (IV) and subcutaneous (SC) induction followed by SC maintenance in moderately to severely active Crohn's disease (CD) in the GALAXI and GRAVITI Ph3 trials.<sup>2,3</sup>
- Previous analysis showed similar changes in serum inflammatory proteins following GUS SC and IV induction.<sup>4</sup> We extended this work to compare serum IL-22 and biopsy transcriptomic profiles following GUS SC or IV induction.

## Objectives

- Compare serum IL-22 changes associated with GUS SC and IV induction in CD patients stratified by previous biologic exposure
- Compare molecular effect of GUS SC and IV induction in ileum and rectum tissue in patients stratified by previous biologic exposure

## Methods

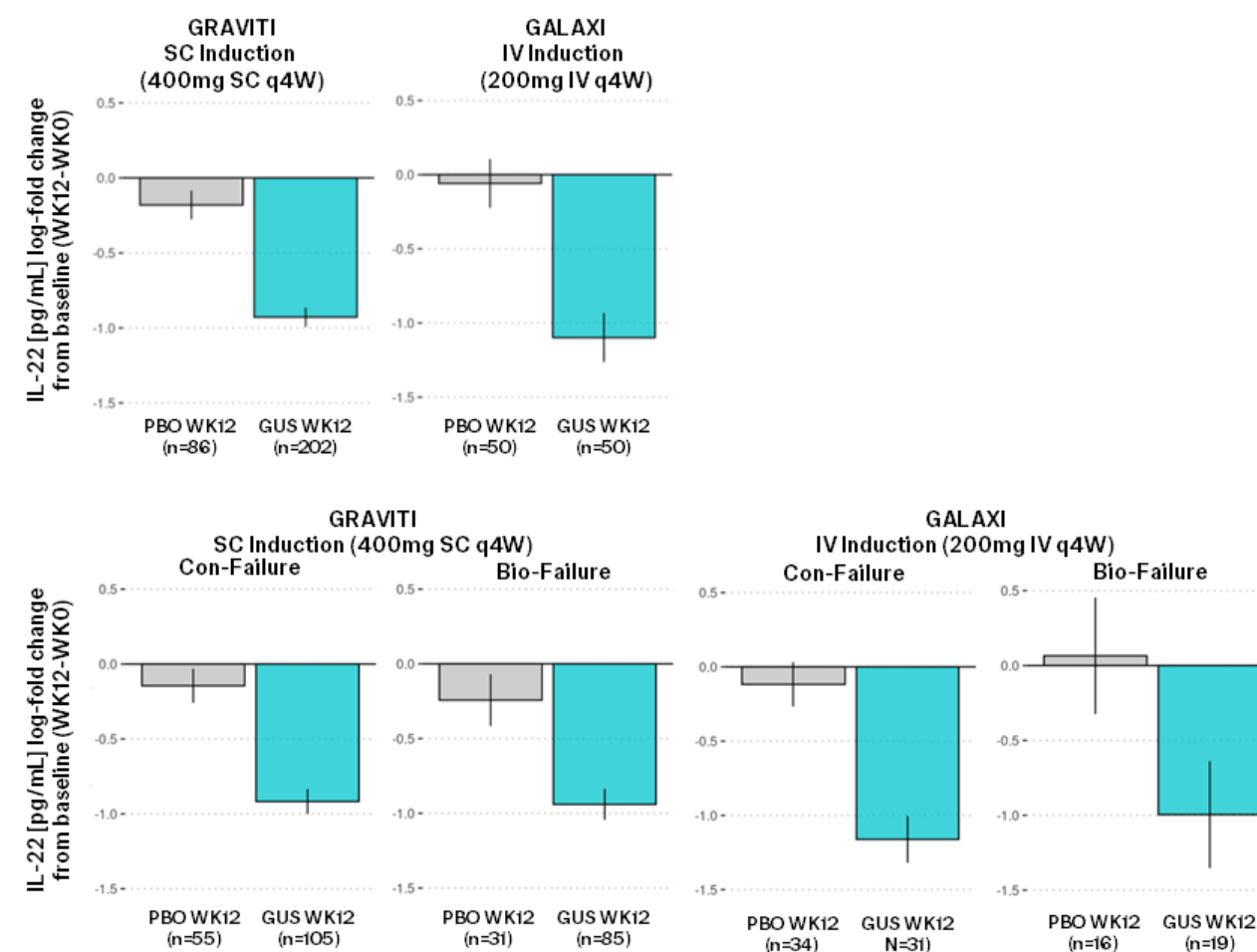
- Serum IL-22 was measured using a high-sensitivity assay and changes in protein abundance were assessed at WK0 and WK12 following GUS 400 mg SC q4w induction (n=202) compared with placebo (PBO) (n=86); GUS 200 mg IV q4w induction (n=50) compared with PBO (n=50), and in independent healthy control sera (n=30).
- Transcriptional profiling from ileum and rectum was analyzed from 277 GRAVITI patients randomized to PBO or GUS 400mg SC q4w, and from 259 GALAXI patients randomized to PBO or GUS 200mg IV q4w. Matched samples were analyzed from baseline (BL) and WK12.
- Transcriptional gene modules were evaluated for differential expression in the bulk RNA-seq dataset in ileum and rectum segments, and in patients stratified by previous biologic exposure.
- Analysis of treatment effect was performed using molecular inflamed samples (defined as bMIS<sup>5</sup> >0) from segments with SES-CD >0 at baseline.



## Results

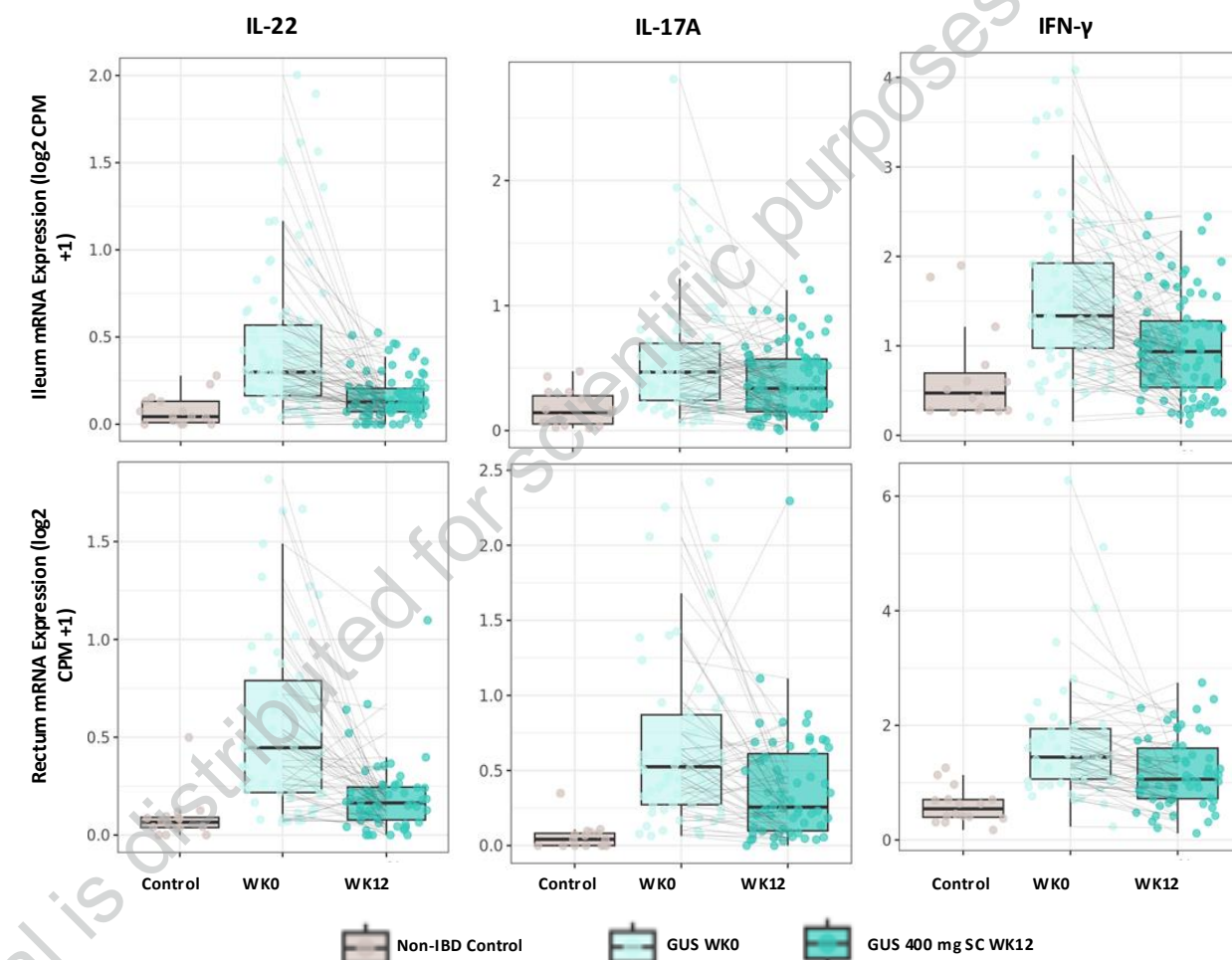
In serum, GUS SC and GUS IV showed similar WK12 decreases in IL-22 at WK12

- Similar decreases in IL-22 were observed in patients stratified by previous biologic exposure following GUS 400 mg SC q4w (GRAVITI) or GUS 200 mg IV q4w (GALAXI) induction



GUS SC vs PBO p<0.05 and GUS IV vs PBO p<0.05.

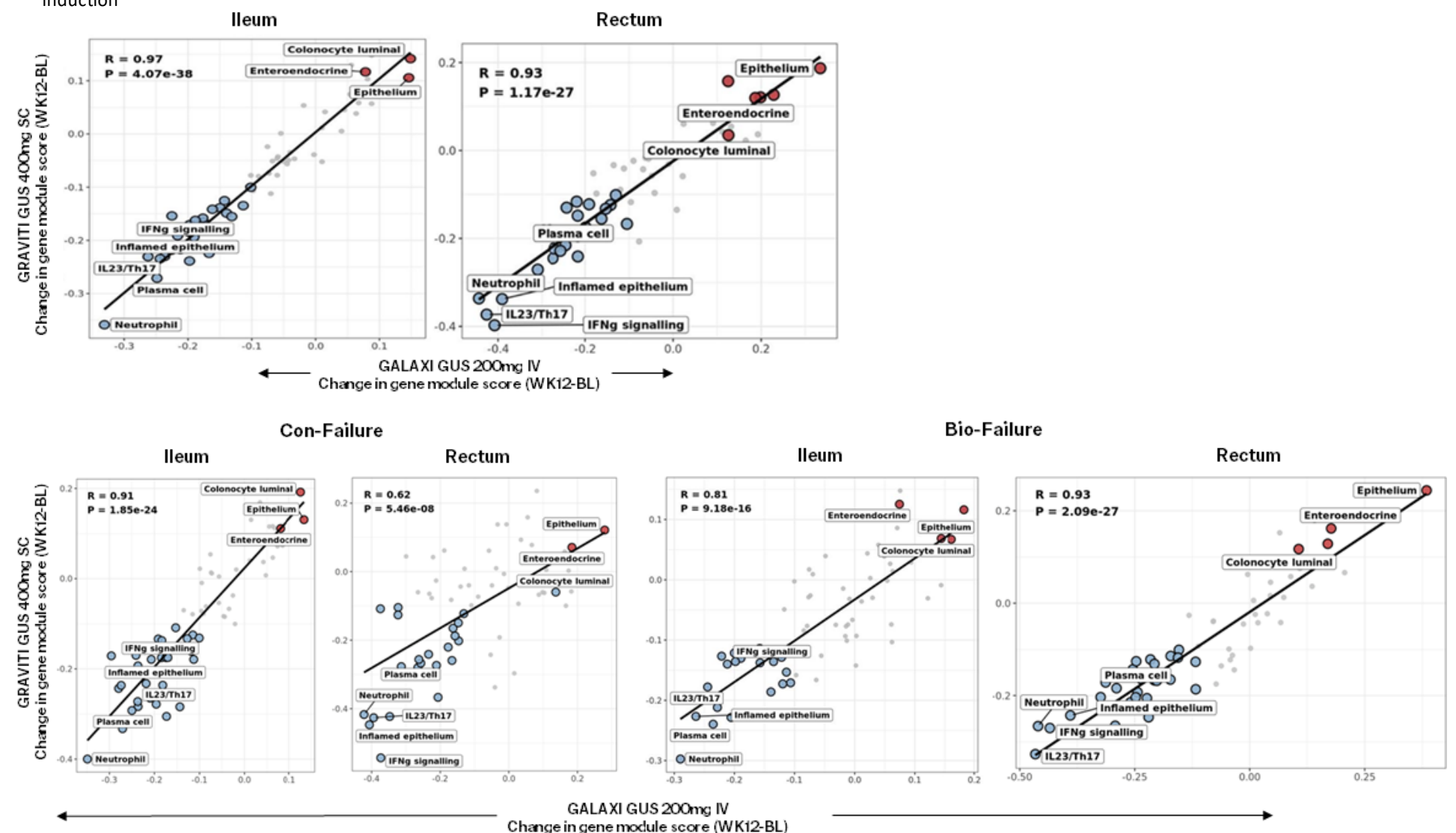
In tissue, IL-22, IL-17A and IFN-γ mRNA expression levels are elevated at baseline and decrease towards non-IBD control levels at WK12 following GUS 400 mg SC induction



RNAseq counts per million (CPM) from combined analyses of ileum and rectum tissue.

In tissue, changes in gene transcriptional modules observed with GUS 400mg SC q4w induction at WK12 in ileum and rectum were significantly correlated with those observed with GUS 200mg IV q4w induction at WK12

- Similar changes in molecular transcriptional modules in ileum and rectum tissue were observed patients stratified by previous biologic exposure following 400 mg SC or 200 mg IV induction



Correlation between 400 mg SC q4w or 200 mg IV q4w in all comers R=0.97, p<0.05 in ileum and R=0.93, p<0.05 in rectum

PRESIDENT: Dr. 3rd United European Gastroenterology Week Congress, October 4-7, 2025, Berlin, Germany. Conflicts of interest: Klebea Sohn, Dylan Richards, Ruchi Patel, Amy Hart, Christopher Sisk, Mobolaji Olurinde, Natalie A. Terry, Bradford McRae, and 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, MSD, Roche, Pfizer, Sobi, Takeda, serving as a consultant for AbbVie, Amgen, ADP Ophtho, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Eli Lilly, Galapagos, Glaxo, Indivior, Janssen, Mediatec, Mitsubishi, 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, Sanofi, and Takeda. Flavio Steinwurz reports serving as consultant, speaker, or researcher for AbbVie, Amgen, Celltrion, Ferring, Janssen, Johnson & Johnson, Pfizer, Sanofi, and Takeda; Remo Panaccione reports consultancy fees from AbbVie, Abbott, AbbVie, Almirall, Almirall (formerly Roberts), Amgen, Anestylabo, Arena Pharmaceuticals, AstraZeneca, Bogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Cosmo Pharmaceuticals, Eisai, Eli Lilly, Ferring, Fresenius Kabi, Galapagos, Genentech, Glaxo Sciences, GlaxoSmithKline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oplivian Pharma, Organon, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Roche, Sanofi, Sandoz, Shire, Summit Therapeutics, Takeda Pharmaceuticals, and Vertex. Geert D'Haens reports consultancy activities for AbbVie, Amgen, Almirall, AstraZeneca, AMI, Bristol Myers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Exelixis, Galapagos, GlaxoSmithKline, GossamerBio, Immunix, Indevco, Johnson & Johnson, Kaleida, Origen, Pfizer, Progenity, Protagonist Therapeutics, Prometheus Biosciences, Progenity, and Protagonist Therapeutics. Ruchi Patel reports consultancy fees from AbbVie, AstraZeneca, Galapagos, and Sanofi Health. References: 1. Saha K, Kammerl O, Sebke M, et al. Guselkumab binds to CD64: IL-23-inhibiting mAb that enhances pathway for maintaining IL-23 signaling. Frontiers in Immunology. 2025; doi:10.3389/fimm.2025.1533822. 2. Panaccione R, Bourne S, Kaplan EG, et al. Efficacy and safety of guselkumab therapy in patients with moderately to severely active Crohn's disease: results of the GALAXI-23, a phase 3 studies. Gastroenterology. 2024;5 (Supplement): p3057b. 3. Hart A, Panaccione R, Steinwurz F, et al. Efficacy and Safety of Guselkumab Subcutaneous Induction and Maintenance in Patients with Moderately to Severely Active Crohn's Disease: Results from the Phase 3 GRAVITI Study. Gastroenterology. 2025;147(2):p3057b. 4. D'Haens G, Klebea S, et al. Comparison of pharmacodynamic and mechanistic response of guselkumab intravenous and subcutaneous induction in moderately to severely active Crohn's disease: molecular analysis of the GRAVITI and GALAXI Phase 3 studies. Journal of Crohn's and Colitis, Volume 19, Issue Supplement\_1, January 2025, Pages: 600-601.P0597. 5. C. Agnam, et al. Biopsy and blood-based molecular biomarker of inflammation in IBD. Gut. 2022;01-17.