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Summary

MOLECULAR CHARACTERISATION OF RESPONDERS TO VEDOLIZUMAB IDENTIFIED BY SYMPTOM RESPONSE TRAJECTORIES, STUDY ENDPOINTS, AND MUCOSAL GENE TRANSCRIPTOMIC ANALYSES

Paresh Thakker

UEG Week Barcelona 2026 | Presentation

Gut Microbiota | Mechanisms & Personalised Medicine | IBD

October 20, 2026

Transcriptomic analysis of the VARSITY trial identified distinct molecular pathways distinguishing vedolizumab and adalimumab responders from non-responders, with faster symptom response trajectories linked to higher rates of comprehensive disease control at week 52.

KEY POINTS

- In 214 vedolizumab and 187 adalimumab patients from VARSITY with RNA-seq samples, symptom-based trajectory modeling identified four response groups: super/fast responders, responders, partial responders, and incomplete/non-responders, with faster responses linked to higher rates of comprehensive disease control at week 52.
- Non-responders to vedolizumab showed elevated fibroinflammatory pathways including angiogenesis, interferon signaling, ECM interactions, neutrophil degranulation, and increased inflammatory fibroblasts, B cells, and myeloid subtypes at baseline and post-treatment.
- Responders to vedolizumab demonstrated gene expression associated with epithelial barrier and metabolic processes at both baseline and post-treatment.
- Targeted analysis revealed molecular signatures linked to TNF and TL1a resistance, characterized by fibroblast, myeloid, and lymphoid cell activity, elevated in non-responders to both vedolizumab and adalimumab.
- The findings identify discrete and shared pathways linked to non-response to vedolizumab or adalimumab, demonstrating that endpoint response and symptom response trajectories define biologically different UC patient subpopulations.

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