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Summary

Immunometabolism as a therapeutic concept in inflammatory bowel disease

Bram Verstockt

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Hepatobiliary | Immunology | Digestive Oncology | Colorectal

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Immunometabolic therapies targeting cellular energy states represent a novel approach in inflammatory bowel disease, with early clinical and preclinical data suggesting potential to complement existing anti-cytokine strategies.

KEY POINTS

- Current IBD therapies block cytokines but do not alter the metabolic state of cells, and a shared therapeutic ceiling persists across mechanisms of action despite decades of drug development.
- A phase 1 study of annexe 13, an nlrx1 agonist designed to shift cells from glycolysis toward mitochondrial oxidative phosphorylation, showed signals for clinical response, endoscopic response, and dose-dependent rectal bleeding improvement in active ulcerative colitis without relevant safety signals, though the sponsor later terminated the global phase 2 program for undisclosed non-safety reasons.
- Mitochondrial pathway and oxidative phosphorylation are substantially downregulated in colonic tissue of newly diagnosed paediatric ulcerative colitis patients, supporting the biological rationale for metabolic intervention.
- Observational data from Scandinavian, US, and Israeli registries suggest IBD patients exposed to GLP-1 agonists experience fewer adverse events, fewer surgeries, and better outcomes, with multiple randomized trials now underway.
- The speaker concludes that immunometabolic agents may serve as combination partners with anti-cytokine therapies in biomarker-rich trials, and calls for investment in biomarkers, patient selection strategies, and dietary intervention studies.

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