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Summary

Transglutaminase inhibition in CeD

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Immunology | Nurses | Small Intestine & Nutrition

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A highly specific oral tissue transglutaminase 2 inhibitor demonstrated dose-dependent prevention of gluten-induced villous atrophy and symptom improvement in coeliac disease patients undergoing controlled gluten challenge, with a completed phase 2 study in nearly 400 patients showing significant histological improvement in the high-dose group.

KEY POINTS

- In a phase 2a study of 160 coeliac patients in remission undergoing 3-gram daily gluten challenge, the speaker reported dose-dependent recovery of villous height to crypt depth ratio and at the highest dose of 100mg intraepithelial lymphocytes remained essentially unchanged.
- The speaker stated that the drug normalized pro-inflammatory and anti-inflammatory gene expression pathways in transcriptome analysis, with the drug-treated group behaving similarly to the gluten-free group.
- A completed phase 2 study in 397 patients with continuous symptoms and minor histological damage showed that histological damage was significantly improved in the high-dose group, though symptoms did not differ between groups.
- The inhibitor is 100-fold more selective for transglutaminase 2 over other transglutaminases, blocks deamidation of gluten peptides, and the mucosa-active oral formulation limits systemic exposure with no relevant side effects reported in the first study.
- The speaker positioned the drug as most promising for patients with significant histological inflammation and damage rather than those with IBS-like symptoms or food sensitivities without true coeliac inflammation, and suggested future scenarios including standby use or longer-term treatment with possible tolerance induction.

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