ASSESSMENT OF HISTOLOGIC ENDPOINTS AND PERFORMANCE IN THE TAK-062 PHASE 2 TRIAL

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A phase 2 trial of TAK-062, an oral glutenase for celiac disease, did not meet endpoints and showed worsening histology compared to placebo, but provided insights into optimal histologic endpoints for future celiac disease studies.

KEY POINTS

- TAK-062 is an orally delivered glutenase designed to degrade immunogenic gliadin peptides in patients with celiac disease; the phase 2 trial (NCT05353985) did not meet primary or secondary endpoints.
- 153 adult patients with symptomatic celiac disease received TAK-062 or placebo three times daily for 24 weeks while exposed to 500 mg of gluten three times per week.
- All histology endpoints except CD8 T cell count significantly worsened from baseline to week 24 in the TAK-062 group relative to placebo, including villus height to crypt depth ratio (Vh:Cd), IEL counts, and Marsh–Oberhuber scoring.
- Analysis of Vh:Cd variability showed 52% was patient-level, 23% biopsy-level, and only 1% reader-related; no endpoint outperformed Vh:Cd in effect size, supporting its use as a key endpoint in celiac disease studies.
- Using a target response criterion of Vh:Cd change of 0.4, more placebo patients (13.3%) achieved improvement compared to TAK-062 patients (3.4%); remission rates (Vh:Cd ≥2.7) were also higher in placebo (8.3%) versus TAK-062 (1.7%).

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