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Summary

CLINICAL, HISTOLOGIC AND SAFETY OUTCOMES OF ZED1227 TREATMENT IN SYMPTOMATIC CELIAC DISEASE PATIENTS: RESULTS FROM THE PHASE 2B CEC-004/CEL RANDOMIZED CLINICAL TRIAL

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The phase 2b CEC-004/CEL trial of oral transglutaminase 2 inhibitor ZED1227 in celiac disease patients with residual symptoms and villous atrophy on a gluten-free diet did not meet its primary combined histology-symptom endpoint, though 50 mg once-daily significantly improved villous height to crypt depth ratio versus placebo.

KEY POINTS

- 397 adult celiac disease patients with residual symptoms and villous atrophy (VH:CrD ≤2.5) despite at least one year on a gluten-free diet were randomized to placebo or ZED1227 (10 mg TID, 25 mg TID, or 50 mg QD) for 12 weeks without gluten challenge.
- The primary endpoint of combined improvement (≥0.4 in VH:CrD and ≥15% in CDSD symptom score) was not met: 27.1% with 10 mg TID, 16.9% with 25 mg TID, 25.3% with 50 mg QD, and 19.3% with placebo achieved the endpoint, with no significant differences between active treatment and placebo.
- Mean change in VH:CrD ratio was 0.26 for 50 mg QD versus 0.12 for placebo ($p<0.05$, the only significant between-group difference), while 10 mg TID and 25 mg TID showed changes of 0.21 and 0.17 respectively.
- Mean changes in CDSD GI total severity score were -1.20 with 50 mg QD, -0.96 with 10 mg TID, -0.95 with 25 mg TID, and -1.05 with placebo, with significant within-group improvements but no significant differences between any treatment arm and placebo.
- Significant within-group improvement in both histology and symptoms in the placebo group highlighted the challenges of trials without gluten challenge in patients with heterogeneous symptoms and histology typical of partially treated celiac disease.

– No notable differences in adverse events or serious adverse events were observed between study arms, no drug-related serious adverse events were reported, and the favorable safety profile of ZED1227 was confirmed with no new safety concerns.

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