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Summary

GUT-TARGETED PDE4 INHIBITION WITH ONCE-DAILY PALI-2108 DEMONSTRATES EARLY CLINICAL AND BIOMARKER IMPROVEMENTS IN FIBROSTENOTIC CROHN'S DISEASE: RESULTS FROM A PHASE 1B STUDY

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In this first-in-Crohn's-disease Phase 1b study, the oral PDE4 inhibitor prodrug PALI-2108 demonstrated a favorable safety profile and early signals of endoscopic activity in five patients with fibrostenotic Crohn's disease over 14 days of treatment.

KEY POINTS

- Mean SES-CD decreased by 47.5% from 8.0 at baseline to 4.2 at Day 14 (nominal $P<0.05$), with 40% of patients achieving endoscopic remission (SES-CD ≤2) and 40% achieving endoscopic response (≥50% reduction).
- PALI-2108 was well tolerated with no serious adverse events, no discontinuations, and no moderate or severe adverse events; importantly, no PDE4-related nausea, vomiting, or diarrhea were observed.
- Steady-state plasma and ileal concentrations of the active metabolite exceeded the IC90, and ileal tissue cAMP increased by approximately 33% in 4 of 5 patients, consistent with PDE4 inhibition.
- Fecal calprotectin decreased by approximately 59% during treatment, with rebound observed after discontinuation.
- The study enrolled patients with long-standing disease (mean 15.4 years), 80% on concomitant biologics, and 40% with prior intestinal resection, representing a refractory fibrostenotic population.
- These findings support further evaluation of PALI-2108 in larger, controlled studies for fibrostenotic Crohn's disease, a condition with no currently approved medical therapies.

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