LINAPRAZAN GLURATE IS HIGHLY EFFECTIVE IN TREATING MODERATE TO SEVERE EROSIVE ESOPHAGITIS: A DOUBLE-BLIND, RANDOMIZED, DOSE FINDING STUDY

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Introduction: There is an unmet medical need in the treatment of patients with moderate to severe (LA grade C or D) erosive esophagitis (EE), and those who do not achieve healing with currently available therapies. Linaprazan glurate (LG), a P-CAB and prodrug of its main metabolite linaprazan, has a favorable pharmacokinetic profile providing excellent acid control (1). This Phase 2 study was designed to support dose selection of LG for Phase 3 studies. Safety results are summarized separately.

Aims & Methods: This is a randomized, double-blind, active comparator-controlled, 5-arm parallel group, dose-finding study of LG, with lansoprazole (LAN) as the active comparator, on the 4-week healing of EE, with safety and tolerability as secondary endpoints. Adult patients with endoscopically confirmed EE with LA grade C or D or with LA grade A or B and a documented history of ≥8 weeks PPI therapy plus at least partial symptom response, were eligible for inclusion. The estimation for sample size calculations was based on the presumed responses in the LA grade C/D cohort dosing groups. Patients were randomized (1:1:1:1:1) to LG (25 mg, 50 mg, 75 mg or 100 mg: all BID doses) or LAN (30 mg QD), followed by 4-week open-label LAN treatment for all patients. All endoscopic images and videos were reassessed by a central review board, and primary endpoint was based on the central review output.

Results: A total of 248 patients were randomized to treatment. Based on the reassessed endoscopic images and videos, 182 patients had EE at screening (Full Analysis Set with EE; FAS-EE); of these, 162 patients had an endoscopy performed at 4 weeks (modified FAS-EE; LG, N=133; LAN, N=29) and were available for evaluation of healing. Modified FAS-EE C/D patients receiving LG (all 4 dosing groups) had a 4-week healing rate of 73.6% (95% CI: 59.7 -84.7), compared to 37.5% (95% CI: 8.5 -75.5) for LAN; for modified FAS-EE A/B patients receiving LG (all 4 dosing groups), the 4-week healing rate was 83.8% (95% CI: 73.8 -91.1), compared to 81.0% (95% CI: 58.1 -94.6) for LAN. The healing rates for the individual LG doses in modified FAS-EE C/D patients are presented in Table 1, showing a clear dose-response trend for LG 25 mg to 75 mg. When analyzing the FAS-EE (N=182, with the 20 patients without a 4-week endoscopy performed being imputed as “not healed”, as per the primary endpoint), data were consistent with the modified FAS-EE cohort. FAS-EE C/D patients receiving LG (all 4 dosing groups) had a 4-week healing rate of 68.4% (95% CI: 54.8 -80.1), compared to 33.3%
(95% CI: 7.5 -70.1) for LAN, and a clear dose-response trend was seen.

LA Grade C or D	LG 25 mg (N=10) n(%)	LG 50 mg (N=10) n(%)	LG 75 mg (N=19) n(%)	LG 100 mg (N=14) n(%)	LAN 30 mg (N=8) n(%)	Total (N=61) n(%)
Healing (%) at 4 weeks	7 (70.0)	8 (80.0)	17 (89.5)	7 (50.0)	3 (37.5)	42 (68.9)
95% CI	(34.8 - 93.3)	(44.4 - 97.5)	(66.9 - 98.7)	(23.0 - 77.0)	(8.5 - 75.5)	(55.7 - 80.1)

Conclusion: High EE healing rates were seen after 4 weeks of LG treatment in the overall LA grade C/D cohort, with the highest healing rate seen for 75 mg BID. In combination with good safety and tolerability results, these findings support further development of LG for the treatment of erosive esophagitis due to GERD.

References

References: **References**
1. Unge P, Andersson K. Gastroenterology, 2018.

Disclosure

Nothing to disclose: No

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Peter Unge: Shareholder of and consultant to Cinclus Pharma AB
Kajsa Larsson, Maria Rosenholm and Elham Yektaei: Employees of Cinclus Pharma AB

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