LINAPRAZAN GLURATE IS WELL TOLERATED IN THE TREATMENT OF PATIENTS WITH EROSIVE ESOPHAGITIS: A DOUBLE-BLIND, RANDOMIZED, DOSE FINDING STUDY

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Abstract selection

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General data

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Abstract body

Introduction:

There is an unmet medical need for the treatment of patients with moderate to severe (LA grade C or D) erosive esophagitis (EE), and those who do not achieve healing with available therapies. Linaprazan glurate (LG), a P-CAB and prodrug of its main metabolite linaprazan, has a favorable pharmacokinetic profile providing an excellent acid-control (1). This Phase 2 study aimed to investigate safety, tolerability, and healing rates after 4 weeks of treatment with LG or lansoprazole (LAN). Efficacy 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 LAN as the active comparator, on the 4-week healing of erosive esophagitis, 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 were based on the presumed responses in the C/D cohort dosing groups. Target dose corresponded to 85% healing. *H. pylori* status of all patients was identified at enrolment, but the presence of infection was not an exclusion criterion. Patients were randomized (1:1:1:1:1) to LG (25, 50, 75, 100 : all BID doses) or LAN (30 mg QD), followed by 4-week open-label LAN treatment for all patients. Safety outcome is reported for the double-blind period (Week 1-4), as well as for the full study period (Week 1-8).

Results:

A total of 248 patients were randomized to treatment. In the double-blind period (Week 1-4), treatment-emergent adverse events (TEAEs) were reported by 18.2% of patients treated with LG, and by 18.0% of patients treated with LAN. 2 patients (0.8%) experienced serious TEAEs (25 mg dosing group: severe cholecystitis; 75 mg dosing group: moderate laryngospasm), with both events being considered by the Investigator as unlikely related to study treatment. 8 patients (3.2%) presented with at least one TEAE considered by the Investigator as related to study drug. Treatment was discontinued in 5 patients (2.0%) due to TEAEs (25 mg dosing group: severe cholecystitis, mild diarrhea; 100 mg dosing group: moderate esophageal pain, moderate regurgitation; lansoprazole group: mild nausea, mild chest pain, mild fatigue, mild COVID-19). For the entire study period (Week 1-8), TEAEs were reported by 23.0% of patients. The most commonly reported TEAEs are presented in Table 1. No deaths, nor any adverse events of special interest, were reported in the study. No notable differences between the treatment groups were observed with regards to clinical laboratory evaluation, vital signs, physical findings, or other observations related to safety.

	LG 25 mg (N=51) n (%)	LG 50 mg (N=48) n(%)	LG 75 mg (N=52) n(%)	LG 100 mg (N=47) n(%)	LAN 30 mg (N=50) n(%)	Total (N=248) n(%)
Any TEAE	14 (27.5)	10 (20.8)	12 (23.1)	11 (23.4)	10 (20.0)	57 (23.0)
Covid-19	1 (2.0)	2 (4.2)	1 (1.9)	4 (8.5)	2 (4.0)	10 (4.0)
Headache	1 (2.0)	3 (6.3)	1 (1.9)	1 (2.1)	1 (2.0)	7 (2.8)
Constipation	2 (3.9)	1 (2.1)	2 (3.8)	0	0	5 (2.0)
Nausea	1 (2.0)	0	0	0	4 (8.0)	5 (2.0)
Nasopharyngitis	1 (2.0)	2 (4.2)	0	1 (2.1)	0	4 (1.6)
Regurgitation	0	2 (4.2)	0	2 (4.3)	0	4 (1.6)
Diarrhea	2 (3.9)	0	1 (1.9)	0	0	3 (1.2)
Eructation	0	0	0	2 (4.3)	0	2 (0.8)

Conclusion:

LG was well-tolerated with no dose-related increase in AEs, and the safety profile was comparable to that of LAN. In combination with promising efficacy results, these findings support further development of LG for the treatment of erosive esophagitis due to GERD.

References

References:

1. Unge P, Andersson K. Gastroenterology, 2018.

Disclosure

Nothing to disclose: No

Disclosure: Prateek Sharma, Michael Vaezi, Ivan Popadiin, Andras Rosztóczy and David Armstrong: Nothing to disclose.
Peter Unge: Shareholder of and consultant to Cinclus Pharma AB
Kajsa Larsson, Maria Rosenholm and Elham Yektaei: Employees of Cinclus Pharma AB

Keywords

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Keyword 2: P-CAB

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