

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

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### **Background**

There is an unmet medical need in treatment of erosive esophagitis, especially in those with LA Grade C/D (moderate to severe), 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 an excellent acid-control (1). This Phase 2 study was designed to support dose selection of LG for Phase 3 studies.

### **Methods**

This was a randomized, double-blind, active comparator-controlled, 5-arm parallel group, dose-finding study of LG, with lansoprazole (LAN) for comparison of safety outcome, on 4-week endoscopic healing of erosive esophagitis, with safety and tolerability as secondary endpoints. Adult LA Grade C/D patients, and patients with unhealed erosive esophagitis (LA Grade A/B) with a history of preceding 8 weeks proton pump inhibitor therapy documented by the investigators, were eligible for inclusion. The sample size was estimated based on the C/D cohort, and dose selection was based on the C/D patient outcome. *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) to LG (25 mg, 50 mg, 75 mg, or 100 mg BID) or LAN (30 mg QD), followed by 4-week open-label LAN treatment for all patients. All endoscopic images and videos were assessed 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, of which 228 underwent a 4-week endoscopy and completed the study. After central adjudication review of the screening videos, 66 (28.9%) patients were re-classified from erosive to non-erosive esophagitis, leaving 162 evaluable patients for the primary endpoint (LG, N=133 [C/D, n=53; A/B, n=80]; LAN, N=29 [C/D, n=8; A/B, n=21]). C/D patients receiving LG (full analysis set; all doses) had a 4-week healing rate of 73.6%, as compared to 37.5% for LAN ( $p=0.04$ ). For A/B patients receiving LG, the 4-week healing rate was 83.8%, as compared to 81.0% for LAN. The healing rates for the individual doses of LG in C/D patients are presented in Figure 1, showing a clear dose-response trend for LG 25 mg to 75 mg. The safety profile was comparable across treatment groups (Table 1). One serious TEAE each was reported in the LG 25 mg and 75 mg groups; both were considered by the Investigator to be mild and unlikely related to study drug.

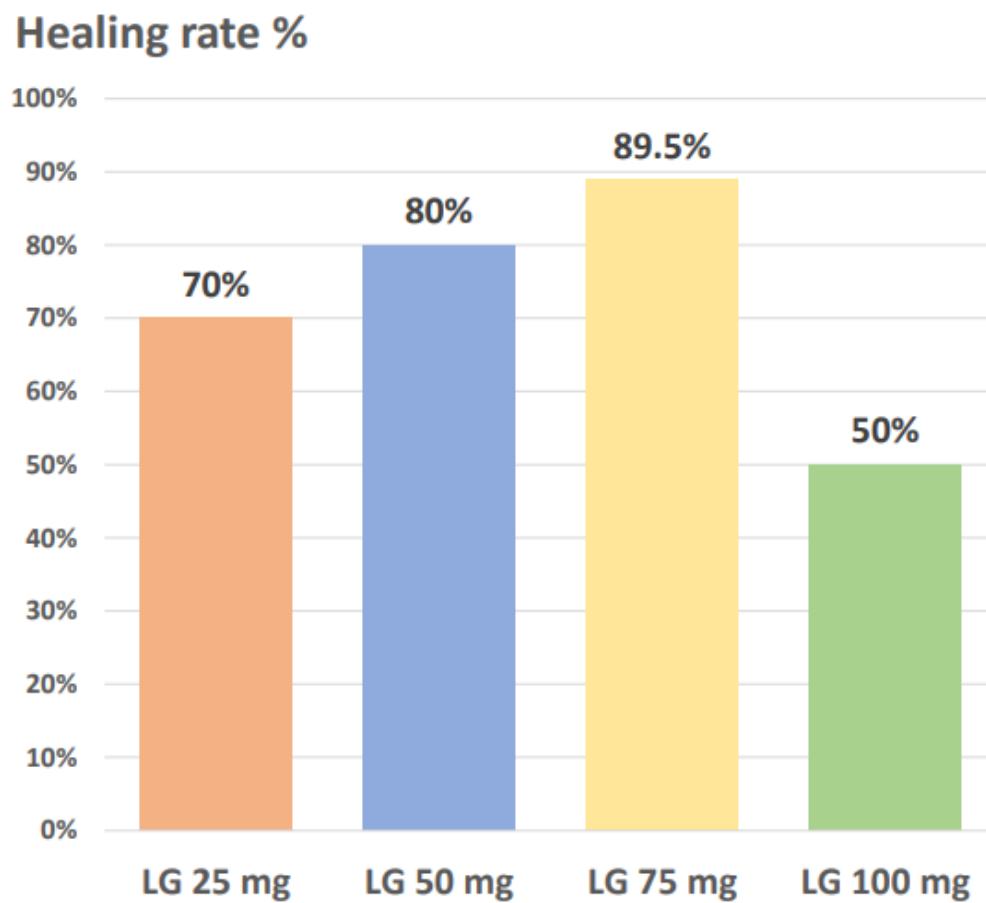
### **Conclusion**

A high healing rate was seen after 4 weeks of LG treatment in the overall C/D cohort, with the highest healing rate seen for 75 mg. LG was generally well-tolerated, and the safety profile was comparable to that of LAN. These results support further development of LG for the treatment of erosive esophagitis.

### **References**

1. Unge P, Andersson K. Gastroenterology, 2017.

## Figure 1. Dose response diagram LA Grade C/D



Abbreviations: LG = Linaprazan glurate.

Healing rates with a clear dose response separation pattern seen in patients with LA Grade C/D with up to 89.5% healing by central review after 4 weeks of treatment.

The 100 mg group had a lower healing rate than expected, where 6 of 7 unhealed patients had improved to LA Grade A.

Table 1. TEAE by preferred term occurring in ≥2% of total study population or >2 patients in any treatment arm in the double-blind phase and full study

Double-blind phase	LG 25 mg	LG 50 mg	LG 75 mg	LG 100 mg	LAN	Total
<b>COVID-19</b>	0	2 (4.2%)	1 (1.9%)	3 (6.4%)	0	6 (2.4%)
<b>Headache</b>	1 (2.0%)	2 (4.2%)	1 (1.9%)	1 (2.1%)	1 (2.0%)	6 (2.4%)
<b>Nausea</b>	1 (2.0%)	0	0	0	4 (8.0%)	5 (2.0%)
<b>Full study (including open-label LAN treatment)</b>	<b>LG 25 mg</b>	<b>LG 50 mg</b>	<b>LG 75 mg</b>	<b>LG 100 mg</b>	<b>LAN</b>	<b>Total</b>
<b>COVID-19</b>	1 (2.0%)	2 (4.2%)	1 (1.9%)	4 (8.5%)	2 (4.0%)	10 (4.0%)
<b>Headache</b>	1 (2.0%)	3 (6.3%)	1 (1.9%)	1 (2.1%)	1 (2.0%)	7 (2.8%)
<b>Nausea</b>	1 (2.0%)	0	0	0	4 (8.0%)	5 (2.0%)
<b>Constipation</b>	2 (3.9%)	1 (2.1%)	2 (3.8%)	0	0	5 (2.0%)

Abbreviations: LAN = Lansoprazole; LG = Linaprazan glurate; TEAE = Treatment-emergent adverse event.