

Review article: esomeprazole, 40 mg once daily, compared with lansoprazole, 30 mg once daily, in healing and symptom resolution of erosive oesophagitis

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SUMMARY

Background: Proton pump inhibitors are the most effective agents for treating erosive oesophagitis, but their relative efficacies have not been well characterized in large clinical trials.

Aim: To compare standard doses of esomeprazole and lansoprazole in healing oesophagitis and resolving accompanying symptoms.

Methods: This was a US, multicentre, randomized, double-blind trial and included 5241 adult patients (intention-to-treat) with endoscopically documented erosive oesophagitis. Patients were randomized to esomeprazole, 40 mg once daily, or lansoprazole, 30 mg once daily, for up to 8 weeks. The primary end-point, endoscopic healing at Week 8, was assessed

using life-table analysis and a log-rank test. Secondary endpoints included healing at Week 4, healing according to baseline severity of oesophagitis, control of heartburn and side-effects.

Results: Healing rates were 92.6% with esomeprazole and 88.8% with lansoprazole at Week 8 ($P = 0.0001$, log-rank test). A significant difference was also observed at Week 4. Sustained resolution of heartburn occurred faster and in a larger proportion of patients treated with esomeprazole. Both agents were well tolerated.

Conclusions: Esomeprazole produced significantly higher oesophagitis healing rates than lansoprazole over all grades of oesophagitis. Esomeprazole also provided better control of heartburn and was associated with a greater proportion of patients with sustained resolution of symptoms.

INTRODUCTION

Proton pump inhibitors are the most effective agents available for treating erosive oesophagitis (EO); however, the relative efficacies of the various proton pump inhibitors have not been well characterized in large clinical trials with sufficient power to detect differences in clinical efficacy. A large, US multicentre trial was designed to compare the efficacies of esomeprazole and lansoprazole for the complete healing and resolution of symptoms in gastro-oesophageal reflux disease (GERD)

patients with EO. Details of this study have been published elsewhere.¹

MATERIALS AND METHODS

This US study was performed in 228 centres, and was a randomized, double-blind, double-dummy trial. It compared the efficacy and safety of esomeprazole, 40 mg administered once daily, and lansoprazole, 30 mg administered once daily, in patients with heartburn and endoscopically proven EO. The severity of oesophagitis was measured using the Los Angeles (LA) grading system. This classification was used because it has a high degree of interobserver reliability.^{2, 3}

Patients were required to have a recent history of heartburn (at least 2 days in the 7 days before the

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baseline endoscopy) to be eligible for entry into the study. Patients were also required to have endoscopic evidence of EO. All patients had a *Helicobacter pylori* serology test at baseline, but the results did not affect their entry into the study.

Randomization was performed at each centre using blinded blocks of four numbers. Information was stored in individual tamper-evident, sealed envelopes (concealed allocation). Esomeprazole and lansoprazole were taken as capsules, swallowed whole before breakfast with a glass of water. Efficacy and safety evaluations were performed at Week 4 and at Week 8, and included endoscopy and symptom assessment. Patients who were healed (no mucosal breaks according to the LA classification) at Week 4 were discharged from the study following a complete physical and laboratory examination. If a patient was not healed at Week 4, an additional 5-week supply of medication was dispensed and the patient was scheduled to return at Week 8 for final endoscopic evaluation and discharge from the study.

Patients assessed and recorded the severity of the most intense episode of heartburn during the previous 24 h on daily diary cards. Heartburn was defined as a burning feeling rising from the stomach or lower part of the chest towards the neck. The presence of nocturnal heartburn was also recorded on daily diary cards. The investigator evaluated the severity of the most intense episode of heartburn within the preceding week at baseline, at Week 4 and at Week 8. Resolution was defined as the complete absence of symptoms.

The primary efficacy variable was the percentage of patients with complete healing of EO (no mucosal erosions or breaks) at Week 8 at endoscopy. Secondary efficacy variables were: complete healing of EO at Week 4; the percentage of patients with complete resolution of heartburn (defined as 7 consecutive days without heartburn, as assessed by the investigator) at Week 4; the times to first resolution (time to the first day without symptoms) and complete resolution (the first of 7 consecutive days without heartburn was used for analysis) of heartburn, as measured by diary card information at Week 4; the percentage of heartburn-free days (a 24-h period) and nights.

A sample size of 2244 patients per treatment arm was calculated to provide 95% power to detect a 3% difference in complete healing rates between the two treatment groups, estimating 93% for esomeprazole.

RESULTS

Patient characteristics

A total of 2624 patients were randomized to esomeprazole, 40 mg once daily, and 2617 patients were randomized to lansoprazole, 30 mg once daily. These patients comprised the intention-to-treat (ITT) population. Most (94%) patients completed the study. Compliance was high (>90% in both treatment groups).

Efficacy

Healing of oesophagitis by life-table analysis occurred in 92.6% (95% CI 91.5–93.6) of patients treated with esomeprazole and 88.8% (95% CI 87.5–90.0) of patients treated with lansoprazole at Week 8 (ITT; $P = 0.0001$, log-rank test). Similar results were seen in the per protocol population (93.1% vs. 89.2%, respectively, at Week 8; $P = 0.0001$, log-rank test).

Symptom control was also better with esomeprazole than with lansoprazole. A larger proportion of patients treated with esomeprazole (62.9%) had complete resolution of heartburn at Week 4 than with lansoprazole (60.2%; $P \leq 0.05$). Sustained resolution of heartburn (the first day of a completely heartburn-free week) occurred significantly earlier with esomeprazole (median, 7 days) than with lansoprazole (8 days; $P \leq 0.01$). Sustained resolution of nocturnal heartburn occurred more rapidly with esomeprazole (1 day) compared with lansoprazole (2 days). The proportion of patients with heartburn-free nights was significantly greater in the esomeprazole group ($87 \pm 21\%$) than in the lansoprazole group ($86 \pm 22\%$; $P < 0.05$).

The 8-week healing rates by baseline grade of oesophagitis were: esomeprazole – Grade A 97.2%, Grade B 92.0%, Grade C 88.3%, Grade D 81.4%; lansoprazole – Grade A 97.0%, Grade B 91.0%, Grade C 77.3%, Grade D 64.4%.

Both drugs were well tolerated and there were no significant differences in the side-effect profiles of the two agents.

DISCUSSION

A new proton pump inhibitor should demonstrate superiority in acid control in intragastric pH studies, improved healing of EO, and better and faster resolution of symptoms of heartburn. It should demonstrate little interindividual variability and have at least the same

high degree of tolerability and safety as demonstrated by currently available proton pump inhibitors.

This large, randomized, double-blind trial shows that esomeprazole, 40 mg once daily, produces higher rates of healing of EO than lansoprazole, 30 mg once daily. Esomeprazole is also associated with a greater proportion of patients who have sustained resolution of symptoms of GERD. Esomeprazole, 40 mg once daily, has been shown to be superior to omeprazole, 20 mg once daily, in two large, randomized, double-blind trials.^{4, 5} In addition to producing higher healing rates than lansoprazole, esomeprazole also provided better control of the most common symptom of GERD, namely heartburn. More patients treated with esomeprazole achieved resolution of heartburn, and these patients also experienced less nocturnal heartburn. Importantly, sustained resolution of heartburn, as well as sustained resolution of nocturnal heartburn, occurred faster with esomeprazole.

Patients with heartburn are frequently treated by primary care physicians without endoscopic assessment of the severity of mucosal disease. Drugs such as esomeprazole that have high efficacy rates across all grades of oesophagitis have clinical advantages in this

setting. It is noteworthy that in this large trial of US patients, 18% of patients had Grade C disease at baseline and 6% had Grade D disease, suggesting that advanced disease is not uncommon in large cohorts of patients with GERD.

REFERENCES

- 1 Castell D, Kahrilas P, Richter J, *et al.* Esomeprazole 40 mg compared with lansoprazole 30 mg in the treatment of erosive esophagitis. *Am J Gastroenterol* 2002; 97: 575–83.
- 2 Lundell LR, Dent J, Bennett JR, *et al.* Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. *Gut* 1999; 45: 172–80.
- 3 Armstrong D, Bennett JR, Blum AL, *et al.* The endoscopic assessment of esophagitis: a progress report on observer agreement. *Gastroenterology* 1996; 111: 85–92.
- 4 Richter JE, Kahrilas PJ, Johanson J, *et al.* Efficacy and safety of esomeprazole compared with omeprazole in GERD patients with erosive esophagitis: a randomized controlled trial. *Am J Gastroenterol* 2001; 96: 656–65.
- 5 Kahrilas PJ, Falk GW, Johnson DA, *et al.* Esomeprazole improves healing and symptom resolution as compared with omeprazole in reflux oesophagitis patients: a randomized controlled trial. The Esomeprazole Study Investigators. *Aliment Pharmacol Ther* 2000; 14: 1249–58.