AstraZeneca

I-649

SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Losec™

ACTIVE INGREDIENT: Omeprazole

Trial Title (number): Recurrence of Stricture – Omeprazole's Role Evaluated (RESTORE)

Development Phase: III
First Subject Recruited: June 1990
Last Subject Completed: March 1993
Approval Date: 21 September 2004

OBJECTIVES

The objective of this study was to compare the recurrence of esophageal strictures complicating gastro-esophageal reflux disease in patients treated with either omeprazole or ranitidine following dilatation of those strictures.

METHODS

Study design

Randomized, double-blind parallel group design.

The study was of double-blind parallel group design with a treatment period of one year. Initial medication was assigned randomly and comprised omeprazole 20 mg or ranitidine 150 mg b.i.d.

Target subject population and sample size

Three hundred and sixty-six patients were randomized, double-blind to either omeprazole 20 mg (n=181) or ranitidine 150 mg b.i.d. (n=185) for one year following endoscopic dilatation of their esophageal stricture to 12-18 mm [36-54 French Gauge].

Investigational product and comparator(s): dosage, mode of administration and batch numbers

- Omeprazole 20 mg capsules, administered orally. Batch numbers: H-431-13-2-1, H431-13-2-2
- Omeprazole placebo capsules, administered orally. Batch numbers: H-459-6-1-1 H-459-6-1-2
- Ranitidine 150 mg tablets, administered orally. Batch numbers H538-5-1-4 H538-5-1-5 H538-5-1-7
- Ranitidine placebo tablets, administered orally. Batch numbers H-539-4-1-2 H-539-4-1-3
- Gaviscon® liquid, administered orally. Batch numbers: J11674 WK048013 WK057494

Duration of treatment

Duration of treatment was for a period of one year.

Criteria for evaluation

Efficacy:

Endoscopy: Subsequent endoscopy and dilatation were performed whenever clinically indicated, and endoscopy on completion of treatment. Symptoms were assessed every 3 months at clinic visits and weekly diary cards were used to record symptoms, diet and alginate/antacid consumption.

Safety

Adverse events, clinical laboratory data, and physical examination were used to evaluate safety.

RESULTS:

Efficacy results

Fewer patients in the omeprazole group required redilatation compared with those receiving ranitidine (43/143, [30%] vs. 66/143 [46%] after 12 months; p<0.01). Patients on omeprazole also required fewer redilatations (0.48/year) compared with ranitidine (1.08/year; p<0.01). On completion of treatment, symptom relief favoured omeprazole with 76% of patients free of dysphasia (64% ranitidine; p<0.05) and 65% in the omeprazole group asymptomatic compared with 43% receiving ranitidine (p<0.001). The proportion of patients requiring no relief medication was greater in the omeprazole group (61% with zero consumption after 12 months against 40% on ranitidine; p<0.05).

Safety results

One hundred and seven patients discontinued treatment during the study for the following reasons: 53 patients due to adverse events (omeprazole n=24, ranitidine n=29), 27 patients non-compliance (omeprazole n=14, ranitidine n=13) and 20 patients because of worsening of oesophageal symptoms (omeprazole n=3, ranitidine n=17; p<0.05), and 7 patients due to malignant stricture at entry (omeprazole n=3, ranitidine n=4).

The overall frequency of adverse events was similar in both treatment groups, the most common adverse events being respiratory e.g., common cold, breathlessness, bronchitis, and gastrointestinal e.g., diarrhea, stomach pains. Sixty-nine adverse events were classified as serious and 12 patients died during the study (n=7 omeprazole, n=5 ranitidine).

Additional safety information is presented in Table 1.

Table 1 Long-term omeprazole study data

Trial	Treatment	Omep dose (mg)	Planned duration (months)	N	Average days of treatment	Total exposure (pt-yrs)	% drop-outs	# CV SAEs	# deaths all cause	# deaths CV	# MIs	# MI fatal	# deaths or MIs	# Non heam. stroke
I-649	Omeprazole	20	12	181	365.0	180.9	24.3	10	7	5	5	3	9	1
	Ranitidine		12	185	365.0	184.9	34.1	5	5	3	0	0	5	1

(mg milligram; N number of patient; CV Cardiovascular; SAE Serious adverse event; MI Myocardial infarction.)

As with any comprehensive clinical trial programme, individual studies may include both approved and non-approved treatment regimens, including doses higher than those approved for clinical use. Before prescribing Losec™ (omeprazole), Healthcare Professionals should view their specific country information.