AstraZeneca

I-655

SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Losec™

ACTIVE INGREDIENT: Omeprazole

Trial Title (number): A comparative study of omeprazole and cimetidine on regression of columnar lined epithelium in patients with Barrett's esophagus.

Development Phase: Phase II
First Subject Recruited: January 1999
Last Subject Completed: November 1991
Approval Date:

OBJECTIVES

To observe the long term effect of reduced acid exposure with omeprazole (OM) and cimetidine (CIM) on the extent of columnar lined epithelium (CLO) in patients with Barrett's esophagus.

METHODS

Study design

Open, randomised, parallel group design. Patients randomized to receive either OM 20 mg daily or CIM 1200 mg daily for 24 months. If a patient had pH≤4 for >5% of a 24 h monitoring period 3-4 weeks after randomisation, the dosage regimen was increased to OM 40 mg daily or CIM 1600 mg daily.

Target subject population and sample size

Adult outpatients with endoscopically and histologically confirmed Barrett's esophagus (i.e.≥5 cm of columnar lined epithelium).
Twenty eight patients (22M, 6F; mean age 59 years) entered the study, 14 were randomised to OM and 14 to CIM.®

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

Omeprazole capsules 20 mg (H431-13-1-3 and H431-12-1-6)
Cimetidine tablets 400 mg (JF2736, JF2737 and BN69970)

Duration of treatment

24 months

Criteria for evaluation

Assessment methods

24h pH monitoring to assess acid suppression and endoscopy to assess the extent of columnar lined epithelium and the number of squamous islands were performed. Reflux symptoms were assessed. Adverse events (AEs) were recorded at each visit.

Statistical methods

There were comparisons between the 2 treatment groups for: a) the number of treatment successes, denoted as a reduction in CLO >2 cm from baseline, at 12 and 24 months (Fischer's Exact test) and b) the change in the number of squamous islands from baseline to 12 and 24 months (Wilcoxon rank sum test). The All Patients Treated (APT) and Per-Protocol (PP) approach were used.

Summary of results

The mean baseline CLO was 8.0 cm (OM 7.3 cm; CIM 8.8 cm). All 28 patients were eligible for the APT analyses with 26 eligible for the PP analyses. Nineteen patients (OM: 10, CIM: 9) completed the study and 8 patients discontinued (2 adverse events; 6 other reasons). Esophageal acid exposure time was reduced in both treatment groups, but not always ≤5% of the 24 h recording time with pH<4. The mean length of CLO was decreased at 24 months in the cimetidine group (-1.7cm-PP), but not in the omeprazole group (+0.6cm-PP). There was a reduction in reflux symptom score in both treatment groups. The number of treatment successes (CLO≥2 cm reduction) was significantly greater with CIM than OM after 12 months ($p<0.05$). After 2 years treatment, 4 OM patients (44%-PP) and 7 CIM patients (78%-PP) had an increased number of squamous islands within the metaplastic epithelium. There were 4 SAEs (2 OM; 2 CIM) and none were considered to be drug-related.

Additional safety information is presented in Table 1 below

Table 1 Long-term omeprazole study data

Trial	Treatment	Omep dose (mg)	Planned duration (months	N	Average days of treatment	Total exposure (pt-yrs)	% dropouts	# CV SAEs	# deaths all cause	# deaths CV	# MIs	# MI fatal	# deaths or MIs	# Non heam. stroke
DC-OMD	Omeprazole	20	24	14	519.8	19.9	28.6	0	0	0	0	0	0	0
	Cimetidine		24	14	382.0	14.6	35.7	0	1	0	0	0	1	0

(mg milligram; N number of patient; CV Cardiovascular; SAE Serious adverse event; MI Myocardial infarction.)
Note: Days of treatment and total exposure unavailable: Days on treatment imputed from trials where data available

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.