AstraZeneca

Drug product		**SYNOPSIS**	(For national authority use only)
Drug substance(s)	Esomeprazole	Referring to part of the dossier	
Document No.	SH-QBE-0091		
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Study code	SH-QBE-0091		
Date	16 November 2005		

A single-centre, open, 2-way crossover, comparative study of esomeprazole 40 mg once daily and lansoprazole 30 mg once daily regarding 24-hour intragastric pH following single and repeated oral administration in patients with symptoms of GERD

STUDY CENTRE

Single-centre study.

PUBLICATION (REFERENCE)

Röhss K, Lind T, Wilder-Smith C. Esomeprazole 40 mg provides more effective intragastric acid control than lansoprazole 30 mg, omeprazole 20 mg, pantoprazole 40 mg and rabeprazole 20 mg in patients with gastro oesophageal reflux symptoms. European Journal of Clinical Pharmacology 2004;60(8):531-9

Study period		**Phase of development**
- **DATE OF FIRST PATIENT ENROLLED**	21 September, 2001	Therapeutic confirmatory
- **DATE OF LAST PATIENT COMPLETED**	8 November, 2001	

OBJECTIVES

The primary objective was to compare the effect on intragastric acidity on day 1 after a single dose and day 5 following repeated once-daily administration of 40 mg esomeprazole and 30 mg lansoprazole in patients with symptoms of gastroesophageal reflux disease (GERD) by

assessment of the percentage of time during which intragastric pH>4 during the 24-hour period.

The secondary objectives were:

- To compare the effect on intragastric acidity on day 1 after a single dose and day 5 following repeated once-daily administration of 40 mg esomeprazole and 30 mg lansoprazole in patients with symptoms of GERD, by assessment of the 24-hour median intragastric pH
- To evaluate the safety of esomeprazole by assessment of adverse events (AEs) and laboratory variables.

STUDY DESIGN

Open, randomized, 2-way crossover study

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION/EXCLUSION

Patients with symptoms of GERD.

TEST PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

Esomeprazole capsule 40 mg administered once in the morning (om) for 5 days.

Batch No. H 1222-04-01-09.

COMPARATOR PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

Lansoprazole (Prevacid®) tablet 30 mg administered om for 5 days.

Batch No. H 0995-05-01-02.

DURATION OF TREATMENT

Two treatment periods of 5 days separated by a wash-out period of at least 13 days.

MAIN MEASUREMENT(S) AND VARIABLE(S):

- **PHARMACOKINETIC**

  This section is not applicable.

- **PHARMACODYNAMIC**

  The percentage of time with intragastric pH>4 during the 24-hour period following drug administration on days 1 and 5.

  The 24-hour median intragastric pH during the 24-hour period following drug administration on days 1 and 5.

- **SAFETY**

  Adverse events and laboratory screening.

METHODS FOR DATA EVALUATION

The Per Protocol (PP) population was used in the statistical analyses of the pharmacodynamic variables since this population is considered relevant for pharmacodynamic studies. Thus, data from patients with major Clinical Pharmacology Study Protocol (CPSP) deviations eg, non-compliance with the study drug, were excluded from the statistical evaluation. Detailed criteria and identification of the PP population were decided before database lock. Missing values were not replaced in the statistical analyses. Thus, patients with data available from only one treatment period were excluded in the Analysis of Variance (ANOVA).

The safety population, defined as patients who received at least 1 dose of any study drug and for whom post-dose data were available, was used for the evaluation of the safety variables.

Pharmacodynamic variables

The percentage of time with intragastric pH>4 during the 24-hour period following drug administration on days 1 and 5 was analysed using a mixed model Analysis of Variance (ANOVA) with fixed effects for period, sequence and treatment and a random effect for patient within sequence. The estimated mean for each treatment and the estimated mean treatment difference are given together with 95% CI and p-values for the test of no difference between the treatments.

Descriptive statistics for the percentage of time with pH>4 during the 24-hour period and the median 24-hour pH are given for the total group as well as for males and females separately.

Demographic variables (age, height, weight, body mass index (BMI)) are presented descriptively.

Safety variables

Adverse Events as well as all laboratory variables are presented descriptively.

PATIENTS

	Total
No. enrolled	45
No. randomized and treated	36
Males/Females	17/19
Mean age (range)	31 (20-49)
No. analysed for pharmacodynamics	Day 1 - 30 Day 5 - 31
No. analysed for safety	
Esomeprazole	36
Lansoprazole	36
No. completed	36

SUMMARY

- **PHARMACOKINETIC RESULTS**

  This section is not applicable.

- **PHARMACODYNAMIC RESULTS**

  Single and repeated once daily administration of esomeprazole 40 mg provided statistically significant longer time with intragastric pH>4 than lansoprazole 30 mg in patients with symptoms of GERD.

  The estimated difference in percentage of time with intragastric pH>4 between esomeprazole 40 mg and lansoprazole 30 mg was 7.16 percentage points (95% CI: 1.31-13.00) and 13.16 percentage points (95% CI: 8.87-17.46) on days 1 and 5 respectively.

  A similar pattern was seen for 24-hour median intragastric pH.

- **SAFETY RESULTS**

  Esomeprazole was well tolerated. Adverse events were reported with a similar frequency during both treatment periods. Flatulence was the most commonly reported AE. There were no serious adverse events (SAEs) reported.