AstraZeneca

DRUG PRODUCT		**Synopsis**	(FOR NATIONAL AUTHORITY USE ONLY)
DRUG SUBSTANCE	Esomeprazole	REFERRING TO PART OF THE DOSSIER	
DOCUMENT NO.	SH-QBE-0099		
VERSION NO.	01		
STUDY CODE	SH-QBE-0099		
DATE	28 November 2005		

A single-centre, open, 2-way crossover, comparative study of esomeprazole 20 mg and pantoprazole 20 mg once daily regarding 24-hour intragastric pH following single and repeated oral administration in healthy male and female subjects

STUDY CENTRE

Single-centre study

PUBLICATION (REFERENCE)

Röhss K, Wilder-Smith C, Jansson L et al. Esomeprazole 20 mg provides more effective intragastric acid control than maintenance-dose rabeprazole, lansoprazole or pantoprazole in healthy volunteers. Clinical Drug Investigation 2004;24(1):1-7

STUDY PERIOD

- **DATE OF FIRST SUBJECT ENROLLED** 11 April 2002
- **DATE OF LAST SUBJECT COMPLETED** 15 July 2002

PHASE OF DEVELOPMENT

Therapeutic confirmatory

OBJECTIVES

The primary objective was to compare the percentage of time with intragastric pH>4 over the 24-hour period on study days 1 and 5 following repeated once daily administration of 20 mg esomeprazole and 20 mg pantoprazole in healthy male and female subjects by using 24-hour pH-recording.

The secondary objectives were:

- To compare the 24-hour median intragastric pH on study days 1 and 5 following repeated once daily administration of 20 mg esomeprazole and 20 mg pantoprazole in healthy male and female subjects by using 24-hour pH-recording.

- 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

Healthy male and female subjects.

TEST PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

Esomeprazole capsule 20 mg administered once in the morning (om) for 5 days.
Batch No. H 1189-04-01-07.

COMPARATOR PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

Pantoprazole (Pantoloc®) tablet 20 mg administered om for 5 days.
Batch No. H 1560-01-01-01.

DURATION OF TREATMENT

Two treatment periods of 5 days separated by a wash-out period of at least 14 days.

MAIN MEASUREMENT(S) AND VARIABLE(S):

- PHARMACOKINETIC

This section is not applicable.

- PHARMACODYNAMIC

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

The 24-hour median intragastric pH following drug administation on study 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 subjects 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, subjects with data available from only one treatment period were excluded in the Analysis of Variance (ANOVA).

The safety population, defined as subjects 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 statistical evaluation

The percentage of time with intragastric pH>4 over the 24-hour period following drug administration on study days 1 and 5 were analysed using a mixed model ANOVA with fixed effects for period, sequence and treatment and a random effect for subject within sequence. The mean for each treatment and the mean treatment difference were estimated with symmetric 95% confidence interval (CI). Study days 1 and 5 were analysed separately. The p-value for each treatment comparison was calculated.

The 24-hour median pH was analysed in the same way as above.

Descriptive statistics for the percentage of time with pH>4 over the 24-hour period and the median 24-hour pH were also calculated for the total group as well as for males and females separately.

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

Safety statistical evaluation

Adverse events and laboratory variables are presented descriptively

SUBJECTS

	Total
No. enrolled	69
No. randomised and treated	44
Males/Females	19/25
Mean age (range)	25 (20-42)
No. analysed for pharmacodynamics	43
No. analysed for safety	44
No. completed	43

SUMMARY

- **PHARMACOKINETIC RESULTS**

This section is not applicable.

- **PHARMACODYNAMIC RESULTS**

Single and repeated once daily administration of esomeprazole 20 mg provided statistically significant longer time with intragastric pH>4 than pantoprazole 20 mg in healthy subjects.

The estimated difference in percentage of time with intragastric pH>4 between esomeprazole 20 mg and pantoprazole 20 mg was 8.78 percentage points (95% CI: 4.73 to 12.84) and 20.13 percentage points (95% CI: 14.84 to 25.42) 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 (AEs) were reported with a similar frequency during both treatment arms. No serious adverse events (SAEs) were reported.