AstraZeneca

DRUG PRODUCT		**Synopsis**	(FOR NATIONAL AUTHORITY USE ONLY)
DRUG SUBSTANCE	H 199/18	REFERRING TO PART OF THE DOSSIER	
DOCUMENT NO.	SH-QBE-0066		
VERSION NO.	1		
STUDY CODE	SH-QBE-0066		
DATE	28 January, 2000		

A comparative study on 40 mg H 199/18 and 40 mg omeprazole with regard to effect on 24-hour intragastric pH in patients with symptomatic gastroesophageal reflux disease

STUDY CENTRE

Single centre study

PUBLICATION (REFERENCE)

This section is not applicable.

STUDY PERIOD

- DATE OF FIRST SUBJECT ENROLLED 4 October, 1999
- DATE OF LAST SUBJECT COMPLETED 22 December, 1999

PHASE OF DEVELOPMENT

Therapeutic confirmatory

OBJECTIVES

The primary objective was to compare the percentage of time with an intragastric pH>4 on day 5 of 40 mg H 199/18 and 40 mg omeprazole after repeated once-daily administration in patients with symptomatic GERD.

The secondary objective was to compare the percentage of time with an intragastric pH>4 after single dose administration of 40 mg H 199/18 and 40 mg omeprazole in patients with symptomatic GERD.

STUDY DESIGN

Open, randomised, two-way cross-over study

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION/EXCLUSION

Patients with symptomatic gastroesophageal reflux disease (GERD).

TEST PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

H 199/18 capsule 40 mg, batch no. H 1222-06-01-05, oral dose of 40 mg o.m.

COMPARATOR PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

Omeprazole, capsule 40 mg, batch no. H 0743-02-05-01, oral dose of 40 mg o.m

DURATION OF TREATMENT

Two periods of five days separated with at least 13 days

MAIN MEASUREMENTS AND VARIABLES:

- PHARMACOKINETIC

  This section is not applicable.

- PHARMACODYNAMIC

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

- SAFETY

  Adverse Events (AE), laboratory assessments, ECG and physical examination.

METHODS FOR DATA EVALUATION

The percentage time with intragastric pH>4 during the 24-hour period following drug administration on day 1 and day 5 was analysed separately, 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 was estimated with 95% confidence intervals.

PATIENTS

	Total
No. planned	130
No. randomised and treated	130
Males/Females	60/70
Mean age (range)	31.7 (20-79)
No. analysed for pharmacodynamics	115
No. analysed for safety	130
No. completed	120

SUMMARY - CONCLUSIONS

- PHARMACOKINETIC RESULTS

This section is not applicable.

- PHARMACODYNAMIC RESULTS

The estimated difference in percentage of time with intragastric pH>4 between 40 mg H 199/18 and 40 mg omeprazole was 8.1% on day 1 and 6.4% on day 5 of repeated once-daily administration (Table 1).

Table 1. Means of percentage of time with intragastric pH>4 and the difference between the means following daily oral doses of H 199/18 capsule 40 mg and omeprazole capsule 40 mg for 5 days in patients with symptomatic GERD. Estimates, limits for 95% CI and p-values for tests of equal means are presented.

	Estimated mean	95% confidence interval lower	upper	p-value
Day 1 (n=115)				
H 199/18	48.6	45.1	52.2	
omeprazole	40.6	37.0	44.1	
H 199/18 - omeprazole	8.1	5.5	10.7	<0.001
Day 5 (n=114)				
H 199/18	68.4	65.4	71.4	
omeprazole	62.0	59.0	65.0	
H 199/18 - omeprazole	6.4	4.0	8.8	<0.001

- SAFETY RESULTS

The adverse events reported were of mild to moderate intensity and of a kind commonly seen in a study population of patients.