ASTRA
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NAME OF COMPANY ASTRA HÄSSLE AB TRADE NAME(S) NAMES OF ACTIVE INGREDIENTS INN H 199/18 omeprazole	**Clinical Study Synopsis** REFERENCE IN THE DOSSIER VOLUME REF. NUMBER PAGE	(FOR NATIONAL AUTHORITY USE ONLY) STUDY CODE SH-QBE-0008 REPORT NO. SH-QBE-0008

TITLE OF THE STUDY

COMPARATIVE STUDY ON 20 AND 40 MG H 199/18 AND 20 MG OMEPRAZOLE WITH REGARD TO EFFECT ON 24-HOUR INTRAGASTRIC pH

STUDY CENTRE

Department of Surgery, Kärnsjukhuset, S-541 85 Skövde, Sweden

STUDY PERIOD

The study was performed between March - June, 1996.

CLINICAL PHASE

Phase II

OBJECTIVES

The primary objective was to compare H 199/18 20 mg with omeprazole 20 mg regarding intragastric pH in patients refereed for investigation of or with established gastroesophageal reflux disease.

The secondary objective was to compare H 199/18 40 mg with H 199/18 20 mg and with omeprazole 20 mg regarding intragastric pH and to study the pharmacokinetics of H 199/18 and omeprazole. The relative bioavailability of H 199/18 20 mg compared to omeprazole 20 mg was determined.

STUDY DESIGN

The study was conducted as a double-blind, randomised, three-way cross-over trial consisting of three study periods separated by a wash-out period of at least two weeks.

NUMBER OF PATIENTS

Thirty-eight patients were included in the study.

CRITERIA FOR INCLUSION

Inclusion criteria: Suspicion of or established gastroesophageal reflux disease, male or female, 30 - 60 years of age, known *Helicobacter Pylori* status, signed informed consent to participate in the study
Study specific exclusion criteria: Treatment with H_2-receptor antagonists, pro-kinetic drugs or proton pump inhibitors in the two weeks preceding the start of the study, symptoms indicating complications of GORD (e.g. melaena, haematemesis), history of oesophagogastric surgery except for simple closure of an ulcer

INVESTIGATIONAL DRUG

Enteric coated pellets of H 199/18 magnesium salt dispensed in hard gelatine capsules, corresponding to 20 mg and 40 mg of H 199/18, respectively. Each of the two formulations were administered orally once daily for five days.
Batch No: H 1189-01-02-01 and H 1222-01-01-01, respectively

REFERENCE DRUG

Enteric coated pellets of omeprazole neutral form dispensed in a hard gelatine capsules, corresponding to 20 mg of omeprazole. Omeprazole was administered orally once daily for five days.
Batch No: H 0431-14-04-01

ASSESSMENT METHODS

At day five in each study period, the patients arrived fasted at the clinic for:

- administration of dose no. 5 of the study drug.
- recording of intragastric pH during 24 hours.
- analysis of plasma concentrations of H 199/18 or omeprazole.

STATISTICAL METHODS

A mixed analysis of variance model with the percentage of time with pH>4 during the 24-hour period, the median 24-hour pH and ln AUC, one at a time as the dependent variable was applied.

SUMMARY OF RESULTS

Thirty-six patients, age 29-58 years, 21 females, completed the study as per protocol and could be included in the statistical evaluation. The effect on intragastric pH is summarised in Table 1 and the AUC values are given in Table 2.

Table 1. Estimates and 95% c.i. for the percentage of time with pH>4 during 24 hrs.

Treatment		Estimate	Lower	Upper
Omeprazole	20 mg	43.7	36.7	50.7
H199/18	20 mg	53.0	46.0	60.0
H199/18	40 mg	69.8	62.8	76.8

The effect on percentage of time with pH>4 was significantly higher after treatment with H 199/18 20 mg as compared to omeprazole 20 mg (p=0.0045). Furthermore, the effect on intragastric pH was significantly higher after treatment with H 199/18 40 mg as compared to H 199/18 20 mg (p<0.0001).

Table 2. Estimates and 95% c.i. for the AUC_{tot} (µmol·h/L).

Treatment		Estimate	Lower	Upper
Omeprazole	20 mg	2.3	1.8	3.0
H199/18	20 mg	4.2	3.3	5.4
H199/18	40 mg	12.6	9.9	16.2

The AUC_{tot} was significantly higher for H 199/18 20 mg than for omeprazole 20 mg, and the AUC_{tot} of H 199/18 40 mg was significantly higher than for both omeprazole 20 mg and H 199/18 20 mg (p<0.0001).

DATE: 1997-04-14