ASTRA
ASTRA HÄSSLE

DRUG PRODUCT	H 199/18	**Synopsis**	(FOR NATIONAL AUTHORITY USE ONLY)
DRUG SUBSTANCE	H 199/18	REFERRING TO PART OF THE DOSSIER	
DOCUMENT NO.	SH-QBE-0019		
VERSION NO.	1		
STUDY CODE	SH-QBE-0019		
DATE	28 May, 1999		

The effect of omeprazole or H 199/18 on the efficacy of clarithromycin plus amoxicillin for the eradication of H. pylori in duodenal ulcer patients

STUDY CENTRE(S)

Multicentre study including 56 centres in Canada, Denmark, France, Germany, Spain and Sweden

PUBLICATION (REFERENCE)

STUDY PERIOD		**PHASE OF DEVELOPMENT**
- DATE OF FIRST ENROLMENT	March 5, 1998	IIIA
- DATE OF LAST PATIENT COMPLETED	November 4, 1998	

OBJECTIVES

Primary:

- To estimate eradication rates of *Helicobacter pylori* (*H. pylori*) in patients with duodenal ulcer disease but with no current ulcer, after treatment with H 199/18 or omeprazole in combination with clarithromycin plus amoxicillin. The patients received one of the following two therapies:
- H 199/18, 20 mg b.i.d., amoxicillin, 1000 mg b.i.d. and clarithromycin, 500 mg b.i.d. (HAC), given for one week
- Omeprazole, 20 mg b.i.d., amoxicillin, 1000 mg b.i.d. and clarithromycin, 500 mg b.i.d. (OAC), given for one week

Secondary:

- To compare the eradication rates of the two treatments
- To evaluate the tolerability of H 199/18 in combination with clarithromycin and amoxicillin

STUDY DESIGN

Randomised, double-blind, international multicentre study with two parallel groups.

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION

History of at least one endoscopically or radiologically verified DU episode. Positive *Helicobacter* urease test (HUT®).

TEST PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

H 199/18, 20 mg twice daily, orally, capsule, batch number: H 1189-04-01
Amoxicillin, 1000 mg twice daily, orally, tablet, batch number: H 1035-03-01
Clarithromycin, 250 mg x 2, twice daily, orally, tablet, batch number: H 1031-04-01

COMPARATOR PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

Omeprazole, 20 mg twice daily, orally, capsule, batch number: H 0431-14-04
Amoxicillin, 1000 mg twice daily, orally, tablet, batch number: H 1035-03-01
Clarithromycin, 250 mg x 2, twice daily, orally, tablet, batch number: H 1031-04-01

DURATION OF TREATMENT

Seven days.

MAIN VARIABLES:

- EFFICACY
  - *H. pylori* eradication rates
- SAFETY
  - Adverse events (AE), laboratory assessments

STATISTICAL METHODS

- ERADICATION

  The proportions of patients with eradicated *H. pylori* were used to estimate the true eradication rates. Two-sided 95% confidence intervals (CI) (exact) were calculated for each treatment group. A two-sided 95% CI for the difference, in eradication rates between the treatment groups was also calculated.

PATIENTS

Planned randomised: 400, actual randomised 448, i.e. safety population 446, intention to treat (ITT)/per protocol (PP) population: 204/192, 196/185 for HAC and OAC, respectively.

	HAC	OAC	Total
No. planned	200	200	400
No. randomised and treated	224	224	448
Males/Females	147/77	138/86	285/163
Mean age (range)	52.9(21-86)	54.3(18-91)	53.6(18-91)
No. analysed for efficacy	204	196	400
No. analysed for safety	224	222	446
No. completed	220	212	432

SUMMARY

- EFFICACY RESULTS

The eradication of *H. pylori* is shown in Table 1 and Table 2.

Table 1. Proportion of patients with eradicated *H. pylori*, estimates and 95% exact CI.

	Treatment	*Hp* negative	*Hp* positive	*Hp* unknown	Eradication rate	Lower limit	Upper limit
ITT	HAC	183	19	2	89.7%	84.7%	93.5%
	OAC	172	18	6	87.8%	82.3%	92.0%
PP	HAC	174	18	0	90.6%	85.6%	94.3%
	OAC	169	16	0	91.4%	86.3%	95.0%

According to the ITT analysis, the CI for the difference in eradication rates ranges from 4% in favour of OAC to 8% in favour of HAC. Thus, there is no statistically significant difference between the two treatments.

Table 2. Difference in eradication rates between HAC and OAC, estimates and 95% CI (normal approximation).

		Estimate	Lower limit	Upper limit
ITT	HAC minus OAC	2.0%	-4.3%	8.2%
PP	HAC minus OAC	-0.7%	-6.5%	5.1%

- SAFETY RESULTS

The treatments were safe and well tolerated with an AE profile and frequency that can be expected when proton pump inhibitors are combined with antibiotics.

DATE OF THE REPORT

28 MAY, 1999