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-0020		
VERSION NO.	01		
STUDY CODE	SH-QBE-0020		
DATE	28 May, 1999		

The effect of omeprazole or H 199/18 on the efficacy of clarithromycin plus amoxicillin for Helicobacter Pylori eradication and duodenal ulcer healing

STUDY CENTRE(S)

Multi-centre study including 29 centres in the Czech Republic, Hungary and Poland

PUBLICATION (REFERENCE)

STUDY PERIOD		**PHASE OF DEVELOPMENT**
- DATE OF FIRST ENROLMENT	March 23, 1998	IIIA
- DATE OF LAST PATIENT COMPLETED	November 1, 1998	

OBJECTIVES

Primary:

- To estimate healing rates at four weeks in duodenal ulcer patients after *Helicobacter pylori* (*H. pylori*) eradication therapy. 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, followed by 3 weeks´ placebo treatment
- Omeprazole, 20 mg b.i.d., amoxicillin, 1000 mg b.i.d. and clarithromycin, 500 mg b.i.d.(OAC), given for one week, followed by 3 weeks´ treatment with omeprazole 20 mg o.d.

Secondary:

- To estimate the eradication rates of *H. pylori* in the two treatment groups
- To compare eradication rates between the two treatment groups
- To compare the healing rates at four weeks between the treatment groups
- To evaluate the tolerability of H 199/18 in combination with clarithromycin and amoxicillin

STUDY DESIGN

Randomised, double blind, international multi centre study with two parallel groups.

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION

Patients with active duodenal ulcer of at least 5 mm in diameter verified by endoscopy, positive *Helicobacter* urease test (HUT test®) and signed Informed consent.

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
Placebo, once daily, orally, capsule, batch number: H 0459-06-03

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
Omeprazole, 20 mg once daily, orally, capsule, batch number: H 0431-14-04

DURATION OF TREATMENT

Four weeks of double-blind medication

MAIN VARIABLES:

- EFFICACY

  Healing rates at four weeks

  H. pylori eradication rates

- SAFETY

  Adverse Events (AE), laboratory assessments

STATISTICAL METHODS

- HEALING

  The proportions of patients with healed duodenal ulcer at visit 3 were used to estimate the true healing rates. Two-sided 95% confidence intervals (exact) were calculated for each treatment group. A two-sided 95% confidence interval for the difference in healing rates between the treatment groups, was also calculated.

- ERADICATION

  The proportions of patients with eradicated *H. pylori* were used to estimate the true eradication rates. Two-sided 95% confidence intervals (exact) were calculated for each

treatment group. A two-sided 95% confidence interval for the difference in eradication rates between the treatment groups, was also calculated.

patients

	HAC + placebo	OAC + omeprazole	Total
No. planned	200	200	400
No. randomised and treated	222	224	446
Males/Females	143/79	135/89	278/168
Mean age (range)	45.7 (18-79)	45.5 (18-77)	45.6 (18-79)
No. analysed for efficacy (ITT)	214	219	433
No. analysed for safety	222	224	446
No. completed	217	216	433

SUMMARY

- EFFICACY RESULTS

The outcome of healing at four weeks and the eradication of *H. pylori* after eight weeks are shown in Table 1 and Table 2.

Table 1. Healing outcome at week four; numbers by healing outcome, and healing rates with 95% exact confidence intervals.

	Treatment	Healed	Not healed	Unknown outcome	Healing rate	Lower limit	Upper limit
ITT	HAC + placebo	195	13	6	91.1%	86.5%	94.6%
	OAC + omeprazole	202	9	8	92.2%	87.9%	95.4%
PP	HAC + placebo	190	12	0	94.1%	89.9%	96.9%
	OAC + omeprazole	194	9	0	95.6%	91.8%	98.0%

Table 2. Proportion of patients with eradicated *H.pylori*, estimates and 95% exact confidence intervals.

	Treatment	Hp negative	Hp positive	Hp unknown	Eradication rate	Lower limit	Upper limit
ITT	HAC + placebo	184	25	5	86.0%	80.6%	90.3%
	OAC + omeprazole	192	21	6	87.7%	82.6%	91.7%
PP	HAC + placebo	176	22	0	88.9%	83.7%	92.9%
	OAC + omeprazole	180	21	0	89.6%	84.5%	93.4%

- SAFETY RESULTS

The treatments were safe and well tolerated but 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