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Clinical Study Synopsis

TRADE NAME(S): Losec NAME OF ACTIVE INGREDIENT(S) INN: Omeprazole	REFERENCE IN THE DOSSIER Volume: Ref. number: Page:	(FOR NATIONAL AUTHORITY USE ONLY) STUDY CODE: I-613

Title of the study: Omeprazole and ranitidine in the treatment of patients with erosive oesophagitis not responding to treatment with H_2-receptor antagonists: A double-blind, controlled, multicentre study

Investigators, study centres: Multicentre study in Sweden and Norway including 7 centres

Publication: Lundell L et al. Scand J Gastroenterol 1991;26:248-256

Study period: March 1987 to April 1989

Clinical phase: III

Objectives: To document the effect of 4 to 12 weeks treatment with omeprazole 40 mg o.m. or ranitidine 300 mg b.i.d. on healing of oesophagitis in patients unhealed after at least 3 months treatment with an H_2-receptor antagonist.

To document the effect of continuous treatment over a 6 month period with omeprazole 20 mg o.m. or ranitidine 150 mg b.i.d. for the prevention of recurrence of oesophagitis. The maintenance treatment period was extended to 12 months while the study was running.

Study design: Parallel groups, double-blind, double-dummy, randomised

Number of patients: Phase a, acute treatment - 98 entered (51 omeprazole, 47 ranitidine).
Phase b, maintenance treatment - 68 entered (46 omeprazole, 22 ranitidine).

Diagnosis, inclusion criteria: Erosive, ulcerative oesophagitis of Grade 2 or greater.

Investigational drugs: Omeprazole 20 mg enteric-coated granules in gelatin capsules, batch nos: H431-9-3, -5, -6, -7, -8, -9.
Omeprazole placebo enteric-coated granules in gelatin capsules, batch nos: H459-3-7, -8, -9.

Reference drugs: Ranitidine 150 mg film-coated tablets, batch nos: H538-1-14, -15, -16, -17, -18, -19, -21.
Ranitidine placebo tablets, batch nos: H-539-1-4, H539-3-1

Duration of treatment: Phase a, acute treatment: 4 to 12 weeks
Phase b, maintenance treatment: 12 months

Assessment methods:	Phase a – Endoscopy, biopsies, symptoms, laboratory screen and physical examination at pre–entry and every 4th week until healing or maximum 12 weeks. Adverse events and compliance every 4th week. Healed patients entered phase b. Phase b – Endoscopy, biopsies, symptoms, laboratory screen, adverse events and compliance every 3rd month, physical examination at completion of treatment. Endoscopy also in case of symptomatic recurrence between visits. Endoscopic recurrence caused withdrawal from study.
Statistical methods:	Intention to treat analysis was performed. Proportion healed patients – Mantel–Haenszel Chi–square test with stratification according to pre–entry grade. The remission curves have been estimated according to the actuarial life table method.
Summary of results:	Phase a – Omeprazole group: 32/51 (63%) patients were healed day 29, 44/51 (86%) day 57 and 46/52 (90%) patients day 85. The corresponding figures for the ranitidine group 8/47 (17%), 18/47 (38%) and 22/47 (47%). Phase b: According to the life–table analysis 67% (53%–81%) of the patients allocated to the omeprazole treatment and 10% (<22%) of the ranitidine patients were in remission at the end of the maintenance period. (95% confidence intervals within brackets.) Histopathology – A normal localization of endocrine cells was observed in all patients. Slight hyperplasia of argyrophil cells was found in 6 omeprazole and 1 ranitidine patient. This hyperplasia was of simple type and observed on only a few of the biopsy occasions. The median gastrin level in the omeprazole group significantly increased during phase a from 15 pmol/l to 28 pmol/l and remained stable at that level during the maintenance phase. There was no change in gastrin levels during treatment in the ranitidine group. Adverse events – The most common adverse events in the omeprazole group were diarrhoea and in the ranitidine group gastro–oesophageal reflux. No serious adverse event was considered to be attributable to study treatment.