AstraZeneca

**STUDY REPORT SUMMARY**

**ASTRAZENECA PHARMACEUTICALS**

**FINISHED PRODUCT:** Nexium®
**ACTIVE INGREDIENT:** Esomeprazole

| **Study No:** SYNCHRONISE study; NCT00524329; Study Code N13 |
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| SYNCHRONISE: Esomeprazole 20 mg once daily for relief of upper gastrointestinal SYmptoms associated with continuous use of NSAIDs including COX-2 selective NSAIDs in DutcH general practice: the influence of Risk-factors fOr NSAID associated GI damage on symptom responSE. |

**Developmental phase:** Non Interventional Study (Phase IV)
**Study Completion Date:** Database lock 31 October 2007
**Date of Report:** August 2008

**OBJECTIVES:**

Primary objective:

- compare the treatment effect of esomeprazole 20 mg on NSAID associated gastric complaints in patients with and without an elevated risk for upper-gastro intestinal damage (as judged by the GP).

Secondary objectives:

- determine nature and severity of the individual NSAID associated gastric complaints in patients with and without an elevated risk for upper gastro-intestinal damage (as assessed by the GP).
- determine agreement between an elevated risk as assessed by the GP and the individual absolute and relative risk factors as provided by the CBO-guideline.
- determine the difference in the amount of days that patients still experience complaints after treatment with esomeprazole 20mg compared to baseline, for patients with and without an elevated risk for upper-gastro intestinal damage.
- determine the percentage of patients that is ultimately completely symptom fee (score of ‘none’) for patients with and patients without an elevated risk for gastro-intestinal damage.
- determine the change in nature and severity of the individual upper-gastro-intestinal complaints after treatment with esomeprazole 20mg compared to baseline, in patients using a conventional NSAID or a COX-2 selective NSAID.

**METHODS:**

The study was an observational study without intervention in the treatment strategy of the patient. Patients eligible for the study were patients with upper gastro-intestinal symptoms (defined as heartburn and/or regurgitation and/or nausea and/or abdominal fullness), which were thought to be related to NSAID use and for which the GP, prior to study participation, planned to prescribe esomeprazole 20 mg once daily. At baseline, visit date, patient characteristics, NSAID use (type, dose, frequency, length and indication), risk assessment for gastric damage (risk according to GP and presence of risk factors), type and frequency of gastro-intestinal symptoms were obtained and esomeprazole treatment was started. At the evaluation visit, (approximately 2 weeks after treatment with esomeprazole) esomeprazole use, change in NSAID use, type and frequency of gastro-intestinal symptoms, adverse events leading to discontinuation of medication (DAE) and serious adverse events (SAE) were registered. Symptoms were measured on a on a 4-point Likert scale. Treatment effect was expressed as the change in the mean symptom score, which was s tested by an ANOVA model. Secondary measures and safety data were summarized by descriptive statistics.

**RESULTS:**

Between October 2006 and June 2007, GPs from 162 centres enrolled 1,233 patients. The IIT population consisted of 1,231 patients.
At baseline, nearly all patients experienced gastric symptoms (99.3%). After esomeprazole treatment, these symptoms were drastically decreased (54%). In the patients with no elevated risk for gastric damage, 50% of patients were completely symptom free after esomeprazole treatment vs 43% in the group with an elevated risk. The mean total symptom score for patients with no elevated risk improved from 1.24 (SD: 0.61) at baseline to 0.23 (SD: 0.32) after esomeprazole treatment. In patients with an elevated risk, total symptom score improved from 1.42 at baseline (SD: 0.62) to 0.28 after esomeprazole treatment (SD: 0.35). The corrected differences (corrected for baseline values) in total symptom score before and after treatment were respectively –1.09 (95% CI: -1.12 - -1.07) and –1.08 (95% CI: -1.11 - -1.06). (p=0.54). For the individual symptoms, the uncorrected changes in symptom score after esomeprazole treatment were higher in the group of patients with elevated risk: -1.45 versus –1.35 for heartburn, -1.01 versus –0.86 for regurgitation, -1.16 versus –1.03 for abdominal fullness and –0.95 versus –0.79 for nausea. Nevertheless, the proportional changes were comparable for both groups.
At baseline, 68% of the patients with an elevated risk had moderate to severe heartburn versus 60% in the group with no elevated risk. Moderate to severe regurgitation was mentioned in respectively 43% and 30% of the patients, abdominal fullness in respectively 52% and 41% and nausea in respectively 34% and 25% of the patients. Esomeprazole reduced the mean number of days with complaints respectively from to 5,1 to 1,36 and from 5,1 to 1,42 in patients without and with an increased risk.
Baseline symptoms scores were somewhat higher in the patients using classic NSAID compared with patients using COX-2 inhibitor (heartburn 1,76 vs 1,62; regurgitation 1,18 vs 1,08; abdominal fullness 1,44 vs 1,23 and nausea 1.05 vs 0,96). In the COX-2 inhibitor group, heartburn symptom score improved with 1.27 (SD: 0.82), regurgitation symptom score improved with 0.86 (SD: 0.85), abdominal fullness symptom score improved with

0.91 (SD: 0.84) and nausea symptom score improved with 0.84 (SD: 0.78). For the classic NSAID group the symptom score improvements respectively were: 1.43 (SD: 0.85), 0.96 (SD: 0.85), 1.13 (SD: 0.88) and 0.89 (SD: 0.87). There seems to be a tendency that symptom score improvements are higher in the classic NSAID group, but the standard deviations are high and differences are small.

Overall agreement in risk assessment between the GP and the CBO guideline was 78,2%. The agreement between GP and CBO guideline regarding risk assessment in patients with the primary risk factors age of above 70 years, a history with ulcus or complications of ulcus and an untreated *H. pylori* infection respectively was 87.7%, 92.1% and 86.7%. The agreement in risk assessment by the GP and the guidelines was 83% for patients with at least two risk factors.

No SAE were reported. In one patient esomeprazole treatment was stopped untimely because of diarrhea.