AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Not applicable, (Non-interventional trial, i.e. therapy according to current practice.)
ACTIVE INGREDIENT:

Study No: SRP-GB-GERD-2006/01
ALEGRIA : An epidemiological, observational study to describe symptom control and impact on daily life of GERD in patients with erosive gastroesophageal reflux disease

Developmental phase: NIS
Study Completion Date: 12 September 2007 (database closure)

Date of Report: 16 April 2008

OBJECTIVES:

Primary objective: to gather the following epidemiological data:
- demographic data
- typical GERD symptoms (frequency and severity)
- treatments prescribed for GERD and treatment changes
- symptom control and impact on daily life from the patient's perspective using the new patient-completed questionnaire GIS (GERD Impact Scale)

Secondary objective: to evaluate the added value of the GIS as a useful tool for the initial and long-term management of GERD patients

METHODS:

This was an observational study (non-interventional trial) in approximately 2000 patients suffering from gastroesophageal reflux disease (GERD) with esophagitis grade A to D according to the Los Angeles classification.

At the first visit (day 1), after having obtained the patient's informed consent, demographic and baseline data were recorded (age, gender, GERD history, current GERD symptoms, clinical judgment and prescribed treatment). At the next two visits (week 4-6 and week 8-14), GERD symptoms, clinical judgment and treatment changes were recorded. In addition, the patients were asked to complete the GERD Impact Scale (GIS) at each visit. All procedures

were routine procedures and not study related, may be except for the completion of the GIS, which was relatively new when the study was conducted.

Number of subjects (planned and analyzed):

Planned: 2000 patients in 400 study centers
Included: 2001 patients in 296 study centers
Analyzed: 2001 patients in the safety analysis set (= all patients enrolled)
1919 in the ITT analysis set (= all patients with visit 2 data)

Diagnosis and main criteria for inclusion:

Male and female patients ≥ 18 years of age suffering from GERD with erosive esophagitis (grade A-D acc. to the Los Angeles classification) currently not treated with a proton pump inhibitor for whom the responsible physician decided to initiate or change the treatment for GERD

Treatment:

Treatment for GERD according to current practice (RIZV/INAMI consensus report 15 May 2003) and according to the summary of product characteristics of the prescribed treatment

Study variables:

- Demographic and life-style characteristics
- Type and extent of esophageal erosion (findings of endoscopy performed before study entry)
- GERD impact scale
- GERD symptoms assessed by physician
- Clinical judgment of GERD symptoms
- Physician's judgment of GIS

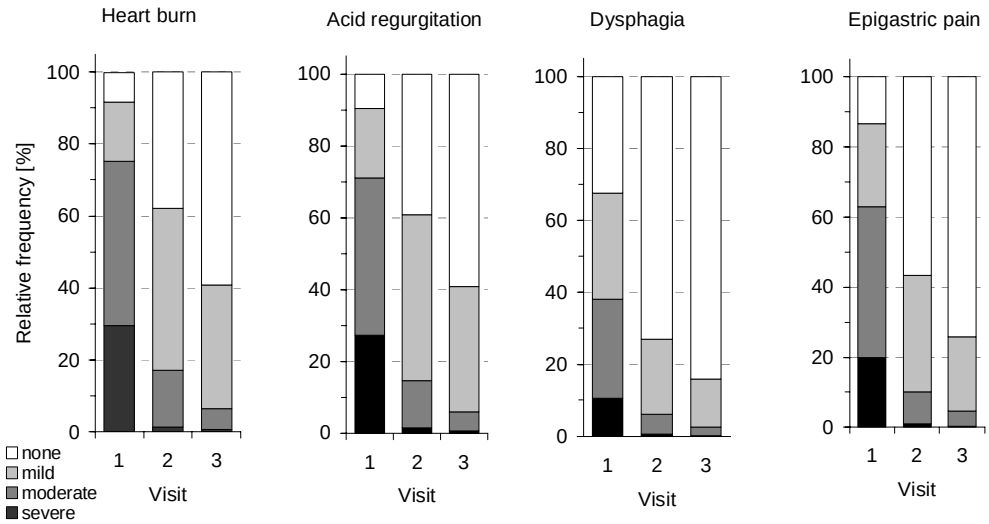
Statistical methods:
All data were listed and summarized with descriptive statistics and frequency tables as appropriate. To investigate the correlation between GIS mean-scores and other variables Spearman's correlation coefficients were calculated.

RESULTS: epidemiological data (ITT analysis set)

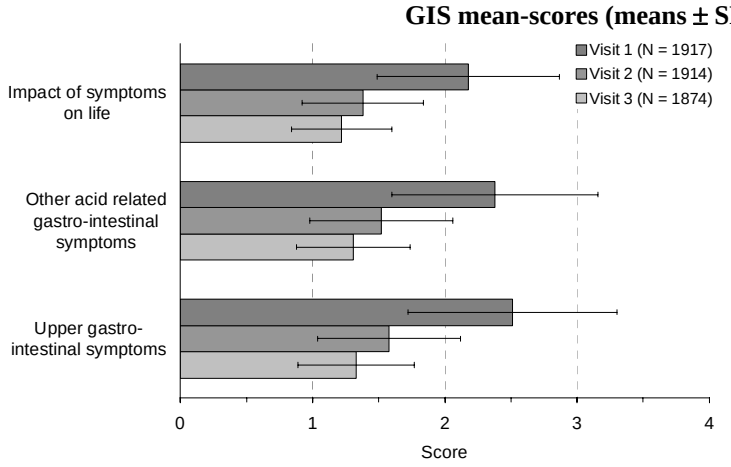
- The mean age was 55 ± 16 years (range: 18 – 95 years), the mean body weight was 75 ± 14 kg (40 – 152 kg) and the mean body mass index (BMI) was 26 ± 4 kg/m2 (16 – 54 kg/m2). The male to female ratio was ~ 1:1 (885 men and 1034 women).
- For about 70% of the patients stress was documented as a GERD-relevant lifestyle characteristic, for ~ 70% consumption of caffeine containing beverages, for ~ 50% consumption of alcohol, and for ~ 40% smoking (smokers and ex-smokers). For about 5% of the patients other relevant factors such as intake of nonsteroidal anti-inflammatory drugs were documented.

The median interval between the first occurrence of GERD symptoms and entry into the study was 1.2 years (range: 0 – 66 years). The mucosal break detected upon endoscopy was Grade A or B in most cases (91%).

- 25% of the subjects had not yet received any treatment for their GERD when they entered the study; 25% received (or had received, see below) antacids, ~ 25% H2-receptor antagonists, 15% empiric therapy with proton pump inhibitors (PPIs), and 30% therapy with PPIs after endoscopy (multiple answers were possible). Omeprazole dominated among the PPIs used for empiric therapy, pantoprazole, esomeprazole and omeprazole among the PPIs used after endoscopy.
- In most cases (99%) the responsible physician prescribed treatment with PPIs, mainly esomeprazole (82% of the patients) with a median daily dose of 40 mg. In about 50% of all patients the prescribed dose was changed between visit 1 and 2.
- During the course of the observation period, the percentage of patients with moderate or severe GERD (as assessed by the physician) decreased substantially (visit 1: ~ 90%; visit 2: ~ 30%; visit 3: ~ 15%).
- At visit 1, heartburn, acid regurgitation and epigastric pain were each documented for about 90% of the patients, dysphagia for about 70%. During the course of the observation period, the percentage of patients presenting with these typical GERD symptoms – in particular in their moderate or severe form – decreased substantially.



- All three GIS mean-scores improved substantially during the course of the observation period.



Results – evaluation of the usefulness of the GIS

- For about 80% the patients (1541 of 1905) the physicians said that the GIS had helped them to find the appropriate treatment for the patient and to evaluate the patient's response to this treatment.
- At all visits, the GIS mean-scores increased markedly with increasing severity of disease (clinical judgment). The correlation between GIS mean-scores and endoscopy findings or the physician's judgment of the usefulness of the GIS was less pronounced.

Correlation of GIS mean-scores with clinical judgment, endoscopy, and usefulness of GIS (Spearman's correlation coefficients) (ITT)

	Clinical judgment			**Endoscopy** (1)	**GIS usefulness** (2)
GIS dimension	**Visit 1** N = 1914	**Visit 2** N = 1911	**Visit 3** N = 1869	**Visit 1** N = 1907	**Visit 1** N = 1897
Upper gastro-intestinal symptoms	0.47	0.45	0.35	0.13	0.02
Other acid related gastro-int. symptoms	0.40	0.43	0.31	0.11	-0.07
Impact of symptoms on life	0.45	0.40	0.35	0.13	-0.06

Source: section 16.1.9
(1) before study entry
(2) visit 3