AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: None
ACTIVE INGREDIENT: None

Study No: NIS-GVN-NEX-2007/1
Epidemiological Study To Assess The Symptoms And Patterns Of Diagnosis And Treatment Of The Gastroesophageal Reflux Disease

Developmental phase: Epidemiological study
Study Completion Date: November 2007
Date of Report: March 2008

OBJECTIVES:

Primary

- To assess the frequency, type and severity of the symptoms in patients visiting the primary care physicians, with symptoms consistent with gastroesophageal reflux disease (GERD).

Secondary

- To assess decision to start and type of treatment by physicians for patients with symptoms of GERD.
- To assess the utilization of diagnostic resources in patients complaining of symptoms of GERD.
- To assess the impact of reflux symptoms in the daily life as perceived by the patients.

STUDY DESIGN

This is an observational, multi-centre study on the diagnostic and therapeutic approach of primary care physicians in the management of GERD; the use of diagnostic methods in this type of patients and the impact of the disease perceived by the patients. Data collection for each patient will take place at one visit.

Before assessment of the first patient, the investigator will fill in opinion survey questionnaire on his/her standard diagnostic and therapeutic approaches in the patient with reflux symptoms. Before assessment by the investigator, patients will complete the GERD impact questionnaire.

The investigator will complete questionnaire on clinical practice data obtained from clinical history and medical records on previous history, symptoms, current diagnostic approach & treatment for GERD.

TARGET SUBJECT POPULATION

The target study population is patients of either gender, aged above 18 years, visiting the primary care clinic with symptoms consistent with gastroesophageal reflux disease, either patients previously diagnosed of GERD or first visiting the clinic for these symptoms.

TARGET VARIABLES

Primary variable
Type, frequency and severity of the symptoms.

Secondary variables

- Type and percent of treatment, diagnosis utilization.
- Percent of patients well controlled of GERD

STATISTICAL METHODS

The statistical analysis was performed from two standpoints, a descriptive and another analytical.

The descriptive analysis analyzed in general the characteristics of the patients with symptoms consistent with GERD visiting primary care clinics. In this analysis for continuous variables, the arithmetic mean, standard deviation, median, minimum and maximum interquartile range were provided. For categorical variables, absolute and relative frequencies were provided.

For continuous variables, a difference of means, 95% confidence interval, and statistical significance of the difference vs. null equality hypothesis were obtained by the Student's t test, and if the normal hypothesis was not complied by the Mann Whitney Wilcoxon test. In the study on the association between categorical variables, the significance of difference was obtained by the Chi-squared test and if the applicability conditions of the previous were not met, by the Exact Fisher test.

The hypothesis tests were only considered statistically significant when $P<0.05$.

No safety analyses were done.

RESULTS:

The result analysis was based on 2,717 patients participating in the study. Analysis of the investigator questionnaire was based on 519 returned questionnaires.

The main demographic and disease-related data are shown in the table below.

Table 1 Patient demographics and baseline characteristics

	N	% *Mean±SD
Age	2,668	43.9 ± 14.3*
Gender		
Male	1205	45%
Female	1474	55%
Previously diagnosed GERD	911	34%
History of GERD < 1 year	260	29%
History of GERD from 1-5 years	549	60%
History of GERD from 5-10 years	73	8%
History of GERD > 10 years	28	3%

Patient Questionnaire (GERD Impact Scale)

100% (n=2,717) patients filled at least one question of patient questionnaire. All data presented here have been calculated taking into account only patients answering the corresponding item in the questionnaire on frequency of GERD symptoms.

Based on the GERD Impact Scales, patients described type and frequency of GERD symptoms in 7 days before the day they visited their doctor. Below (table 2) is the type and frequency of GERD symptoms:

Table 2 Type and frequency of GERD symptoms perceived by patients (n=2,717)

Type of symptom in the past 7 days	**Frequency of symptom (%)**			
	Daily	Often	Sometimes	Never
Pain in the chest or behind the sternum	15% (414)	29% (796)	33% (896)	22% (611)
Feeling of burning in the chest or behind the sternum	22% (593)	39% (1058)	29% (776)	11% (290)
Regurgitations or acid tast in the mouth	21% (565)	37% (993)	29% (795)	13% (364)
Pain or burning in the upper stomach	16% (427)	35% (956)	31% (829)	19% (505)
Sore throat or hoarness related to heartburn or acid reflux	7% (187)	15% (411)	32% (877)	46% (1242)

Based on the GERD Impact Scales, the impact of GERD symptoms on patients' daily life as perceived patients as follows:

Table 3 Impact of GERD symptoms perceived by patients (n=2,717)

Impact on patients' daily life	Frequency (%)			
	Daily	Often	Sometimes	Never
Having problems to sleep well at night due to the symtoms	9% (242)	23% (637)	41% (1118)	26% (720)
Being prevented from eating or drinking by the symptoms	15% (420)	34% (921)	26% (700)	25% (676)
Being prevented from being completely productive at work or in daily life activities	8% (214)	30% (822)	39% (1050)	23% (631)
Taking some additional medicine other than indicated by doctors (such as Maalox, Phosphalugel)	4% (98)	14% (371)	26% (710)	57% (1538)

Case Report Form

In the Case Report Form, investigators assessed the type, frequency and severity of GERD symptoms for 2,717 patients.

Table 4 Type and frequency of GERD symptoms assessed by investigators (n=2,717)

Type of symptom	Frequency in the past 7 days			
	None	1 day / week	≥ 2 days / week	Daily
Heartburn	7% (191)	12% (316)	48% (1298)	34% (912)
Acid regurgitation	10% (265)	11% (305)	46% (1242)	33% (905)
Chronic coughing	55% (1488)	19% (512)	17% (473)	9% (244)
Chest pain due to reflux	27% (740)	20% (541)	36% (991)	16% (445)
Hoarseness due to reflux	60% (1625)	20% (533)	15% (401)	6% (158)
Sleep disturbance due to reflux	32% (881)	20% (552)	31% (839)	16% (445)

Table 5 Severity of GERD symptoms assessed by investigators (n=2,717)

Type of symptom	Severity of symptoms in the past 7 days			
	None	Mild	Moderate	Severe
Heartburn	8% (227)	18% (480)	56% (1533)	18% (477)
Acid regurgitation	12% (320)	19% (529)	53% (1451)	15% (417)
Chronic coughing	56% (1510)	24% (640)	17% (451)	4% (116)
Chest pain due to reflux	29% (795)	26% (705)	36% (987)	8% (230)
Hoarseness due to reflux	60% (1627)	23% (629)	14% (389)	3% (72)

Type of symptom	Severity of symptoms in the past 7 days			
	None	Mild	Moderate	Severe
Sleep disturbance due to reflux	34% (923)	27% (729)	30% (816)	9% (249)

Level of control of GERD symptoms:

Based on the answers of patients in GERD Impact Scale, we assessed the level of control of GERD symptoms. The following definition of treatment control is suggested.

- Very well controlled: all ticks in the "never" box
- Fairly well controlled: all but 3 ticks in the "never" box
- Uncontrolled: more than 3 ticks outside the "never" box
- Poorly controlled: more than 5 ticks outside the "never" box
- Very poorly controlled: no ticks in the "never" box

Table 6 Level of control based on GERD Impact Scale filled by patient (n=2,717)

Level of control of GERD symptoms	Percentage
Very well controlled	0% (8)
Fairly well controlled	7% (189)
Uncontrolled	19% (518)
Poorly controlled	58% (1569)
Very poorly controlled	16% (433)

Investigator Questionnaire

100% of the 519 investigators participating in the study filled and returned the investigator questionnaires.

According to investigators:

- Percentage of patients doctors can establish the diagnosis based on the symptoms only: 26.5 ± 14.5 (%)
- Cases where doctors ask for complementary investigation: No response to trial treatment with a PPI: 68% (n=352); There are alarm symptoms leading to suspect complicated forms (odynophagia, dysphagia, anemia, digestive bleeding, weight loss): 67% (n=350); The symptoms are severe (impact on patient's life, work, study): 54% (n=282); Always ask for endoscopy: 35% (n=180); The diagnosis is not clear: 68% (n=354).
- Asking about the symptoms GERD can manifest through, 96% (n=499) doctors think about chestpain; 95% (n=491) about epigastric pain; 86% (n=447) about sleep

disturbance; 83% (n=429) about dysphagia; 82% (n=427) about cough; 82% (n=424) about hoarseness and 57% (n=294) about asthma.

- In total of 2,717 GERD patients participating in the study, 10% (n=276) patients were not ordered any diagnostic tests because they were already diagnosed before, 66% (n=1795) patients were diagnosed with endoscopy, 39% (n=1052) were empirically treated with PPI, 3% (n=77) patients had contrast radiology, and 2% (n=49) patients were referred to specialists for diagnosis and treatment for requiring special tests.
- 98% (n=508) doctors consider the impact of reflux symptoms on patients' daily life when they make the diagnosis and treatment for GERD.
- 81% (n=415) doctors have treatment option based on the severity or frequency of symptoms
- 97% (n=498) doctors consider a better acid controller (for example PPI) to treat GERD cases which failed with previous medicines
- In total of 2,717 GERD patients participating in the study, 96% (n=2558) patients were treated with PPIs, 29% (n=781) with antacids, 26% (n=680) with prokinetics, 7% (n=189) with H2 antagonists and only 0.55% (n=15) with no medicines

Safety analysis

This was not a therapeutic or safety study. Only serious adverse events were to be registered through the study. No serious adverse event was experienced by any of subjects