AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: PPIs
ACTIVE INGREDIENT: PPIs

Study No: NIS-GRO-DUM-2009/1
A prospective, non-interventional study to evaluate the change in symptom scores and treatment response after 4 weeks of systematic treatment with PPIs in GERD patients in primary care setting in Romania, using the validated GerdQ questionnaire.

Developmental Phase: post marketing, non-interventional observational study
Study Completion Date: 20.12.2010
Date of Report: 03.08.2011

OBJECTIVES:

Primary objective

- To describe the change in GerdQ sum scores, after a 4-week period of systematic treatment with PPIs(GerdQ)

Secondary objectives

- To measure the response at the current treatment after a 4-week period of systematic treatment with PPIs(GerdQ)

- To identify the percentage of patients which require alterations of their treatment after a 4-week period of systematic treatment with PPIs(GerdQ)

METHODS:

This prospective, non-interventional, multicentre study included **952** patients with GERD.
The target population were patients:

- known or newly diagnosed with GERD

- typical symptoms of GERD (heartburn and regurgitation) (GerdQ sum score≥8 in absence of PPI treatment)

- age≥18 years.
- each patient must meet all of the inclusion criteria and none of the exclusion criteria for this study. Under no circumstances can there be exceptions to this rule.

Observation duration was 4 weeks and the patients were treated with PPIs as per routine clinical practice or decision of treating physician.

VISIT PLAN

	Visit 1 Day 0 (Baseline evaluation)	**Visit 2** After 4 weeks
Informed Consent	x	
Visit date	x	x
GerdQ (completed by the patient)	x	x
Demography (initials, sex, date of birth)	x	
History of GERD	x	
Actual symptoms	x	x
Medication for GI symptoms at enrolment(including last week before enrolment) and during the study (except PPIs)	x	x
PPIs	x	x
Adverse events	x	x

All information regarding eligible patients were entered by the physicians in a pCRF. The patients completed PROs questionnaires prospectively during V1 and V2. The administration of the PRO were carried out in the beginning of Visit1, after informed consent had been obtained.
PRO for the current study consists in GerdQ.
GerdQ has been developed to identify the patients with GERD and to monitor the response to treatment.

GerdQ questionnaire is a validated self-administered questionnaire consisting of 6 questions regarding the symptoms from the **preceding week (last 7 days)**: **4 are positive markers** for diagnose of GERD (box **A** and **C**) and **2 are negative markers**(box **B**). Scores ranging from **0-3** were applied for the positive predictors (from box **A** and **C**) and from **3 to 0** (reversed order, where 3=none) for negative predictors (box **B**).
Gerd Q was calculated as a **sum of these scores** giving a total score ranging from **0-18.**
Interpretation of scores:

Identification of patients with GERD, without previous treatment:

Total score(boxes A+B+C)	Impact score(box C)	GERD probability
<7		Low probability
≥8	**<2**	High probability of GERD with symptoms depend on life style
≥8	**≥3**	High probability of GERD with recurrent symptoms

Identification of necessity of treatment alteration in patients previously treated:

Any question from box A and C has the score	**0 or 1**	Treatment alteration not necessary
At least one question from box A and C has the score	**2 or 3**	Treatment alteration necessary

Spontaneous adverse events reporting followed routine pharmacovigilance practice during all study length.

Inclusion criteria

- Provision of informed consent
- Female or male, age ≥ 18
- Patients known or newly diagnosed with GERD or patients with typical symptoms of GERD- heartburn, regurgitation (in the last case, GerdQ sum score should be ≥8, in the absence of PPI treatment)

All eligible patients included in the study have received information in advance and have signed consent to grant access to the data collected with regard to their condition during the observation interval proposed

Exclusion criteria

- Any symptoms at visit 1 suggesting a need for further investigation, judged by the Investigator (alarm symptoms).

- Previous participation in the present study

According to the guidelines for the diagnosis and treatment of gastro-esophageal reflux disease, the alarm symptoms suggesting complicated disease are: dysphagia, odynophagia, bleeding, weight loss without intention or anemia

Statistical methods

Data collection and processing has been followed by a simple descriptive statistical analysis. Due to the exploratory objectives of the study, there are no hypotheses to test with statistical methods to predetermine a needed sample size. The choice of target sample is pragmatic and based on patient addressability to selected physicians.

RESULTS:

Subject population:

Characteristics		**Statistic n**	**Statistic %**
Sex	**Male** **Female**	**359** **593**	**37.7** **62.3**
Age(years)	**Mean** **Median** **SD** **Minimum** **Maximum**	**53.57** **55** **15.9** **18** **88**	
Duration of disease(years)	**Mean** **Median** **SD** **Minimum** **Maximum**	**3.65** **2.00** **4.10** **1** **40**	
BRGE previously diagnosed (no. of patients)		**532**	**55.9**
BRGE newly diagnosed(V1)(no. of patients)		**420**	**44.1**

Efficacy results:

The change in **symptoms scores,** after 4 weeks of systematic treatment with PPIs:

	Score A(V1)	Score B(V1)	Score C(V1)	**Score GerdQ(V1)**	Score A(V2)	Score B(V2)	Score C(V2)	**Score GerdQ(V2)**
No. patients	951	951	951	951	951	951	951	951
Missing	1	1	1	1	1	1	1	1
Mean	4.48	3.15	3.45	**11.09**	1.27	4.69	1.06	**7.04**
Median	5.00	3.00	3.00	**11.00**	1.00	5.00	1.00	**7.00**
SD	1.19	1.61	1.63	2.35	1.25	1.65	1.13	2.27

The total mean score GerdQ(A+B+C) has changed from **11.09** at enrolment(V1) to **7.04** at V2, after 4 weeks of treatment with PPIs.

QoL-change in GerdQ scores at V2, at previously diagnosed patients:

	QoL V1	**QoL V2**
No. of patients	532	532
Missing	0	0
Mean	**16.68**	**9.32**
Median	**17.00**	**8.00**
Std. dev.	3.15	3.20
Range	16.00	20.70
Minimum	8.00	6.00
Maximum	24.00	26.70

Paired Samples Test

		Paired Differences							
					95% Confidence Interval of the Difference				
		Mean	**Std. Deviation**	**Std. Error Mean**	**Lower**	**Upper**	**t**	**df**	**Sig. (2-tailed)**
Pair 1	**QoL1 - QoL2**	**7.36147**	**3.97018**	**.17213**	**7.02333**	**7.69960**	**42.767**	**531**	**<0.001**

Paired Samples Test –the difference of 7.3 points between V1 and V2 shows that this difference is not random, at the patients previously diagnosed with GERD.

The change in symptoms scores, after 4 weeks of systematic treatment with PPIs**, in patients with previously diagnosed GERD and in newly diagnosed patients:**

	GERD present at enrolment(V1)		**GERD newly diagnosed at V1**	
	Score GerdQ V1	**Score GerdQ V2**	**Score GerdQ V1**	**Score GerdQ V2**
No. patients	532	532	418	418
Missing	0	0	1	1
Mean	**11.08**	**7.30**	**11.10**	**6.71**
Median	**11.00**	**7.00**	**11.00**	**7.00**
SD	2.41	2.25	2.27	2.27

The change in symptoms scores for **heartburn("A" box, first question),** after 4 weeks of systematic treatment with PPIs**(How often did you experience heartburn in the last 7 days?):**

	V1		**V2**	
	Frequency	**%**	**Frequency**	**%**
never	**10**	**1.1**	**376**	**39.5**
1 day	88	9.2	436	45.8
2-3 days	416	**43.7**	96	**10.1**
4-7 days	438	**46.0**	44	**4.6**
total	952	100.0	952	100.0

The % of patients which experience **heartburn>2 days** in the last 7 days has changed from **89.7%(854 patients) at V1** to **14.7(140 patients) at V2,** after 4 weeks of treatment with PPIs .

The change in symptom scores for **regurgitations("A" box, second question),** after 4 weeks of systematic treatment with PPIs**(How often did you experience regurgitations in the last 7 days?):**

	V1		**V2**	
	Frequency	**%**	**Frequency**	**%**
never	**43**	**4.5**	**597**	**62.7**
1 day	140	14.7	266	27.9
2-3 days	450	**47.3**	62	**6.5**
4-7 days	319	**33.5**	27	**2.8**
total	952	100.0	952	100.0

The % of patients which experience **regurgitations>2days** in the last 7 days has changed from **80.8%(769 patients) at V1 to 9.3%(89 patients) at V2,** after 4 weeks of treatment with PPIs **.**

The change in symptom scores for **sleep disturbances("C" box, first question)**, after 4 weeks of systematic treatment with PPIs**(How often did you experience sleep disturbances in the last 7 days?):**

	V1		**V2**	
	Frequency	**%**	**Frequency**	**%**
never	**150**	**15.8**	**723**	**75.9**
1 day	250	26.3	169	17.8
2-3 days	352	37.0	42	4.4
4-7 days	200	21.0	18	1.9
total	952	100.0	952	100.0

The % of patients which did not experience sleep disturbances in the last 7 days has changed from **15.8%(150 patients) at V1 to 75.9%(723 patients) at V2,** after 4 weeks of treatment with PPIs **.**

The change in symptom scores for rescue medication(antiacides) **("C" box, second question)**, after 4 weeks of systematic treatment with PPIs**(How often did you use rescue medication-antiacides in the last 7 days?):**

	V1		**V2**	
	Frequency	**%**	**Frequency**	**%**
never	**165**	**17.3**	**753**	**79.1**
1 day	168	17.6	141	14.8
2-3 days	338	35.5	36	3.8
4-7 days	281	29.5	22	2.3
total	952	100.0	952	100.0

The % of patients which did not use rescue medication in the last 7 days has changed from **17.3%(165 patients) at V1 to 79.1%(753 patients) at V2,** after 4 weeks of treatment with PPIs.

The % of patients which required alterations of their treatment after a 4-week period of systematic treatment with PPIs

	Frequency	**%**
yes	**238**	**25.0**
no	713	75.0
total	951	100.00
withdrawn	1	
total	952	

75 %(713 patients) did not require alterations of their treatment after 4 weeks of systematic treatment with PPIs.

Safety results:
There were no AEs reported in the study.
No deaths were reported.