Non-Interventional Study (NIS) Report Synopsis	
NIS Name/Code	NIS-GKR-ATC-2011/1
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Recurrence rate, risk factors for the recurrence, and quality of life in patients with GERD in Korea-an observational study (Refresh study)

Study dates:	First Subject In: 07 Dec 2011 Last Subject Last Visit: 21 Sep 2013
Phase of development:	Not applicable
Co-ordinating Investigator:	Not applicable
Sponsor's Responsible Medical Officer:	Astrazeneca Korea 16th FL Luther Building 42 Olympic-ro 35 da-gil, Soul, 138-240, Korea

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

Study Site(s)

23 study sites with 857 enrolled subjects.

Publications

No publication in academic journals at the time of preparation of this clinical study report.

Medicinal products and concomitant medication

Not applicable.

Objectives

1) To assess the response rate to proton pump inhibitor (PPI) treatment and post-treatment recurrence rate in Korean gastroesophageal reflux disease (GERD) patients.

2) To investigate factors associated with the recurrence of GERD after PPI treatment and the difference between GERD and nonerosive reflux disease (NERD) in terms of rate of complete resolution with the treatment, quality of life, and rate of recurrence.

Study design

This non-interventional study was a prospective, multicenter, observational study in patients with typical reflux symptoms. A total of 857 patients participated in the study at 23 study sites. There were no experimental elements associated with this study, and all observational activities, except the measuring of quality of life by validated questionnaires, were carried out as part of the routine treatment visits. A total of 2 to 4 on-site visits (maximum 4 visits) and 1 to 3 phone call contacts (maximum 3 contacts) were carried out according to the extent of alleviation of symptoms of the subject as well as the investigator's judgment. Data were collected by visit and the visit schedules were as follows: Baseline (Week 0), Week 4, Week 8 (only in subjects without alleviation of symptoms at Week 4), and an optional visit upon the first recurrence (optional, if the visit was performed upon recurrence, end-of-treatment phone call contacts were not carried out, except at the last Month 12.).

Target subject population

Patients with typical reflux symptoms (pyrosis, reflux) by upper endoscopy.

Study variable(s)

Primary outcome variable:

- Rate of recurrence after PPI treatment in GERD patients.

- Response rate after PPI treatment in GERD patients.

Secondary outcome variables:

- Factors associated with the recurrence of GERD.
- Comparisons between the erosive reflux disease (ERD) versus NERD for;
    - Rate of complete resolution
    - Rate of recurrence
    - Quality of life

Statistical methods

Descriptive statistics were presented for the distributions of demographic variables and endoscopic findings in the subjects. For categorical variables, number and percentage of subjects belonging to each category were provided. For continuous data, mean, standard deviation, median, minimum, and maximum were presented, and these were categorized and summarized as appropriate. Response rate to PPI treatment and post-treatment recurrence rate were determined in GERD patients. In addition, the relationships between GERD recurrence and other variables were assessed by univariate analysis or appropriate statistical analyses were carried out. As this study did not suggest a specific hypothesis, the analyses and assessments were performed in an exploratory manner. All statistical analyses were carried out using SAS.

Subject population

A total of 857 subjects participated in this non-interventional study. Among those, 33 subjects (3.9%) violated the inclusion/exclusion criteria. The primary objective, i.e., response rate to PPI treatment and recurrence status, could be verified in 611 subjects among the total study subjects.

Demographic statistics are summarized in Table S1. Mean age ± standard deviation was 53.7 ± 12.3 years old. 43.8% were male and 56.2% were female. Diagnosis of GERD was ERD in 58.6% (483/824 subjects) and NERD in 41.4% (341/824 subjects). Among 824 subjects who experienced typical symptoms, pyrosis occurred to 621 subjects (75.4%) and regurgitation phenomenon was experienced by 543 subjects (65.9%). Atypical symptoms experienced by 711 subjects included epigastric burning in 542 subjects (76.2%), globus in 389 subjects (54.7%), chest pain in 303 subjects (42.6%), cough in 250 subjects (35.2%), hoarseness in 155 subjects (21.8%), and wheezing in 78 subjects (11.0%) (Table S1).

Table S1. Subject baseline information

Item	Category		Total evaluable subjects	Subjects assessed for response
Age (years old)		N	824	611
		Mean[SD]	53.7[12.3]	54.2[12.2]
Gender		N	824	611

Table S1. Subject baseline information

Item	Category		Total evaluable subjects	Subjects assessed for response
	Male	n(%)	361(43.8)	266(43.5)
	Female	n(%)	463(56.2)	345(56.5)
GERD diagnosis		N	824	611
	Erosive	n(%)	483(58.6)	358(58.6)
	Non-erosive	n(%)	341(41.4)	253(41.4)
Typical symptom		N*	824	611
	Pyrosis	n(%)	621(75.4)	458(75.0)
	Regurgitation	n(%)	543(65.9)	399(65.3)
Atypical symptom		N*	711	530
	Epigastric burning	n(%)	542(76.2)	402(75.8)
	Globus	n(%)	389(54.7)	284(53.6)
	Chest pain	n(%)	303(42.6)	212(40.0)
	Cough	n(%)	250(35.2)	176(33.2)
	Hoarseness	n(%)	155(21.8)	111(20.9)
	Wheezing	n(%)	78(11.0)	51(9.6)

* Overlapping counting

Summary of results

Responses following PPI treatment were collected from 611 subjects. The responses were complete resolution in 65.6% (401/611 subjects), satisfactory resolution in 21.6% (132/611 subjects), partial response in 11.5% (70/611 subjects), and refractory response in 1.3% (8/611 subjects). Rate of recurrence following complete resolution was assessed in 343 out of 401 subjects with complete resolution; 57 subjects without optional and phone call visits and 1 subject with a phone call visit data error were excluded. The rate of recurrence was 47.8% (164/343 subjects) and its 95% confidence interval (CI) was (42.4, 53.2) (Table S2).

Table S2. Response and recurrence rates following PPI treatment in GERD patients

Item	Category	Statistics		95% CI√
Response to PPI treatment*		N	611	
	Complete resolution	n(%)	401(65.6)	
	Satisfactory resolution	n(%)	132(21.6)	

Table S2. Response and recurrence rates following PPI treatment in GERD patients

Item	Category	Statistics		95% CI[√]
	Partial response	n(%)	70(11.5)	
	Refractory response	n(%)	8(1.3)	
Recurrence following complete resolution		N	343	
		n(%)	164(47.8)	42.4, 53.2

* Complete resolution: at least 80% of symptoms are resolved.
Satisfactory resolution: 50% or below symptoms are observed.
Partial response: 50% or above symptoms are observed.
Refractory response: No responses to 4 weeks treatment with PPI.
[√] Exact confidence interval, unit (%)

Results from the univariate analyses on the status of recurrence by gender, age, hypertension, body mass index, abdominal obesity, smoking history, drinking history, status of past GERD medication (PPI, H2 blocker) and typical/atypical symptoms, and diagnosis of GERD indicated that there were no factors showing significant differences at a 0.05 significance level.