AstraZeneca

Non-Interventional Study (NIS) Report Synopsis

NIS Name/Code	NIS-GRU-NEX-2009/1
Edition Number	1.0
Date	29 April 2014

Observational study to evaluate *Helicobacter pylori* at the end of routine triple eradication therapy with duodenal ulcer relapse control

Study dates:
November 2010 – November 2013

First Subject In: 09 November 2010
Last Subject Last Visit: 08 November 2013

NIS REPORT SYNOPSIS

Observational study to evaluate *Helicobacter pylori* at the end of routine triple eradication therapy with duodenal ulcer relapse control

STUDY SCHEDULE

First patient inclusion date: 09 November 2010

Last patient end of treatment: 08 November 2013

CENTERS

There are five Russian clinical centers participating in the study.

STUDY OBJECTIVES

Primary objective

The primary objective of this study is to estimate *H.Pylori* eradication rate at the end of routine triple eradication therapy

Secondary objectives

Secondary objectives of the study are:

- To evaluate recurrence rate of duodenal ulcer (in patients with ulcer defects in inclusion stage)
- To evaluate frequency of duodenal ulcer relapses based on gastroscopy data and recurrence rate of *H.Pylori* infection based on breath test data after 52 weeks from the start of the therapy.

STUDY DESIGN

This was a non-interventional prospective study. Data were collected based on patient examination during four visits to the research center and in accordance with routine clinical practice of management of patients with duodenal ulcer. The inclusion criteria stipulated that the written informed consent is provided by a patient with established diagnosis of duodenal ulcer recurrence and positive ^{13}C-urea breath test (UBT) for diagnosis of *H. pylori*, and who in accordance with routine clinical practice received the standard 7-day eradication therapy including esomeprazole 20 mg bd, amoxicillin 1000 mg bd and clarithromycin 500 mg. Between 14 and 28 days from the start of treatment patients with ulcer defects in inclusion stage underwent control esophagogastroduodenoscopy (EGDS). Patients in whom control EGDS showed incomplete healing of ulcer defect received esomeprazole monotherapy (20 mg

bd) for up to 8 weeks. ^{13}C-urea breath test (UBT) was performed after 8 weeks of treatment in patients with healed ulcer defect and after 12 weeks of treatment in patients who required a course of esomeprazole monotherapy. On week 52 from the start of treatment patients were invited for Visit 4 during which the information about disease dynamics was collected and the ^{13}C-urea breath test (UBT) and endoscopic examination was performed (for patients with no acute ulcer in inclusion stage the EGDS examination during visit 4 was performed at the investigator's discretion).

PATIENT SELECTION CRITERIA

Inclusion criteria

1) Age ≥ 18 years old.

2) Active duodenal ulcer with duodenal ulcer exacerbation confirmed by endoscopic signs of duodenal ulcer disease (acute ulcer or scar deformity of the duodenal bulb) and anamnesis data.

3) *H. pylori* positive status by ^{13}C-Urea Breath Test (UBT).

4) Prescription of the standard 7-day eradication therapy including esomeprazole 20 mg bd, amoxicillin 1000 mg bd and clarithromycin 500 mg bd.

5) Written informed consent provided prior to the start of participation in the study.

Exclusion criteria

1) Subjects unable or unwilling to provide informed consent.

2) Current complication of duodenal ulcer disease, e.g. perforation, bleeding or pyloric stenosis.

3) History of esophageal/gastric/duodenal surgery except of the patients who underwent perforated ulcer closure or endoscopic hemostasis 6 or more months before the beginning of the study.

4) Contraindications to esomeprazole, amoxicillin or clarythromycin including their known or suspected hypersensitivity or allergy.

5) Treatment with amoxicillin, clarythromycin or bismuth-containing drugs one month prior to the study inclusion.

6) More than one previous attempt to eradicate *H. pylori*.

EVALUATION CRITERIA

Primary evaluation criteria

- *H. pylori* eradication – as a number (n) and percentage (%) of patients with negative ^{13}C-Urea Breath Test (UBT) following a 7-day routine triple eradication therapy (8-12 weeks from the treatment start).

Secondary evaluation criteria

- Healing of duodenal ulcer – as a number (n) and percentage (%) of patients with endoscopic signs of formation of post-ulcerative scarring between 14 and 28 days of treatment (in patients with ulcer defects at inclusion stage).

- Duodenal ulcer recurrence rate according to gastroscopic examination – as a number (n) and percentage (%) of patients with ulcer defect according to EGDS in 52 weeks after treatment.

- Number (n) and percentage (%) of patients with positive ^{13}C-Urea Breath Test (UBT) on week 52 from the start of treatment as an indicator of *H. pylori* infection.

PATIENT POPULATIONS FOR ANALYSIS

Data from all research centers were pooled into a cumulative set of data. All statistical analysis was carried out as a Full Analysis Set (FAS) using all available data across all patients included in the study. Missed data were left blank. All subjects receiving routine triple therapy were included in safety analysis.

RESULTS

One hundred patients were enrolled in the study. The Full Analysis Set (FAS) included data obtained from 96 patients.

Study population

A total of 96 patients were included in FAS inclusive of 45 (46.9%) women and 51 (53.1%) men. Subjects from Caucasian racial groups comprised the absolute majority (94, 97.9%). The average age of patients at the inclusion stage was 45.8±15.5 years. The majority of participants were employed (70, 72.9%), also 14 (14.6%) were retired, 5 (5.2%) were students, 6 (6.3%) were unemployed and one was a disabled person.
According to patients' anamnesis 68 (70.8%) subjects were non-smokers, 18 (18.8%) were smokers and 10 (10.4%) were former smokers. Sixty-five patients (67.7%) didn't consume alcohol and 31 patients (23.3%) drank alcohol occasionally. The median duration of disease (duodenal ulcer) at the study inclusion stage was 1.5 years (the interquartile range is between 0 and 7.0 years), with the maximum duration of 47.0 years.
Twenty (20.8%) patients had no history of duodenal ulcer. Sixteen (16.7%) patients had one exacerbation of duodenal ulcer disease, and 16 (16.7%) patients had two exacerbation

episodes. Twelve subjects had a history of previous *H. pylori* eradication therapy of whom 6 (50.0%) achieved positive treatment results.
Half of patients (49, 51.0%) had no history of significant co-morbidities or those at the study inclusion stage, 21 (21.9%) patients had one, and 17 (17.7%) patients had two co-morbid conditions.
Ulcer defect at baseline EGDS examination was found in 66 patients, of those 61 (63.5%) patients had one ulcer and 5 (5.2%) patients had two ulcers. At inclusion stage all patients had positive ^{13}C-Urea Breath Test (UBT).

Primary outcome measures

The results of ^{13}C-Urea Breath Test on visit 2 (8-12 weeks after the treatment start) were available for 92 patients (82 patients with complete healing of ulcer defect by day 14-28 from the treatment start and 10 patients with incomplete healing on the same point of time).
Negative ^{13}C-Urea Breath Test was observed in 81 patients with ulcer defect epithelization by day 14-28 from the treatment start and in 9 patients without complete ulcer healing by that time.
Therefore, the *H. pylori* eradication rate after 8-12 weeks of the standard 7-day eradication therapy included esomeprazole 20 mg bd, amoxicillin 1000 mg bd and clarithromycin 500 mg bd was **97.8% (90 out of 92 patients)**.

Secondary outcome measures
On days 14-28 from the treatment start (Visit 2) the EGDS results were analyzed for 58 patients. Complete healing of duodenal ulcers (absence of all previously detectable ulcers) was observed in **50 patients (86.2%)**.

The results of EGDS examination performed in 52 weeks after the treatment start were analyzed for 29 patients. Duodenal ulcer relapse (presence of ulcer defect) was noted in **3 patients (10.3%).** One of them had one ulcer that persisted from the inclusion stage and the other patient with two ulcers at baseline had only one ulcer defect by the 52th week. In third patient ulcer defect had disappeared on visit 2 (days 14-28 from the treatment start) and then reappeared on visit 4. In all patients with endoscopic signs of relapse the ^{13}C-Urea Breath Test was positive by week 52 of treatment.

After 52 weeks after treatment start the results of ^{13}C-Urea Breath Test were available for 58 patients, **23 of whom (39.7%)** had positive UBT results.

Safety

Over the whole study period two adverse events (AE) have been reported: allergic stomatitis involving the throat mucosa and the right hypochondrium pain accompanied by nausea and bitter taste in the mouth. Both AEs were considered as non-serious and resulted in full patient recovery without the discontinuation or adjustment of therapy.