Statistical Analysis Report

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A multicenter, randomized, open-label Phase IV study exploring symptom control rate in co-diagnosed NERD and chronic gastritis patients treated with 8 weeks esomeprazole treatment regimen and 2 weeks esomeprazole treatment regimen

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Study Statistician

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Abbreviations and Acronyms Used in this Document

Abbreviation or special term	Explanation
AE	Adverse event
BP	Blood pressure
DAE	Discontinuation of Investigational Product due to Adverse Event
GERD	Gastroesophageal reflux disease
GerdQ	Gastroesophageal reflux disease Questionnaire
IP	Investigational Product
ITT	Intent-to-treat
MITT	Modified intent-to-treat
NERD	Non- erosive reflux disease
NSAID	Non-steroidal anti-inflammatory drugs
PP	Per-protocol
PPI	Proton pump inhibitor
qd	Once daily
SAE	Serious adverse event (see definition in Section 6.4.2).
SD	Standard deviation

1.

DESCRIPTION OF THE PROTOCOL

1.1 Study Objectives

Primary objective

- To compare the symptom control rate between 8 weeks esomeprazole treatment regimen group and 2 weeks esomeprazole treatment regimen group in co-diagnosed NERD (Non- erosive reflux disease) and chronic gastritis patients, as evaluated by GerdQ after 24 weeks maintenance treatment/follow up.

Secondary objectives

- To compare the success rate between 8 weeks esomeprazole treatment regimen group and 2 weeks esomeprazole treatment regimen group in co-diagnosed NERD and chronic gastritis patients. Success is defined as patients who relieved after 8 weeks or 2 weeks esomeprazole treatment, and also get symptom controlled after 24 weeks maintenance treatment/follow up period.
- To assess time to first relapse, defined as the time to patients first come to see the investigator because of symptom recur and need for treatment after 8 weeks or 2 weeks esomeprazole treatment in the two treatment regimen groups.
- To assess symptom control rate after 8 /16 weeks visits in 24 weeks maintenance treatment/follow up period, as evaluated by GerdQ.
- To assess the symptom relief rate after 8 weeks or 2 weeks esomeprazole treatment in the two different treatment regimen groups.
- In the 8 weeks treatment regimen group, to compare the symptom relief rate after 2 weeks and 8 weeks treatment.
- To compare the number of unscheduled hospital visit between the two different treatment regimen groups.
- To measure patient satisfaction in the two different treatment regimen groups.

1.2 Study Design

This was a randomized, open-label design. Patients with endoscope diagnosed chronic gastritis (non- atrophic, and mild atrophic gastritis) and GerdQ ≥ 8 were randomized into two groups. Around 300 patients were needed to be randomized.

One group was the 8 weeks treatment regimen group, patients received esomeprazole 20 mg qd treatment for 8 weeks, the patients whose symptom relieved (defined as no more than one day with mild symptoms of GERD during the previous 7 days) had another 24 weeks on-demand maintenance treatment.

The second group was the 2 weeks treatment regimen group, patients received 2 weeks esomeprazole 20 mg qd treatment, if symptom relieved, they entered 24 weeks follow-up period.

During the followed up period, if the patients' symptoms recurred and needed treatment in the opinion of investigator, they would be given another 2-week esomeprazole 20 mg qd recurrent treatment, and no limitation for the times of recurrent treatment in 24 weeks follow up period. The patients whose symptoms were not relieved after 8 weeks treatment in 8 weeks treatment regimen group or 2 weeks treatment in 2 weeks treatment regimen group were withdrawn from the study and treated according to clinical routines

There are three scheduled visits (8, 16 and 24 weeks) in 24 weeks' on-demand maintenance treatment/ follow up period. Any unscheduled visits are guided by the patient's symptom recur,

need for extra treatment, or the patients' need for medical consultation. GerdQ was assessed when the patients entered the study and at 8, 16 and 24 weeks' visit in maintenance treatment/ follow-up period to assess the symptom control in two groups.

Controlled patients were defined as patients with all the items ≤1 in A and C category (Questions 1,2, 5 and 6) of GerdQ. The symptom control rate was compared between two treatment regimen groups at the three scheduled visits (8, 16 and 24 weeks in 24 weeks' maintenance treatment/ follow-up period).

1.3 Number of Patients

The primary objective of this study is to compare the symptom control rate in 8 weeks treatment regimen group, and 2 weeks treatment regimen group after 24 weeks maintenance treatment/ follow-up. Since we do not have previous data for the symptom control rate in the two treatment regimens, the sample size was calculated based on clinical experience. With a total of 170 evaluable patients, 85 in the 8 weeks treatment regimen group and 85 in the 2 weeks treatment regimen group, the power would be over 80% to detect a difference of 20% in symptom control rate between two treatment groups at two-sided 0.05 significance level using Fisher exact test, assuming the symptom control rate was around 66% in 2 weeks treatment regimen group and 86% in 8 weeks treatment regimen group (based on data from BU-NEG-0005 study). Considering the PPI response rate was around 70% and drop off rate was 20%, around 300 patients were needed to be randomized.

1.4 Personnel for Analyses

The statistical analysis of the trial was done by the Biostatistics Team, using SAS software (version 9.1.3).

2. ANALYSIS SETS

2.1 Definition of Analysis Sets

Analyses on efficacy endpoints were performed for intent-to-treat (ITT) population, modified intent-to-treat (MITT) population. Efficacy analyses were also repeated in per-protocol (PP) population including ITT-per protocol (ITT-PP) and MITT-PP populations. The MITT population was the primary analysis population. The randomized treatment regimen was used for the efficacy analyses while the actual treatment regimen for the safety analyses.

1. ITT was defined as all patients who were randomized.

2. MITT wasa defined as patients in ITT population whose symptoms relieved after 8 weeks or 2 weeks esomeprazole treatment.

3. ITT-PP (ITT-Per protocol) population was defined as all ITT subjects without significant protocol deviations while MITT-PP population defined as all MITT subjects without significant protocol deviations. Detailed criteria and identification of the Per Protocol population were decided in the data review prior to database lock.

4. Safety population was defined as all patients who took at least one dose of study drug and for whom post-dose data had been collected.

Table 1. Summary of outcome variables and analysis populations

Outcome variable	*Populations*
Demography	*ITT, MITT*
Concomitant medication	*ITT*
Symptom control rate, Time to first relapse, patient satisfaction, number of unscheduled visit	*MITT, MITT-PP*
Symptom relief rate, success rate	*ITT, ITT-PP*
Exposure	*Safety*
SAE/DAE	*Safety*
Laboratory measurements	*Safety*
Vital Signs	*Safety*
Physical examination	*Safety*

2.2 Protocol Deviations

A protocol deviation is defined as the failure to meet all inclusion criteria and the infringement of at least one of the exclusion criteria, or the non-compliance with protocol during the course of trial important protocol deviations that may lead to exclusion of patients from analysis sets are detailed in appendix a. prior to the database lock, the study team reviewed all important protocol deviations that occurred during the trial and made a determination for each patient regarding patient inclusion in the analysis set.

3. PRIMARY AND SECONDARY ENDPOINTS

3.1 Efficacy Endpoints

3.1.1 Primary Efficacy Endpoint

The symptom control rate in 8 weeks treatment regimen group, compared with 2 weeks treatment regimen group after 24 weeks on-demand maintenance treatment/ follow up. Symptom control rate is calculated as the proportion of patients whose symptoms are controlled during the follow-up phase.

Controlled patients are defined as patients with all items ≤1 in A and C category (Questions 1,2, 5 and 6) of GerdQ. (MITT, and MITT-PP)

3.1.2 Secondary Efficacy Endpoints

1. The success rate in 8 weeks treatment regimen group, compared with 2 weeks treatment regimen group after 24 weeks on-demand maintenance treatment/ follow up. Success is defined as patients who relieved after 8 weeks or 2 weeks esomeprazole treatment, and also get symptom controlled after 24 weeks maintenance treatment/follow up period.

2. Time to first relapse, defined as the time to the patients first come to see the investigator because of symptom recur and need for treatment after 8 weeks or 2 weeks treatment in the two treatment regimen groups.

3. The symptom control rate after 8 and 16 weeks on-demand maintenance treatment/ follow up in the two different treatment regimen groups. Controlled patients are defined as patients with all items ≤1in A and C category (Questions 1,2, 5 and 6) of GerdQ.

4. The symptom relief rate after 8 weeks or 2 weeks treatment in the two treatment regimen groups (Symptoms relief are defined as no more than one day with mild symptoms of GERD during the previous 7 days).

5. In the 8 weeks treatment regimen group, the symptom relief rate after 2 weeks and 8 weeks treatment (Symptoms relief are defined as no more than one day with mild symptoms of GERD during the previous 7 days).

6. The number of unscheduled hospital visit in the two treatment regimen groups.

7. The proportion of patients satisfied (scores 1-4) or very satisfied (scores 1-2) in the two different treatment regimen groups after 8, 16 and 24 weeks on-demand maintenance treatment/follow up.

3.2 Safety Endpoints

Tolerability and safety were assessed for all treated patients via serious adverse events (SAEs), discontinuations due to adverse events (DAEs) while the physical examinations, vital signs, laboratory measurements were available at Visit 1 only.

Safety assessments included:
SAEs/DAEs

SAEs would be captured from time of signature of informed consent. DAEs would be captured from time of first dose of IP (investigational product), throughout the treatment period and including the follow-up period in 2 weeks treatment regimen group.

4. ANALYSIS METHODS

4.1 General Principles

4.1.1 Significant Level

For all endpoints when statistical testing was performed, the significance level was 5% and 2-sided tests were used throughout.

4.1.2 Summary or Descriptive Statistics

Summary or descriptive statistics (n, mean, standard deviation, median, minimum, and maximum values) are presented for continuous variables by treatment regimen and visit. Categorical variables are summarized by fraction and percentage

For summary statistics, the minimum and maximum have the same decimal places as the measure collected; the mean and median have 1 more decimal place than the measure; the SD and 95% CI have 2 more decimal places than the measure. For frequency distributions, % have 1 decimal place. If the frequency is zero for a particular table cell, only “0”, properly aligned, may be displayed (i.e., “0 (0.0%)” may not be displayed).

4.1.3 Primary and Secondary Populations

The efficacy variables are summarized and analysed in ITT, MITT, ITT-PP and MITT-PP populations as noted in table 1. The MITT population is the primary analysis population. The analysis for safety variables is based on safety population.

4.1.4 Multiplicity

No adjustment for multiplicity during the analyses were performed for the only one primary comparison

4.1.5 Missing Values Handling

Patients with missing information of GerdQ by which the controlled patients are defined, are considered uncontrolled during the comparison of proportion. Similar handling applies to symptom relief rate. No missing value was imputed for summary or descriptive statistics. No data or date imputation was performed for safety analyses.

4.2 Analysis Methods

4.2.1 Efficacy

4.2.1.1 Primary Endpoint Analysis - Symptom Control Rate 24 Weeks on Follow-up

Summary statistics (number and percentage of patients in each category) and treatment regimen group comparison of proportion of patients controlled after 24 weeks of follow-up are conducted. This analysis is conducted for MITT and MITT-PP populations. Fisher's exact test was performed by using the following SAS procedure:

```
proc freq data=XXX;
  tables REGIMEN*RESPONSE / fisher;
run;
```

where REGIMEN - treatment regimen group, RESPONSE – response category.

4.2.1.2 Success Rate

Success is defined as patients who relieved after 8 weeks or 2 weeks esomeprazole treatment, and also get symptom controlled after 24 weeks maintenance treatment/follow up period. This analysis was conducted for ITT and ITT-PP populations. Summary statistics and comparison were conducted in the same manner as described in Section 4.2.1.1.

4.2.1.3 Time to First Relapse

Time to first relapse (days) was defined as from the date of last dose the 8 weeks or 2 weeks treatment regimen to the date of first time patient comes to see the investigator due to symptom relapse (Days = Date of event - Date of last dose). Patients who were lost to follow-up or whose symptom failed to relapse during study were censored at the last reported date of 24 weeks of follow-up. Median and percentiles (75%, 25%) of time to relapse, and Kaplan-Meier survival figure is presented. This analysis was conducted for MITT and MITT-PP populations. Treatment regimen group comparison by Log-Rank test and the above analyses were performed by the following SAS procedure:

```
proc lifetest data=XXX;
  time TIME*CENSORED(1);
  strata REGIMEN;
run;
```

where REGIMEN - treatment regimen group, CENSORED – censored flag

4.2.1.4 Symptom Control Rate 8 and 16 Weeks on Follow-up

Summary statistics and comparison were conducted in the same manner as described in Section 3.2.1.1.

4.2.1.5 Symptom Relief Rate in 2 Treatment Regimen

Symptom relief was defined as no more than 1 day of mild symptoms of GERD during the previous 7 days after 8 weeks or 2 weeks of treatment. Summary statistics (number and percentage of patients in each category) for the 2 treatment regimen groups were performed. This analysis was conducted for ITT and ITT-PP populations.

4.2.1.6 Symptom Relief Rate After 2 Weeks and 8 Weeks in 8 Weeks Treatment Regimen Group

Symptom relief was defined as no more than 1 day of mild symptoms of GERD during the previous 7 days. Summary statistics (number and percentage of patients in each category) after 2 weeks and 8 weeks of treatment for the 8 weeks treatment regimen group were performed. This analysis was conducted for ITT and ITT-PP populations.

4.2.1.7 Number of Unscheduled Hospital Visit

Group comparison of proportion of patients with unscheduled visit will be conducted using Fisher's exact test, and a weighted least square regression will also be performed to model and compare mean unscheduled visit between two arms using the following SAS procedure:

```
proc catmod data=XXX;
  response means;
  model UNSCH=REGIMEN /freq prob;
run;
```

where REGIMEN - treatment regimen group, UNSCH – number of unscheduled visits.

4.2.1.8 Proportion of Patient Satisfaction

Patients who were satisfied with satisfaction scores 1-4 or very satisfied with score 1-2 after 8, 16 and 24 weeks of follow-up. Summary statistics (number and percentage of patients in each category) were performed. Treatment regimen group comparison of proportion of patients satisfied and very satisfied were performed respectively with Fisher's exact test by using the SAS procedure described in Section 3.2.1.1. This analysis was conducted for MITT and MITT-PP populations.

4.2.2 Tolerability and Safety

Summary tables are presented for Safety population. No formal statistical testing was performed for tolerability and safety variables.

4.2.2.1 Adverse events (AE)

All adverse events leading to withdrawal of trial treatment (DAEs) were summarised and listed.

Where SAEs were collected from the time of the informed consent, DAEs from the time of first dose of IP, and both were followed throughout the study including the 24 weeks follow-up.

4.2.2.2 Laboratory measurements

Collected at Visit 1 only, hematology and clinical chemistry are summarized by treatment regimen received using mean, median, SD, minimum, maximum, and number of subjects.

Similarly the urinalysis results are presented by treatment regimen received using mean, median, SD, minimum, maximum, and number of subjects, where appropriate. Qualitative urinalysis results are listed.

All laboratory measurement results are also listed.

4.2.2.3 Vital signs

Vital sign measurements collected only at Visit 1 are summarized by treatment regimen received using descriptive statistics.

4.2.2.4 Physical examination

Physical examination findings performed at Visit 1 only by treatment regimen received are summarized. Listings of physical examination results are presented for each physical examination item.

4.2.2.5 Withdrawal

The number and percentage of patients who withdrew from the trial treatment for any reason are summarised by treatment regimen received.

4.2.2.6 Extent of Exposure

Extent of exposure was defined as the number of days between the start and the end dates of study therapy, where the start date of study therapy was the date of the first dose of investigative or comparator treatment regimen, and the end date of study therapy is the last known dose of investigative or comparator treatment regimen during the treatment period, i.e., Extent of exposure = Last dosing date - First dosing date + 1.

The extent of exposure is summarized by treatment regimen received by mean, median, SD, minimum, maximum, and number of subjects.

4.2.3 Other Summaries

4.2.3.1 Demographic and Baseline Characteristics

Patient characteristics (age, sex, race, heart rate, blood pressure, weight (kg), height (cm), HP infection status) at baseline are summarised by randomised treatment regimen for populations of ITT and MITT.

4.2.3.2 Protocol Violation/Deviations

Patients with protocol deviations are summarized and listed with deviation reasons.

4.2.3.3 Study Drug Compliance

Patients were asked to return all unused medication and empty bottles. The number of tablets (20 mg tablets) issued minus the number of tablets(20 mg tablets) returned during the treatment period of 8 weeks or 2 weeks for the 2 treatment group regimen were used to calculate the tablets/capsules taken. The number of tablets which should have been taken were 14 for 2 weeks regimen and 56 for 8 weeks regimen. From this information compliance was calculated.

$$\textbf{Compliance} = \left(\frac{\#Tablets \cdot taken \cdot during \cdot the \cdot period}{\#Tablets \cdot which \cdot should \cdot have \cdot been \cdot taken} \right) \textbf{x 100}$$

The treatment compliance is classified into 4 categories: <80%, 80-120%, >120% and unknown. Number and percentage of each category are presented by treatment group regimen.

4.2.3.4 Concomitant Therapy

Concomitant therapy taken at baseline and during the trial are summarised by the number and proportion of patients in each treatment regimen group receiving each drug within each therapeutic class. The WHO drug dictionary was used to classify concomitant medications by therapeutic class and preferred term. Multiple drug usage by a patient was counted only once for that therapeutic class. If the stop date of a given medication was missing, then the medication was classified as concomitant.

5. INTERIM ANALYSES

No interim analysis was planned or performed.

6. CHANGES FROM PLANNED ANALYSES

The analyses are consistent with the planned analyses.

7. RESULTS OF THE STUDY PATIENTS OF THE TRIAL

7.1 Brief Summary of Study Patients

Patients were enrolled in 10 centers in the People's Republic of China. The first patient was screened on 14 Apr 2010, the last patient completed the last visit on 01 Jun 2011 and the date of database lock was 04 Aug 2011.

7.2 Disposition of Patients

A total of 311 patients were screened (informed consent signed and CRF started) and 305 patients were randomized for this study. There were 6 patients who were not randomised in the study. The most common reasons that a patient was a screen failure, patients randomized, patients who entered or completed treatment phase and maintenance phase respectively, are displayed in Table 1.

Table 1. Patient Disposition (All Enrolled Patients)

	2 Weeks Regimen	*8 Weeks Regimen*	*Total*
Patients enrolled*			311
Patients who did not randomized			6
Subject Decision			3
Subject Lost to Follow-up			2
Other			1
Patients randomized	151(100.0%)	154(100.0%)	305(100.0%)
Patients who did not receive treatment	0	0	0
Patients who entered treatment phase	151(100.0%)	154(100.0%)	305(100.0%)
Patients who discontinued treatment	1 (0.7%)	11 (7.1%)	12 (3.9%)
Adverse Event	1 (0.7%)	5 (3.2%)	6 (2.0%)
Subject Lost to Follow-up	0	3 (1.9%)	3 (1.0%)
Eligibility Criteria Not Fulfilled	0	2 (1.3%)	2 (0.7%)
Severe Non-Compliance to Protocol	0	1 (0.6%)	1 (0.3%)

Patients completed 2 or 8 weeks treatment* **	150(99.3%)	143(92.9%)	293(96.1%)
Patients not relieved	24 (15.9%)	7 (4.5%)	31 (10.2%)
Patients relieved	126(83.4%)	136(88.3%)	262(85.9%)
Patients relieved but did not enter maintenance/follow up	2 (1.3%)	0	2 (0.7%)
Eligibility Criteria Not Fulfilled	1 (0.7%)	0	1 (0.3%)
Subject Lost to Follow-up	1 (0.7%)	0	1 (0.3%)
Patients who entered maintenance/follow up	124(82.1%)	136(88.3%)	260(85.2%)
Patients completed maintenance/follow up	122(80.8%)	135(87.7%)	257(84.3%)
Patients who discontinued maintenance/follow up	2 (1.3%)	1 (0.6%)	3 (1.0%)
Severe Non-Compliance to Protocol	0	1 (0.6%)	1 (0.3%)
Subject Decision	1 (0.7%)	0	1 (0.3%)
Subject Lost to Follow-up	1 (0.7%)	0	1 (0.3%)

*Informed consent received.
**Percentages were calculated based on the number of randomized subjects.
***Patients completed treatment but not relieved are considered 'completed'
Source table 14.1.1.1

7.3 Data Sets Analyzed

There were 305 patients in ITT population and also Safety population with 151 patients in 2 weeks Regimen and 154 in 8 weeks Regimen. Patient analysis sets are summarized in Table 2, where there were 126 patients in 2 weeks Regimen and 136 in 8 weeks Regimen in MITT population. Patients excluded from MITT included 25 patients in 2 weeks Regimen and 18 in 8 weeks Regimen. Patients whose symptoms were not relived included 24 patients in 2 weeks Regimen and 7 in 8 weeks Regimen. There were more patients in 8 weeks regimen being excluded from MITT analysis because of treatment discontinuation, and less being excluded because of not relieving.

Table 2. Analysis Data Sets

Important protocol deviation	*2 Weeks Regimen*	*8 Weeks Regimen*	*Total*
Patients included in ITT Population	151(100.0%)	154(100.0%)	305(100.0%)
Patients excluded from ITT Population			6
Subject Decision			3
Subject Lost to Follow-up			2
Other			1
Patients included in ITT-PP Population	149(98.7%)	141(91.6%)	290(95.1%)
Patients excluded from ITT-PP Population	2 (1.3%)	13 (8.4%)	15 (4.9%)
Compliance < 80% or > 120%.	0	8 (5.2%)	8 (2.6%)
Unknown compliance.	1 (0.7%)	5 (3.2%)	6 (2.0%)
Not met inclusion criteria No. 04	1 (0.7%)	1 (0.6%)	2 (0.7%)
Patients included in Safety Population	151(100.0%)	154(100.0%)	305(100.0%)
Patients excluded from Safety Population	0	0	0
Patients included in MITT Population	126(83.4%)	136(88.3%)	262(85.9%)
Patients excluded from MITT Population	25 (16.6%)	18 (11.7%)	43 (14.1%)
Patients who discontinued treatment	1 (0.7%)	11 (7.1%)	12 (3.9%)
Adverse Event	1 (0.7%)	5 (3.2%)	6 (2.0%)
Subject Lost to Follow-up	0	3 (1.9%)	3 (1.0%)

Eligibility Criteria Not Fulfilled	0	2 (1.3%)	2 (0.7%)
Severe Non-Compliance to Protocol	0	1 (0.6%)	1 (0.3%)
Patients not relieved	24 (15.9%)	7 (4.5%)	31 (10.2%)
Patients included in MITT-PP Population	125(82.8%)	135(87.7%)	260(85.2%)
Patients excluded from MITT-PP Population	1 (0.7%)	1 (0.6%)	2 (0.7%)
Compliance < 80% or > 120%.	0	1 (0.6%)	1 (0.3%)
Not met inclusion criteria No. 04	1 (0.7%)	0	1 (0.3%)

Note: One patient may have multiple reasons for exclusion from analysis population.
Note: Safety population is defined as all patients who take at least one dose of study drug and for whom post-dose data has been collected.
Note: ITT is defined as all patients who are randomized while MITT is defined as patients in ITT population whose symptoms relieved after 8 weeks or 2 weeks esomeprazole treatment.
Note: ITT-PP (ITT-Per protocol) population is defined as all ITT subjects without significant protocol deviations while MITT-PP population defined as all MITT subjects without significant protocol deviations.
Source table: Table 14.1.1.3 (data listing refer to Listing 16.2.1.1, 16.2.3.1-16.2.3.3)

7.4 Important Protocol Deviations

- There were 15 patients with important protocol deviations among 305 randomised patients as summarized in Table 3, with 2 (1.3%) in 2 weeks Regimen and 13 (8.4%) in 8 weeks Regimen who had at least one protocol deviations. The individual protocol deviations are detailed in Listing 16.2.2.1.

Table 3. Summary of Important Protocol Deviations (ITT Population)

Important protocol deviation	*2 Weeks Regimen*	*8 Weeks Regimen*	*Total*
Number of patients with at least 1 important protocol deviation	2 (1.3%)	13 (8.4%)	15 (4.9%)
Important eligibility deviation	1 (0.7%)	1 (0.6%)	2 (0.7%)
Not met inclusion criteria No. 04	1 (0.7%)	1 (0.6%)	2 (0.7%)
Important post entry deviation	1 (0.7%)	13 (8.4%)	14 (4.6%)
Compliance < 80% or > 120%.	0	8 (5.2%)	8 (2.6%)
Unknown compliance.	1 (0.7%)	5 (3.2%)	6 (2.0%)

Note: Deviations are not mutually exclusive.
Note: Denominator of percentage is N.
Source Table: Table 7.1.2Demographics and Baseline Characteristics

7.4.1 Demographics

Demographics and key characteristics are presented by regimen and overall in Table 4 for all ITT patients. Overall, more females (56.1%) than males (43.9%) were randomized in the study. Among male patients there were 54 patients in 2 weeks regimen and 80 in 8 weeks regimen while among female patients there were 97 patients in 2 weeks regimen and 74 in 8 weeks regimen. The overall mean age was 45.4 years with standard deviation of 12.91 for ITT populaiton. Except for sex, the rest characteristics seemed comparable between the 2 treatment regimen. Those for MITT are presented in Table 14.1.2.2

Table 4. Summary of Demographic and Key Characteristics (ITT Population)

Parameter	*2 Weeks Regimen (N=151)*	*8 Weeks Regimen (N=154)*	*Total (N=305)*
Age(yrs)			
n	151	154	305

Mean(SD)	44.9(13.12)	45.9(12.72)	45.4(12.91)
Median	45	47	46
Min	20	21	20
Max	74	73	74
Sex			
Male	54 (35.8%)	80 (51.9%)	134(43.9%)
Female	97 (64.2%)	74 (48.1%)	171(56.1%)
Race			
Asian	151(100.0%)	154(100.0%)	305(100.0%)
Heart Rate(beats/min)			
n	151	154	305
Mean(SD)	74.1(6.81)	75.6(6.28)	74.8(6.58)
Median	74	76	75
Min	60	55	55
Max	96	96	96
Systolic BP(mmHg)			
n	151	154	305
Mean(SD)	118.0(11.80)	120.3(12.09)	119.2(11.98)
Median	120	120	120
Min	90	90	90
Max	160	160	160
Diastolic BP(mmHg)			
n	151	154	305
Mean(SD)	75.8(9.78)	78.4(8.50)	77.1(9.23)
Median	78	80	80
Min	55	60	55
Max	100	108	108
Height(cm)			
n	151	154	305
Mean(SD)	163.7(8.05)	165.9(8.19)	164.8(8.18)
Median	162	165	164
Min	149	146	146
Max	183	189	189
Weight(Kg)			
n	151	154	305
Mean(SD)	61.3(10.72)	63.6(11.91)	62.5(11.38)
Median	60	63	61
Min	40	43	40
Max	94	107	107

Note: Age was calculated as the difference between date of consent and date of birth
Source table: Table 14.1.2.1

7.4.2 History of NERD

The NERD history is summarized in Table 5 for ITT population and were well balanced in two regimen. NERD history of MITT is displayed in Table 14.1.3.2.

Table 5. Summary of NERD History (ITT Population)

NERD History	*Parameter*	*2 Weeks Regimen (N=151)*	*8 Weeks Regimen (N=154)*	*Total (N=305)*
Heart Burn Symptom	Yes	136(90.1%)	142(92.2%)	278(91.1%)
	No	15 (9.9%)	12 (7.8%)	27 (8.9%)
	Total	151(100.0%)	154(100.0%)	305(100.0%)
Heart Burn duration (months)	N	136	142	278
	Mean(S.D)	35.8(49.05)	36.3(56.47)	36.1(52.87)
	Median	24	17	18
	Min,Max	3, 240	2, 360	2, 360
Regurgitation Symptom	Yes	135(89.4%)	138(89.6%)	273(89.5%)
	No	16 (10.6%)	16 (10.4%)	32 (10.5%)
	Total	151(100.0%)	154(100.0%)	305(100.0%)
Regurgitation duration (months)	N	135	138	273
	Mean(S.D)	34.9(47.41)	36.4(56.72)	35.6(52.24)
	Median	18	15	15
	Min,Max	2, 240	2, 360	2, 360
Other NERD Symptoms	Yes	89 (58.9%)	92 (59.7%)	181(59.3%)
	No	62 (41.1%)	62 (40.3%)	124(40.7%)
	Total	151(100.0%)	154(100.0%)	305(100.0%)
Specify of Other NERD Symptoms	Non Cardiac Chest Pain Present	28 (18.5%)	32 (20.8%)	60 (19.7%)
	Sleep Disturbance Because Of Acid Regurgitation Present	63 (41.7%)	62 (40.3%)	125(41.0%)
	Cough Because Of Acid Regurgitation	15 (9.9%)	16 (10.4%)	31 (10.2%)
	Others	16 (10.6%)	16 (10.4%)	32 (10.5%)

Note: One patient was counted at most once per category.
Note: Denominator of percentage is N.
Source table: Table 14.1.3.1

7.4.3 History of Chronic Gastritis

History of patient chronic gastritis is summrized in Table 6 for ITT population with128(84.8%) cases in 2 weeks regimen and 118(76.6%) cases in 2 weeks regimen respectively for positive symptom, and those of MITT are displayed in Table 14.1.3.2.

Table 6. Summary of History of Chronic Gastritis (ITT Population)

NERD History	*Parameter*	*2 Weeks Regimen (N=151)*	*8 Weeks Regimen (N=154)*	*Total (N=305)*
Chronic Gastritis Symptom	Yes	128(84.8%)	118(76.6%)	246(80.7%)
	No	23 (15.2%)	36 (23.4%)	59 (19.3%)
	Total	151(100.0%)	154(100.0%)	305(100.0%)
Chronic Gastritis Specify	Epigastric discomfort	55 (36.4%)	43 (27.9%)	98 (32.1%)
	Abdominal fullness	60 (39.7%)	54 (35.1%)	114(37.4%)
	Belching	61 (40.4%)	59 (38.3%)	120(39.3%)
	Nausea	47 (31.1%)	37 (24.0%)	84 (27.5%)
	Other Chronic Gastritis Symptom specify	18 (11.9%)	20 (13.0%)	38 (12.5%)

Note: One patient was counted at most once per category.
Note: Denominator of percentage is N.
Source table: Table 14.1.4.1

7.4.4 Summary of HP Detection Test (ITT Population)

There are 44 (29.1%) cases with positive HP test in 2 weeks regimen and 48 (31.2%) in 8 weeks regimen respectively, as summarized in Table 7.

Table 7. Summary of HP Detection Test (ITT Population)

HP Detection Test	*2 Weeks Regimen (N=151)*	*8 Weeks Regimen (N=154)*	*Total (N=305)*
Urea Breath Test			
Negative	36 (23.8%)	32 (20.8%)	68 (22.3%)
Positive	20 (13.2%)	18 (11.7%)	38 (12.5%)
Missing	95 (62.9%)	104(67.5%)	199(65.2%)

Rapid Urease Test			
Negative	36 (23.8%)	44 (28.6%)	80 (26.2%)
Positive	24 (15.9%)	30 (19.5%)	54 (17.7%)
Missing	91 (60.3%)	80 (51.9%)	171(56.1%)
Pathologic Test			
Negative	19 (12.6%)	19 (12.3%)	38 (12.5%)
Positive	5 (3.3%)	3 (1.9%)	8 (2.6%)
Missing	127(84.1%)	132(85.7%)	259(84.9%)
Any HP Test			
Negative	91 (60.3%)	95 (61.7%)	186(61.0%)
Positive	44 (29.1%)	48 (31.2%)	92 (30.2%)
Missing	16 (10.6%)	11 (7.1%)	27 (8.9%)

* Missing includes un-measurable, sample lost and not tested.
Source table: Table 14.1.5.1.

7.4.5 Baseline GerdQ Score

The mean baseline GERDQ score for 2 weeks regimen is 10.4 and that of 8 weeks regimen 10.7, as summarized in Table 8 for ITT population.

Table 8. Summary of GerdQ Score at baseline (ITT Population)

GerdQ		*2 Weeks Regimen (N=151)*	*8 Weeks Regimen (N=154)*	*Total (N=305)*
Total GerdQ Score	N	151	154	305
	Mean(S.D)	10.4(1.89)	10.7(1.78)	10.5(1.84)
	Median	10	11	10
	Min,Max	8, 16	8, 15	8, 16
Heartburn	0 Day	17 (11.3%)	18 (11.7%)	35 (11.5%)
	1 Day	10 (6.6%)	8 (5.2%)	18 (5.9%)
	2-3 Days	41 (27.2%)	38 (24.7%)	79 (25.9%)
	4-7 Days	83 (55.0%)	90 (58.4%)	173(56.7%)
	Total	151(100.0%)	154(100.0%)	305(100.0%)
Regurgitation	0 Day	18 (11.9%)	17 (11.0%)	35 (11.5%)
	1 Day	16 (10.6%)	17 (11.0%)	33 (10.8%)
	2-3 Days	33 (21.9%)	37 (24.0%)	70 (23.0%)

	4-7 Days	84 (55.6%)	83 (53.9%)	167(54.8%)
	Total	151(100.0%)	154(100.0%)	305(100.0%)
Upper Abd. Pain	0 Day	94 (62.3%)	101(65.6%)	195(63.9%)
	1 Day	25 (16.6%)	25 (16.2%)	50 (16.4%)
	2-3 Days	21 (13.9%)	14 (9.1%)	35 (11.5%)
	4-7 Days	11 (7.3%)	14 (9.1%)	25 (8.2%)
	Total	151(100.0%)	154(100.0%)	305(100.0%)
Nausea	0 Day	106(70.2%)	123(79.9%)	229(75.1%)
	1 Day	19 (12.6%)	15 (9.7%)	34 (11.1%)
	2-3 Days	18 (11.9%)	11 (7.1%)	29 (9.5%)
	4-7 Days	8 (5.3%)	5 (3.2%)	13 (4.3%)
	Total	151(100.0%)	154(100.0%)	305(100.0%)
Difficulty in Sleep due to Heartburn and/or Regurgitation	0 Day	91 (60.3%)	94 (61.0%)	185(60.7%)
	1 Day	11 (7.3%)	16 (10.4%)	27 (8.9%)
	2-3 Days	33 (21.9%)	24 (15.6%)	57 (18.7%)
	4-7 Days	16 (10.6%)	20 (13.0%)	36 (11.8%)

Table 8. Summary of GerdQ Score at baseline (ITT Population)*(Continued)*

GerdQ		*2 Weeks Regimen (N=151)*	*8 Weeks Regimen (N=154)*	*Total (N=305)*
	Total	151(100.0%)	154(100.0%)	305(100.0%)
Additional Medication for Heartburn and/or Regurgitation	0 Day	132(87.4%)	134(87.0%)	266(87.2%)
	1 Day	6 (4.0%)	3 (1.9%)	9 (3.0%)
	2-3 Days	8 (5.3%)	7 (4.5%)	15 (4.9%)
	4-7 Days	5 (3.3%)	10 (6.5%)	15 (4.9%)
	Total	151(100.0%)	154(100.0%)	305(100.0%)

Source table: Table 14.1.6.1

7.4.6 Medical History

The medical history is summarized in Table 9 for ITT and that for MITT in Table 14.1.7.2. The summary of surgical history is displayed in Table 14.1.8.1, 14.1.8.2.

Table 9. Summary of Medical History (ITT Population)

Medical History	*2 Weeks Regimen (N=151)*	*8 Weeks Regimen (N=154)*	*Total (N=305)*
PATIENTS WITH AT LEAST ONE OTHER MEDICAL HISTORY	25 (16.6%)	39 (25.3%)	64 (21.0%)
Vascular disorders	9 (6.0%)	16 (10.4%)	25 (8.2%)
Hypertension	9 (6.0%)	16 (10.4%)	25 (8.2%)
Hepatobiliary disorders	4 (2.6%)	9 (5.8%)	13 (4.3%)
Hepatic steatosis	2 (1.3%)	7 (4.5%)	9 (3.0%)
Hepatitis A	0	1 (0.6%)	1 (0.3%)
Bile duct stone	0	1 (0.6%)	1 (0.3%)
Cholangitis	1 (0.7%)	0	1 (0.3%)
Cholelithiasis	1 (0.7%)	0	1 (0.3%)
Gastrointestinal disorders	3 (2.0%)	3 (1.9%)	6 (2.0%)
Duodenal ulcer	1 (0.7%)	2 (1.3%)	3 (1.0%)
Appendicitis	1 (0.7%)	0	1 (0.3%)
Gastric ulcer	1 (0.7%)	0	1 (0.3%)
Reflux oesophagitis	0	1 (0.6%)	1 (0.3%)
Metabolism and nutrition disorders	1 (0.7%)	4 (2.6%)	5 (1.6%)
Diabetes mellitus	0	3 (1.9%)	3 (1.0%)
Hyperlipidaemia	1 (0.7%)	0	1 (0.3%)
Hyperuricaemia	0	1 (0.6%)	1 (0.3%)
Cardiac disorders	2 (1.3%)	2 (1.3%)	4 (1.3%)
Coronary artery disease	1 (0.7%)	1 (0.6%)	2 (0.7%)
Myocardial bridging	1 (0.7%)	0	1 (0.3%)
Ventricular tachycardia	0	1 (0.6%)	1 (0.3%)
Infections and infestations	4 (2.6%)	0	4 (1.3%)
Appendicitis	1 (0.7%)	0	1 (0.3%)
Hepatitis A	1 (0.7%)	0	1 (0.3%)
Schistosomiasis	1 (0.7%)	0	1 (0.3%)
Urinary tract infection	1 (0.7%)	0	1 (0.3%)
Musculoskeletal and connective tissue disorders	0	3 (1.9%)	3 (1.0%)
Intervertebral disc protrusion	0	1 (0.6%)	1 (0.3%)
Osteonecrosis	0	1 (0.6%)	1 (0.3%)

Spondyloarthropathy	0	1 (0.6%)	1 (0.3%)

Note: One patient was counted at most once per category.
Note: The summary will be sorted by descending frequency of SOC and then PT based on the total counts.
Note: Denominator of percentage is N.

Table 9. Summary of Other Medical History (ITT Population)*(Continued)*

Medical History	*2 Weeks Regimen (N=151)*	*8 Weeks Regimen (N=154)*	*Total (N=305)*
Renal and urinary disorders	2 (1.3%)	1 (0.6%)	3 (1.0%)
Cystitis glandularis	1 (0.7%)	0	1 (0.3%)
Cystitis noninfective	1 (0.7%)	0	1 (0.3%)
Proteinuria	0	1 (0.6%)	1 (0.3%)
Endocrine disorders	1 (0.7%)	1 (0.6%)	2 (0.7%)
Hyperthyroidism	1 (0.7%)	1 (0.6%)	2 (0.7%)
Immune system disorders	1 (0.7%)	1 (0.6%)	2 (0.7%)
IgA nephropathy	1 (0.7%)	1 (0.6%)	2 (0.7%)
Investigations	0	2 (1.3%)	2 (0.7%)
Blood cortisol decreased	0	1 (0.6%)	1 (0.3%)
ECG signs of myocardial ischaemia	0	1 (0.6%)	1 (0.3%)
Respiratory, thoracic and mediastinal disorders	1 (0.7%)	1 (0.6%)	2 (0.7%)
Pharyngitis	1 (0.7%)	0	1 (0.3%)
Pulmonary tuberculosis	0	1 (0.6%)	1 (0.3%)
Eye disorders	1 (0.7%)	0	1 (0.3%)
Diplopia	1 (0.7%)	0	1 (0.3%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	1 (0.6%)	1 (0.3%)
Uterine leiomyoma	0	1 (0.6%)	1 (0.3%)
Reproductive system and breast disorders	1 (0.7%)	0	1 (0.3%)
Prostatitis	1 (0.7%)	0	1 (0.3%)

Note: One patient was counted at most once per category.
Note: The summary will be sorted by descending frequency of SOC and then PT based on the total counts.
Note: Denominator of percentage is N.
Source table: Table 14.1.7.1

7.5 Treatment Compliance and Concomitant Therapy

7.5.1 Measurements of Treatment Compliance

The 2 treatment regimen were comparable with respect to treatment compliance. During the Treatment Period, mean percent of compliance was 99.76% for the 2 weeks regimen and 96.40% for the 8 weeks regimen for Safety population. The number of tablets which should have been taken were 14 for 2 weeks regimen and 56 for 8 weeks regimen.

Table 10. Summary of Study Drug Compliance (Safety Population)

	2 Weeks Regimen (N=151)	*8 Weeks Regimen (N=154)*	*Total (N=305)*
Compliance through Treatment Period			
n	150	149	299
Mean(SD)	99.76(1.530)	96.40(15.215)	98.09(10.907)
Median	100.0	100.0	100.0
Min	85.7	7.1	7.1
Max	100.0	112.5	112.5
Compliance category			
< 80%	0	8 (5.2%)	8 (2.6%)
Between 80% and 120%	150(99.3%)	141(91.6%)	291(95.4%)
Unknown	1 (0.7%)	5 (3.2%)	6 (2.0%)

Note:Compliance=(Tablets taken during then period/Tablets which should have been taken)*100%,during treatment period.
Note: The treatment compliance is classified into 4 categories: <80%, 80-120%, >120% and unknown.
Source: Table 14.3.2.

7.5.2 Concomitant Therapy

Concomitant medications used during the randomized treatment are summarized in the following table (Table 11.) for ITT population. Listing of individual patients are detailed in Listing 16.2.2.2.

Table 11. Summary of Concomitant Medications (ITT Population)

Concomitant Medications	*2 Weeks Regimen (N=151)*	*8 Weeks Regimen (N=154)*	*Total (N=305)*
Patients with at least one concomitant medication	46 (30.5%)	46 (29.9%)	92 (30.2%)
Comb/complexes aluminium, calcium, magnesium comps	20 (13.2%)	19 (12.3%)	39 (12.8%)
HYDROTALCITE	19 (12.6%)	15 (9.7%)	34 (11.1%)
TALCID	0	4 (2.6%)	4 (1.3%)
ALUMINIUM W/MAGNESIUM	1 (0.7%)	1 (0.6%)	2 (0.7%)
Propulsives	7 (4.6%)	5 (3.2%)	12 (3.9%)
DOMPERIDONE	4 (2.6%)	3 (1.9%)	7 (2.3%)
DOMPERIDONE MALEATE	3 (2.0%)	2 (1.3%)	5 (1.6%)
Proton pump inhibitors	4 (2.6%)	7 (4.5%)	11 (3.6%)
OMEPRAZOLE	2 (1.3%)	2 (1.3%)	4 (1.3%)
NEXIUM ORAL	1 (0.7%)	2 (1.3%)	3 (1.0%)
ESOMEPRAZOLE	0	1 (0.6%)	1 (0.3%)
LOSEC (OMEPRAZOLE)	0	1 (0.6%)	1 (0.3%)
RABEPRAZOLE	1 (0.7%)	0	1 (0.3%)
RABEPRAZOLE SODIUM	0	1 (0.6%)	1 (0.3%)
Angiotensin II antagonists, plain	5 (3.3%)	5 (3.2%)	10 (3.3%)
VALSARTAN	3 (2.0%)	1 (0.6%)	4 (1.3%)
TELMISARTAN	1 (0.7%)	2 (1.3%)	3 (1.0%)
LOSARTAN	1 (0.7%)	1 (0.6%)	2 (0.7%)
CANDESARTAN	0	1 (0.6%)	1 (0.3%)
Dihydropyridine derivatives	4 (2.6%)	5 (3.2%)	9 (3.0%)
AMLODIPINE BESILATE	1 (0.7%)	1 (0.6%)	2 (0.7%)
NORVASC	1 (0.7%)	1 (0.6%)	2 (0.7%)
AMLODIPINE	0	1 (0.6%)	1 (0.3%)
AMLODIPINE BESYLATE	0	1 (0.6%)	1 (0.3%)
FELODIPINE	0	1 (0.6%)	1 (0.3%)
NIFEDIPINE	1 (0.7%)	0	1 (0.3%)
NITRENDIPINE	1 (0.7%)	0	1 (0.3%)
Beta blocking agents, selective	2 (1.3%)	3 (1.9%)	5 (1.6%)
BETALOC	1 (0.7%)	2 (1.3%)	3 (1.0%)

BISOPROLOL FUMARATE	1 (0.7%)	1 (0.6%)	2 (0.7%)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	4 (2.6%)	1 (0.6%)	5 (1.6%)

Note: One patient was counted at most once per category.
The summary will be sorted by descending frequency of ATC and then drug name based on the total counts.
Note: Denominator of percentage is N.
Source: Table 14.1.9.1

Table 11. Summary of Concomitant Medications (ITT Population)(Continued)

Concomitant Medications	*2 Weeks Regimen (N=151)*	*8 Weeks Regimen (N=154)*	*Total (N=305)*
COUGH AND COLD PREPARATIONS	1 (0.7%)	0	1 (0.3%)
Fibrates	1 (0.7%)	0	1 (0.3%)
FENOFIBRATE	1 (0.7%)	0	1 (0.3%)
Glucocorticoids	0	1 (0.6%)	1 (0.3%)
PREDNISONE ACETATE	0	1 (0.6%)	1 (0.3%)
Imidazole derivatives	1 (0.7%)	0	1 (0.3%)
METRONIDAZOLE	1 (0.7%)	0	1 (0.3%)
LIPID MODIFYING AGENTS, COMBINATIONS	1 (0.7%)	0	1 (0.3%)
LIPID MODIFYING AGENTS, COMBINATIONS	1 (0.7%)	0	1 (0.3%)
LIVER THERAPY, LIPOTROPICS	0	1 (0.6%)	1 (0.3%)
LIVER THERAPY, LIPOTROPICS	0	1 (0.6%)	1 (0.3%)
OTHER ANALGESICS AND ANTIPYRETICS	1 (0.7%)	0	1 (0.3%)
OTHER ANALGESICS AND ANTIPYRETICS	1 (0.7%)	0	1 (0.3%)
Organic nitrates	0	1 (0.6%)	1 (0.3%)
ISOSORBIDE MONONITRATE	0	1 (0.6%)	1 (0.3%)
Other drugs for bile therapy	1 (0.7%)	0	1 (0.3%)
ANETHOLE TRITHIONE	1 (0.7%)	0	1 (0.3%)
Other peripheral vasodilators	1 (0.7%)	0	1 (0.3%)
GINKGO BILOBA LEAF EXTRACT	1 (0.7%)	0	1 (0.3%)
Penicillins with extended spectrum	1 (0.7%)	0	1 (0.3%)
AMOXICILLIN	1 (0.7%)	0	1 (0.3%)
Rauwolfia alkaloids and diuretics in combination	1 (0.7%)	0	1 (0.3%)
DIHYDRALAZINE+HYDROCHLOROTHIAZIDE+RESERPINE	1 (0.7%)	0	1 (0.3%)
Sulfonamides, plain	0	1 (0.6%)	1 (0.3%)
INDAPAMIDE	0	1 (0.6%)	1 (0.3%)
Sulfonamides, urea derivatives	0	1 (0.6%)	1 (0.3%)
GLICLAZIDE	0	1 (0.6%)	1 (0.3%)
Synth anticholinergics,esters/tertiary amino group	0	1 (0.6%)	1 (0.3%)
TRIMEBUTINE	0	1 (0.6%)	1 (0.3%)

THROAT PREPARATIONS	1 (0.7%)	0	1 (0.3%)
THROAT PREPARATIONS	1 (0.7%)	0	1 (0.3%)
Thiazolidinediones	0	1 (0.6%)	1 (0.3%)
ROSIGLITAZONE MALEATE	0	1 (0.6%)	1 (0.3%)

Note: One patient was counted at most once per category.
The summary will be sorted by descending frequency of ATC and then drug name based on the total counts.
Note: Denominator of percentage is N.
Source: Table 14.1.9.1

Table 11. Summary of Concomitant Medications (ITT Population)(Continued)

Concomitant Medications	*2 Weeks Regimen (N=151)*	*8 Weeks Regimen (N=154)*	*Total (N=305)*
DRUGS FOR FUNCTIONAL GASTROINTEST. DISORDERS	4 (2.6%)	1 (0.6%)	5 (1.6%)
ACE inhibitors, plain	0	4 (2.6%)	4 (1.3%)
BENAZEPRIL	0	1 (0.6%)	1 (0.3%)
CAPTOPRIL	0	1 (0.6%)	1 (0.3%)
FOSINOPRIL	0	1 (0.6%)	1 (0.3%)
ZESTRIL	0	1 (0.6%)	1 (0.3%)
ANTIHYPERTENSIVES AND DIURETICS IN COMBINATION	1 (0.7%)	2 (1.3%)	3 (1.0%)
ANTIHYPERTENSIVES AND DIURETICS IN COMBINATIO	1 (0.7%)	2 (1.3%)	3 (1.0%)
Anilides	1 (0.7%)	2 (1.3%)	3 (1.0%)
TYLENOL COLD	1 (0.7%)	1 (0.6%)	2 (0.7%)
PARACETAMOL	0	1 (0.6%)	1 (0.3%)
Fluoroquinolones	3 (2.0%)	0	3 (1.0%)
LEVOFLOXACIN	2 (1.3%)	0	2 (0.7%)
CIPROFLOXACIN HYDROCHLORIDE	1 (0.7%)	0	1 (0.3%)
H2-receptor antagonists	1 (0.7%)	1 (0.6%)	2 (0.7%)
RANITIDINE	1 (0.7%)	1 (0.6%)	2 (0.7%)
INTESTINAL ADSORBENTS	1 (0.7%)	1 (0.6%)	2 (0.7%)
BISMUTH HYDROXIDE+PECTIN	1 (0.7%)	1 (0.6%)	2 (0.7%)
Platelet aggregation inhibitors excl. heparin	1 (0.7%)	1 (0.6%)	2 (0.7%)
ASPIRIN	0	1 (0.6%)	1 (0.3%)
PLAVIX	1 (0.7%)	0	1 (0.3%)
Third-generation cephalosporins	1 (0.7%)	1 (0.6%)	2 (0.7%)
CEFDINIR	1 (0.7%)	0	1 (0.3%)
CEFOPERAZONE	0	1 (0.6%)	1 (0.3%)
ALL OTHER THERAPEUTIC PRODUCTS	1 (0.7%)	0	1 (0.3%)
HERBAL NOS	1 (0.7%)	0	1 (0.3%)

Antibiotics	1 (0.7%)	0	1 (0.3%)
AZITHROMYCIN	1 (0.7%)	0	1 (0.3%)
Antidiarrheal microorganisms	0	1 (0.6%)	1 (0.3%)
BIFIDOBACTERIUM+LACTOBACILLUS+SACCHAROMYCES	0	1 (0.6%)	1 (0.3%)
BILE THERAPY	1 (0.7%)	0	1 (0.3%)
BILE THERAPY	1 (0.7%)	0	1 (0.3%)
COUGH AND COLD PREPARATIONS	1 (0.7%)	0	1 (0.3%)

Note: One patient was counted at most once per category.
The summary will be sorted by descending frequency of ATC and then drug name based on the total counts.

Note: Denominator of percentage is N.
Source: Table 14.1.9.1

8. Efficacy Results

8.1 Brief Summary of Efficacy

With the successful 2 weeks regimen and 8 weeks treatment regimen of esomeprazole respectively in treatment of co-diagnosed NERD and chronic gastritis, the symptom control rate of the 8 weeks regimen during follow-up period for MITT population has consistently demonstrated better result than those of 2 weeks regimen. Patients with symptom control were 109(80.1%) vs. 95 (75.4%) in 8 weeks follow-up visit, 116(85.3%) vs. 101(80.2%) in 16 weeks follow-up visit, and 129(94.9%) vs. 110(87.3%) in 24 weeks follow-up visit. Fisher exact test to compare the control rate between the 2 treatment regimen showed a statistical significance (p-value = 0.0473) in 24 weeks follow-up. Analysis on MITT-PP population showed a similar result on the control rate. Analysis on the success rate demonstrated the 8 weeks regimen had a better result than that of 2 weeks regimen on both ITT (129(83.8%) cases in 8 weeks regimen vs. 110(72.8%) cases in 2 weeks regimen) and ITT-PP populations. In addition, first relapse of symptoms for the 8 weeks regimen was shown later than that of 2 weeks regimen (p-value=0.0003), less number of unscheduled visits during follow-up period, and higher proportion of patients who claimed treatment satisfaction than that of 2 weeks regimen, supporting that the 8 weeks regimen have a better control rate for relieved patients over 2 weeks regimen in the maintenance period for those with co-diagnosed NERD and chronic gastritis.

8.2 Result of Efficacy

8.2.1 Primary Efficacy Endpoint

The primary analyses were conducted using the MITT and same analyses were also conducted using the MITT-PP.

The analysis on the control rate during follow-up is summaried in Table 12 for MITT, where consistent better control rates were shown along the follow-up visits. At 24 weeks follow-up visit, patients with symptom control were 129(94.9%) vs. 110(87.3%) with p-value of 0.0473 by Fisher exact test.

The result from MITT-PP population is presented on Table 14.2.1.2, which is supportive to the result of MITT.

Table 12. Symptom Control Rate on Follow-Up (MITT Population)

	2 Weeks Regimen (N=126)	*8 Weeks Regimen (N=136)*
8 weeks		
Controlled	95 (75.4%)	109(80.1%)
Not Controlled	31 (24.6%)	27 (19.9%)
Treatment difference in symptom control rate		
8 Weeks Regimen - 2 Weeks Regimen	4.8%	
95% CI	-5.3%, 14.8%	
P value	0.3748	
16 weeks		

Controlled	101(80.2%)	116(85.3%)
Not Controlled	25 (19.8%)	20 (14.7%)
Treatment difference in symptom control rate		
8 Weeks Regimen - 2 Weeks Regimen	5.1%	
95% CI	-4.0%, 14.3%	
P value	0.3258	
24 weeks		
Controlled	110(87.3%)	129(94.9%)
Not Controlled	16 (12.7%)	7 (5.1%)
Treatment difference in symptom control rate		
8 Weeks Regimen - 2 Weeks Regimen	7.6%	
95% CI	0.7%, 14.4%	
P value	0.0473	

Note: The denominator of percentage is N.
Note: Fisher's exact test compared the symptom control rate between the 2 treatment regimen after 8, 16 and 24 weeks of follow-up.
Note: Controlled patients are defined as patients with all items ⩽ 1 in A and C category (Questions 1, 2, 5 and 6) of GerdQ.
Source: Table 14.2.1.1.

8.2.2 Secondary Efficacy Endpoints

Success Rate

Success rate is summaried in Table 13 for ITT population while the analysis on ITT-PP population is summaried in Table 14.2.2.2. In ITT, there were 110(72.8%) and 129(83.8%) patients with success in 2 weeks regimen and 8 weeks regimen respectively. Success comparison between the 2 regimen showed p-value of 0.0258 by Fisher exact test.

Table 13. Symptom Success Rate in 2 Treatment Regimen (ITT Population)

	2 Weeks Regimen (N=151)	*8 Weeks Regimen (N=154)*
8 weeks		
Success	95 (62.9%)	109(70.8%)
Not Success	56 (37.1%)	45 (29.2%)
Treatment difference in symptom success rate		
8 Weeks Regimen - 2 Weeks Regimen	7.9%	
95% CI	-2.7%, 18.4%	
P value	0.1806	
16 weeks		
Success	101(66.9%)	116(75.3%)
Not Success	50 (33.1%)	38 (24.7%)
Treatment difference in symptom success rate		
8 Weeks Regimen - 2 Weeks Regimen	8.4%	
95% CI	-1.7%, 18.6%	
P value	0.1292	
24 weeks		
Success	110(72.8%)	129(83.8%)
Not Success	41 (27.2%)	25 (16.2%)
Treatment difference in symptom success rate		
8 Weeks Regimen - 2 Weeks Regimen	10.9%	
95% CI	1.7%, 20.1%	
P value	0.0258	

Note: The denominator of percentage is N.
Note: Fisher's exact test compared the symptom success rate between the 2 treatment regimens after 24 weeks of follow-up.
Note: Success is defined as patients who relieved after 8 weeks or 2 weeks esomeprazole treatment, and also get symptom controlled during maintenance treatment / follow up period.
Souce: Table 14.2.2.1.

Time to First Relapse

There were 59 (43.4%) patients with symptom relapse in 8 weeks regimen while there were 80 (63.5%) patients in 2 weeks regimen (Table 14 and Figure 1). Log-rank test showed a p-value=0.0003 that it evidently takes a longer time for first symptom to relapse in the 8 weeks regimen than that of the 2 weeks regimen. There were 80 (63.5%) and 59 (43.4%) patients having relapse for 2 weeks regimen and 8 weeks regimen respectively, with 46（37%）and 77(57%) censored cases in 2 weeks regimen and 8 weeks regimen respectively at the end of study without symptom relapse during study in MITT. Hazard ratio of 0.543 was estimated from Cox hazard model favouring 8 regimen group. Analysis on MITT-PP is on Table 14.2.3.2 and Figure 14.2.3.4 showing a similar result.

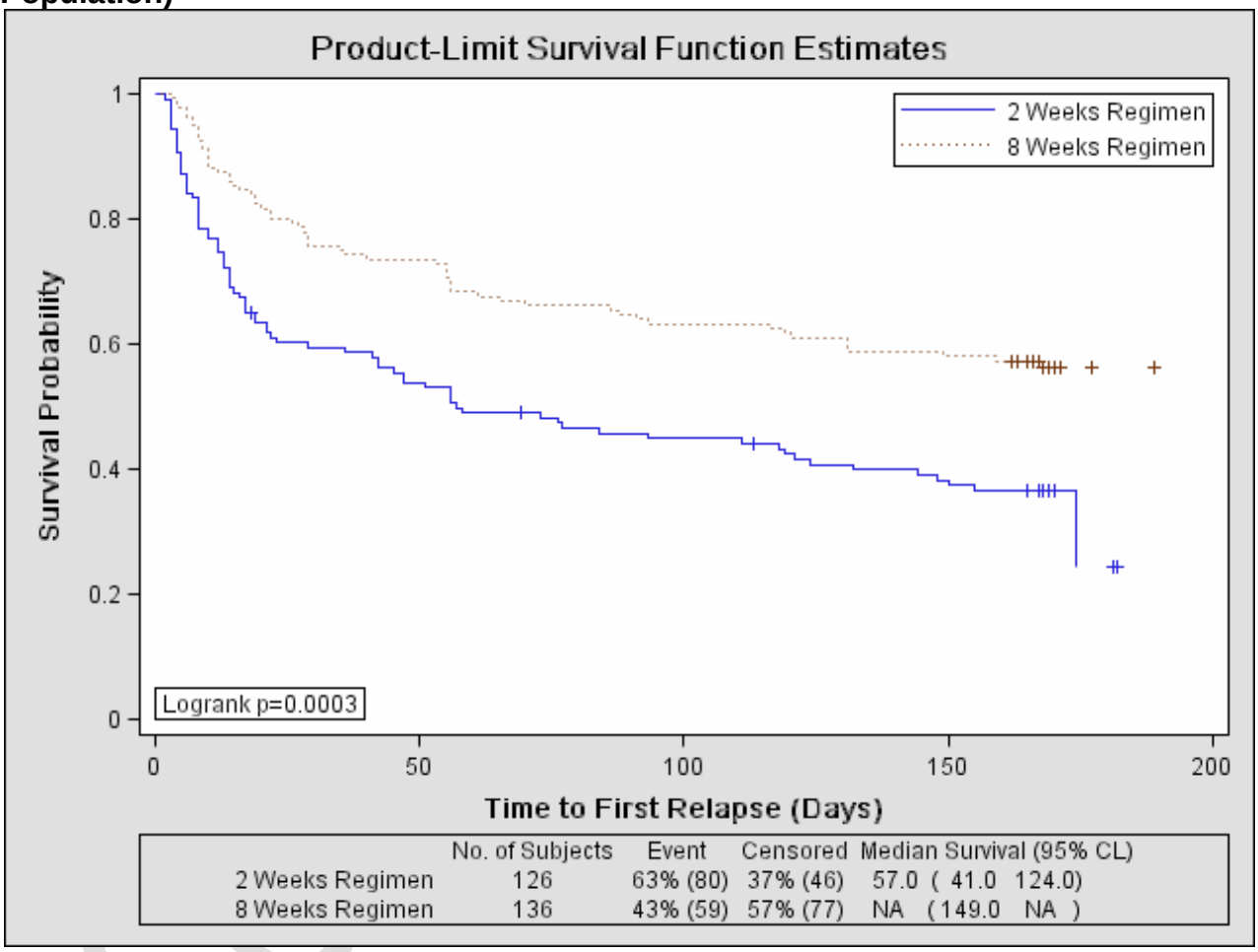
Table 14. Time to First Relapse (MITT Population)

	2 Weeks Regimen (N=126)	*8 Weeks Regimen (N=136)*
No. of patients with relapse	80 (63.5%)	59 (43.4%)
No. of patients censored	46 (36.5%)	77 (56.6%)
Kaplan-Meier estimate of relapse free duration (days)		
Minimum*	2	3
25% percentile (95% CI)	12.0 (8.0 , 17.0)	35.5 (22.0 , 65.0)
Median (95% CI)	57.0 (41.0 , 124.0)	NA (149.0 , NA)
75% percentile (95% CI)	174.0 (174.0 , NA)	NA (NA , NA)
Maximum*	174	168
Relapse free rate		
8 weeks relapse free rate (95% CI)	0.506 (0.419, 0.594)	0.684 (0.606, 0.762)
Relapse free rate difference (8 weeks regimen - 2 weeks regimen) (95% CI)	0.178 (0.060, 0.295)	
Rate difference p value	0.0030	
16 weeks relapse free rate (95% CI)	0.441 (0.354, 0.528)	0.632 (0.551, 0.713)
Relapse free rate difference (8 weeks regimen - 2 weeks regimen) (95% CI)	0.191 (0.072, 0.310)	
Rate difference p value	0.0016	
24 weeks relapse free rate (95% CI)	0.366 (0.281, 0.451)	0.563 (0.479, 0.647)
Relapse free rate difference (8 weeks regimen - 2 weeks regimen) (95% CI)	0.197 (0.078, 0.317)	
Rate difference p value	0.0012	
Hazard Ratio (95% CI)		0.543 (0.388, 0.761)
Log-Rank Test		
p-Value		0.0003

* Minimum and maximum only applies to patients with relapse.
Note: The denominator of percentage is N.
Note: Time to first relapse is from the last dose during the treatment period to date of first time patient comes to the investigator due to symptom recur and need for treatment.
Note: Relapse free rate was estimated from survival analysis.

Note: Log-Rank Test compared the relapse free survival function between the 2 treatment regimens.
Note: Unadjusted HR (Hazard Ratio) from COX model with treatment as the only explanatory factor. HR < 1.0 favors 8 weeks regimen.
Source: Table 14.2.3.1.
Note: For subject data listing refer to Listing 16.2.6.3.

Figure 1. Time to First Relapse Survival Curve - Kaplan-Meier Method (MITT Population)



Source: Figure 14.2.3.3.

Symptom Control Rate 8 and 16 Weeks on Follow-up

See Table 12 for MITT and Table 14.2.1.2 for MITT-PP population with similar results that the 8 weeks regimen had a consistent better symptom control over the 2 weeks regimen.

Symptom Relief Rate in 2 Treatment Regimen

The symptom relief rate is summarized in Table 15 for ITT population. There were 136(88.3%) patients in 8 weeks regimen and 126(83.4%) in 2 weeks regimen respectively and the difference is not statistically significant (p-value=0.2513). Analysis on ITT-PP population is on Table 14.2.4.2 showing a result with a similar but stronger tendency.

Table 15. Symptom Relief Rate in 2 Treatment Regimen (ITT Population)

	2 Weeks Regimen (N=151)	*8 Weeks Regimen (N=154)*
Relieved	126(83.4%)	136(88.3%)
Not Relieved	25 (16.6%)	18 (11.7%)
Treatment difference in symptom relief rate		
8 Weeks Regimen - 2 Weeks Regimen	4.9%	
95% CI	-2.9%, 12.7%	
P value	0.2513	

Note: The denominator of percentage is N.
Note: Fisher's exact test compared the symptom success rate between the 2 treatment regimens after 24 weeks of follow-up.
Note: Symptom relief is defined as no more than 1 day of mild symptoms of GERD during previous 7 days after 8 weeks or 2 weeks of treatment.
Source: Table 14.2.4.1.

Symptom Relief Rate after 2 Weeks and 8 Weeks in 8 Weeks Treatment Regimen Group

Within the 8 weeks regimen, there were 84 (54.5%) patients with symptom relieved at 2 weeks and 136 (88.3%) at 8 weeks during treatment period (Table 16). The analysis on ITT-PP population is on Table 14.2.5.2 with a similar result.

Table 16. Symptom Relief Rate after 2 Weeks and 8 Weeks in 8 Weeks Treatment Regimen Group (ITT Population)

	8 Weeks Regimen (N=154)
2 weeks	
No. of patients with symptom relieved	84 (54.5%)
No. of patients with symptom not relieved	70 (45.5%)
8 weeks	
No. of patients with symptom relieved	136(88.3%)
No. of patients with symptom not relieved	18 (11.7%)
Difference comparison of symptom relief rate	
8 weeks - 2 weeks	33.8%
95% CI	24.4%, 43.1%
P value	< 0.0001

Note: The denominator of percentage is N.
Note: Fisher's exact test compared the symptom relief rate between 2 weeks and 8 weeks of treatment period in 8 weeks regimen.
Note: Symptom relief is defined as no more than 1 day of mild symptoms of GERD during previous 7 days after 8 weeks or 2 weeks of treatment.
Source: Table 14.2.5.1

Number of Unscheduled Hospital Visit

The number of patients with unscheduled hospital visits are summarized in Table 17 for MITT population, where there are 59 (43.4%) for the 8 weeks regimen and 80 (63.5%) for 2 weeks regimen. The comparison of proportion of patients with unscheduled visits between 2 regimen showed a statistical significance with p-value of 0.0013. By the weighted least square regression the estimated number of unscheduled visits per patient were 1.4841 and 0.8529 for 2 weeks regimen and 8 weeks regimen respectively and a statistical significance was shown (p-value 0.0009) in comparison. A similar table is shown in Table 14.2.6.2 for MITT-PP population.

Table 17. Total Number of Unscheduled Hospital Visits during 24 Weeks of Follow-Up (MITT Population)

	2 Weeks Regimen (N=126)	*8 Weeks Regimen (N=136)*	*Total (N=262)*
Number of patients with unscheduled visit(s)	80 (63.5%)	59 (43.4%)	139(53.1%)
Number of patients without unscheduled visit(s)	46 (36.5%)	77 (56.6%)	123(46.9%)
Difference in the proportion of patients with unscheduled			
8 Weeks Regimen - 2 Weeks Regimen	-20.1%		
95% CI	-31.9%, -8.3%		
P value (Fisher's exact test)	0.0013		
Total number of unscheduled visit(s)			
0	46 (36.5%)	77 (56.6%)	123(46.9%)
1	30 (23.8%)	31 (22.8%)	61 (23.3%)
2	24 (19.0%)	14 (10.3%)	38 (14.5%)
3	12 (9.5%)	7 (5.1%)	19 (7.3%)
4	6 (4.8%)	3 (2.2%)	9 (3.4%)
5	3 (2.4%)	2 (1.5%)	5 (1.9%)
6	3 (2.4%)	1 (0.7%)	4 (1.5%)
8	2 (1.6%)	1 (0.7%)	3 (1.1%)
Estimated number of unscheduled visits per patient	1.4841	0.8529	
P value	0.0009		

Note: The denominator of percentage is N.
Note: Regimen comparison of the proportion of patients with unscheduled hospital visit is performed with Fisher's exact test, and the number of unscheduled visits per patient was modeled by weighted least square regression using regimen as the only predictor.
Source: Table 14.2.6.1.

Proportion of Patient Satisfaction

The proportion of patients with satisfaction after 24 weeks of follow-up in the 8 weeks regimen was 100% while that of the 2 weeks regimen was 96% with p-value of 0.0247 (Table 18) favoring 8 weeks regimen. Proportion of very satisfied after 24 weeks of follow-up were 24.6% and 48.5% for 2 weeks regimen and 8 weeks regimen respectively and Fisher exact test showed a strong statistical significance (p-value 0.0001) favoring 8 weeks regimen. A similar MITT-PP results are shown in Table 14.2.7.2.

Table 18. Proportion of Patient Satisfaction during Follow-Up (MITT Population)

	2 Weeks Regimen (N=126)	*8 Weeks Regimen (N=136)*	*Total (N=262)*	*Fisher Exact Test p-Value*
Satisfied				
After 8 weeks	114(90.5%)	133(97.8%)	247(94.3%)	0.0148
After 16 weeks	111(88.1%)	133(97.8%)	244(93.1%)	0.0025
After 24 weeks	121(96.0%)	136(100.0%)	257(98.1%)	0.0247
Very satisfied				
After 8 weeks	26 (20.6%)	69 (50.7%)	95 (36.3%)	< 0.0001
After 16 weeks	33 (26.2%)	63 (46.3%)	96 (36.6%)	0.0008
After 24 weeks	31 (24.6%)	66 (48.5%)	97 (37.0%)	0.0001

Note: The denominator of percentage is N.
Note: Satisfied - satisfaction score of 1-4 while very satisfied - satisfaction score of 1-2.
Source: Table 14.2.7.1.

9. SAFETY EVALUATION

9.1 Brief Summary of Safety Data

The drug exposure of 2 treatment regimen were different. No SAEs or deaths were observed. Summary of DAEs showed more cases of DAEs of GI in 8 weeks regimen than that of 2 weeks regimen. Otherwise DAEs of the 2 treatment regimen were not remarkable with one case DAE of blurred vision, back pain, dysuria and cough respectively during study.

9.2 Extent of Exposure

In the Safety population, the treatment duration(days) is summarized in Table 19.1 for 2 treatment regimens respectively for treatment period. Since the 2 treatment regimen had 2 weeks regimen and 8 weeks regimen respectively and cannot be compared, mean duration in days are still presented for the 2 treatment regimen in Table 19.

Table 19.1 Summary of Study Drug Exposure in Treatment Period (Safety Population)

	2 Weeks Regimen (N=151)	8 Weeks Regimen (N=154)
Treatment duration (days)		
n	151	154
Mean(SD)	13.9(0.99)	52.8(10.86)
Median	14	56
Min	2	4
Max	14	56

Note: Treatment duration (days) = Last dosing date - First dosing date + 1.
Treatment duration in treatment period longer than 14 days for 2 weeks regimen, or longer than 56 days for 8 weeks regimen were hardcoded to 14 days and 56 days respectively for the 2 treatment regimen.
Source: Table 14.3.1.

Summary of drug exposure in maintenance phase is presented in Table 19.2 for MITT population where 79(62.7%) of patients in 2 weeks regimen and 58(42.6%) in 8 weeks regimen received Osomeprazole respectively. Higher percentage in 2 weeks regimen received esomeprazole during the maintenance period. Fisher exact test was conducted to compare the reat and p-value of 0.0013 was obtained. Average days of treatment duration in maintenance phase for nonzero data were 36.7 and 49.7 respectively for 2 weeks regimen and 8 weeks regimen. There was averagely longer treatment duration in 8 weeks regimen than 2 weeks regimen for patients who received esomeprazole during the maintenance period. P-value of the comparison between the 2 means was 0.0093.

Table 19.2 Summary of Study Drug Exposure in Maintenance/Follow-Up Phase (MITT population)

	2 Weeks Regimen (N=126)	*8 Weeks Regimen (N=136)*	*Total (N=262)*
No. of patients with treatment	79 (62.7%)	58 (42.6%)	137(52.3%)
No. of patients without treatment	47 (37.3%)	78 (57.4%)	125(47.7%)
Difference in the proportion of Patients			

without treatment			
8 Weeks Regimen - 2 Weeks			20.1%
95% CI			8.2%, 31.9%
P value (Fisher's exact test)			0.0013
Treatment duration (days) for nonzero data			
n	79	58	137
Mean(SD)	36.7(24.96)	49.7(32.77)	42.2(29.14)
Median	28	42	28
Min	14	7	7
Max	124	135	135
Mean difference (8 weeks-2weeks)			13.0
95% CI			3.3, 22.8
P value (student t test)			0.0093

Note: Treatment duration (days) is a few segments summed up together, date of last dose - date of first dose + 1 for each segment(in maintenance phase). Denominator of percentage is N.
Source: Table 14.3.1.a1.

The study drug exposure in whole study duration for the safety population is summarized in Table 19.3 where the average treatment duration for 2 weeks regimen was 33.1 days while that for the 8 weeks regimen 71.5. Percentage of days with treatment for 8 weeks regimen was 35.2% and that for 2 weeks regimen 21.6%.

Table 19.3 Summary of Study Drug Exposure in Whole Study Duration (Safety Population)

	2 Weeks Regimen (N=151)	*8 Weeks Regimen (N=154)*	*Total (N=305)*
Treatment duration (days)			
n	151	154	305
Mean(SD)	33.1(25.82)	71.5(34.88)	52.5(36.21)
Median	28	56	56
Min	2	4	2
Max	138	191	191
Total No. of days with treatment	5001	11018	16019
Total No. of days in whole study duration	23103	31274	54377
Percentage of days with treatment	21.6%	35.2%	29.5%

Note: Treatment duration (days) is a few segments summed up together, date of last dose - date of first dose + 1 for each segment. First segment is treatment period, rest segments is in maintenance phase.
Treatment duration in treatment period longer than 14 days for 2 weeks regimen, or longer than 56 days for 8 weeks regimen were hardcoded to 14 days and 56 days respectively for the 2 treatment regimen.
Total No. of days with treatment is the number of days for the treatment duration defined above summed up for the patients of the regimen.
Total No. of days in whole study duration is summation of date of end of study - date of randomization visit + 1, for the patients of the regimen.
Source: Table 14.3.1.a2.

9.3 Adverse Events

AE: Any untoward medical occurrence in a patient or clinical investigation subject occurring following or during exposure to study medication until last follow-up visit. Only DAE and SAE were captured and reported.

9.3.1 Brief Summary of Adverse Events

Only SAEs and DAEs were captured and reported. There were no observed SAEs during the trial. AEs leading to discontinuation of study medication are summarized in Table 20 with AE listing in Listing 16.2.7. There were more cases of DAEs of GI in 8 weeks regimen than that of 2 weeks regimen. Otherwise DAEs of the 2 treatment regimen were not remarkable.

9.3.2 Display of Adverse Events

Adverse events leading to study medication discontinuation experienced in patients by SOC and preferred term are summarized in Table 20 and the relationship with the study medication summarized in Table 21. Adverse events are summarized for the Safety Set by MedDRA dictionary. There were 2 moderate cases and 3 mild cases in the 8 weeks regimen while only 1 moderate case in the 2 weeks regimen. There were 3 cases of AEs related to study medication and 2 cased unrelated. See CSR.

Table 20. Table 14.3.3.2 Adverse Event(s) Leading to Discontinuation of Study Medication by System Organ Class and Preferred Term (Safety Population)

	2 Weeks Regimen (N=151)			*8 Weeks Regimen (N=154)*			*Total (N=305)*		
	Mild	*Moderate*	*Severe*	*Mild*	*Moderate*	*Severe*	*Mild*	*Moderate*	*Severe*
Patients with at least one AE	0	1 (0.7%)	0	3 (1.9%)	2 (1.3%)	0	3 (1.0%)	3 (1.0%)	0
Gastrointestinal disorders	0	0	0	2 (1.3%)	2 (1.3%)	0	2 (0.7%)	2 (0.7%)	0
Nausea	0	0	0	1 (0.6%)	1 (0.6%)	0	1 (0.3%)	1 (0.3%)	0
Abdominal discomfort	0	0	0	1 (0.6%)	0	0	1 (0.3%)	0	0
Constipation	0	0	0	0	1 (0.6%)	0	0	1 (0.3%)	0
Frequent bowel movements	0	0	0	1 (0.6%)	0	0	1 (0.3%)	0	0
Eye disorders	0	0	0	1 (0.6%)	0	0	1 (0.3%)	0	0
Vision blurred	0	0	0	1 (0.6%)	0	0	1 (0.3%)	0	0
Musculoskeletal and connective tissue disorders	0	1 (0.7%)	0	0	0	0	0	1 (0.3%)	0
Back pain	0	1 (0.7%)	0	0	0	0	0	1 (0.3%)	0
Renal and urinary disorders	0	1 (0.7%)	0	0	0	0	0	1 (0.3%)	0
Dysuria	0	1 (0.7%)	0	0	0	0	0	1 (0.3%)	0
Respiratory, thoracic and mediastinal disorders	0	0	0	0	1 (0.6%)	0	0	1 (0.3%)	0

Cough	0	0	0	0	1 (0.6%)	0	0	1 (0.3%)	0

Note: One patient was counted at most once per category. Denominator of percentage is N. Discontinuation :Permanent Discontinuation. One patient may be counted in multiple categories. The most severe one was counted for the same symptom if it occurs more than once.
Source: Table 14.3.3.2.

Table 21. Relationship of Adverse Event(s) Leading to Discontinuation of Study Medication by System Organ Class and Preferred Term (Safety Population)

	2 Weeks Regimen		*8 Weeks Regimen*		*Total*	
	(N=151)		*(N=154)*		*(N=305)*	
	Related	*Not Related*	*Related*	*Not Related*	*Related*	*Not Related*
Patients with at least one AE	0	1 (0.7%)	3 (1.9%)	2 (1.3%)	3 (1.0%)	3 (1.0%)
Gastrointestinal disorders	0	0	3 (1.9%)	1 (0.6%)	3 (1.0%)	1 (0.3%)
Nausea	0	0	1 (0.6%)	1 (0.6%)	1 (0.3%)	1 (0.3%)
Abdominal discomfort	0	0	1 (0.6%)	0	1 (0.3%)	0
Constipation	0	0	1 (0.6%)	0	1 (0.3%)	0
Frequent bowel movements	0	0	1 (0.6%)	0	1 (0.3%)	0
Eye disorders	0	0	0	1 (0.6%)	0	1 (0.3%)
Vision blurred	0	0	0	1 (0.6%)	0	1 (0.3%)
Musculoskeletal and connective tissue disorders	0	1 (0.7%)	0	0	0	1 (0.3%)
Back pain	0	1 (0.7%)	0	0	0	1 (0.3%)
Renal and urinary disorders	0	1 (0.7%)	0	0	0	1 (0.3%)
Dysuria	0	1 (0.7%)	0	0	0	1 (0.3%)
Respiratory, thoracic and mediastinal disorders	0	0	0	1 (0.6%)	0	1 (0.3%)
Cough	0	0	0	1 (0.6%)	0	1 (0.3%)

Note: One patient was counted at most once per category. Denominator of percentage is N.
Discontinuation: Permanent Discontinuation

Individual patient data listings of AEs can be found in Listing 16.2.7

9.4 Deaths, Other Serious Adverse Events

9.4.1 Deaths

No deaths occurred during the study.

9.4.2 Other Serious Adverse Events

There were no SAEs reported in the trial.

9.5 Clinical Laboratory Evaluation

Hematology, chemistry and urinalysis were performed only at screening visit and results are summarized in Table 14.3.4, 14.3.5 and 14.3.6.

9.6 Vital Signs, Physical Findings, and Other Observations Related to Safety

9.6.1 Shift of Vital Signs

Vital signs were performed only at screening visit and the result is summarized in Table 4. Listing of data can be found in Listing 16.2.9.1.

9.6.2 Physical Examination

Physical examination was performed at screening visit only and the findings is summarized for Safety Set in Table 14.3.7. Listing of the findings can be found in Listing 16.2.9.2.

9.6.3 Other Observations Related to Safety

Not applicable.

9.7 Safety Conclusions

See CSR.

10. OVERALL STATISTICAL CONCLUSIONS

This was a randomized, open-labeled, 2 or 8 weeks treatment regimen of esomeprazole followed by 24 weeks of follow-up period in the patients of co-diagnosed of NERD and chronic gastritis. The hypothesis of the trial was that 8 weeks treatment regimen had a better control of symptoms in 24 weeks of follow-up period than that of 2 weeks treatment regimen. This trial was conducted in 305 randomized patients with 1:1 regimen ratio, in 10 centers.

Controlled patients were defined as patients with all the items ≤1 in A and C category (Questions 1,2, 5 and 6) of GerdQ and the primary analysis population MITT was defined as randomized patients whose symptoms relieved after 8 weeks or 2 weeks esomeprazole treatment, regardless of patient entrance into maintenance period. The primary analysis on the control rate at 24 weeks follow-up visit demonstrated a statistical significance between the 2 treatment regimen (p-value 0.0473), indicating that the 8 weeks esomeprazole treatment regimen likely has a better control rate in follow-up period than that of 2 weeks treatment regimen. The both 8 weeks and 16 weeks follow-up control rates have consistently shown a better control rate in the 8 weeks treatment

regimen. The analyses on secondary endpoints including success rate at 8, 16, and 24 weeks follow-up visit, time to first symptom relapse, number of unscheduled hospital visits, and satisfaction proportion between the 2 treatment regimen are all supportive to the conclusion of better symptom control in follow-up period for 8 weeks treatment regimen.

Patients in this trial had a high compliance reflecting a good exposure with the treatment in both treatment regimen.

No SAEs or death were reported during the study.

The AEs leading to treatment discontinuation are summarized and the 8 weeks regimen had a few more mild/moderate cases of the AEs relating GI than that of the 2 weeks regimen.

The 8 weeks treatment regimen seems more effective in relieving GERD symptoms during maintenance period than the 2 weeks treatment regimen from this study. However the price of the benefit is with 6 weeks longer drug exposure, with possibly unknown safety concern for patients, apart from th e additional cost of esomeprazole.

More details are given in the CSR.

The source of bias of this study may have included the following. This study was designed as an open-label study which potentially allowed analysis approach/SAP to be modified along the open-labeled live data collection. In addition, the primary efficacy endpoint of this study was of subjective assessment from patient self-reported outcome on GERD questionnaire. It is also worth noting that the patients were allowed different strategy of esomeprazole rescue use in the maintenance period, which might have confounded the effectiveness of esomeprazole whose effect was supposed to carry over from its use in treatment period.

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13. REFERENCE LIST

Not applicable.