

**Clinical trial results:**

**A Randomized Double-blind, Double Dummy, Active Comparator-controlled Dose-finding Study in Patients With Erosive Esophagitis Due to Gastro-esophageal Reflux Disease (GERD) Los Angeles Grade C or D, and Patients With at Least Partial Symptom Response But Endoscopically Still Unhealed After 8 Weeks History of Standard Treatment Healing Course With Proton-pump Inhibitor (PPI), to Investigate Safety, Tolerability, and Healing Rates After 4 Weeks Treatment of X842 or Lansoprazole, and Symptom Pattern During Subsequent 4 Weeks Treatment With Lansoprazole**

**Summary**

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2020-003319-91    |
| Trial protocol           | HU CZ BG          |
| Global end of trial date | 01 September 2022 |

**Results information**

|                                |                   |
|--------------------------------|-------------------|
| Result version number          | v1                |
| This version publication date  | 15 September 2023 |
| First version publication date | 15 September 2023 |

**Trial information****Trial identification**

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | CX842A2201 |
|-----------------------|------------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT05055128 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Cinclus Pharma AG  |
| Sponsor organisation address | Gartenstrasse 101, Basel, Switzerland,   |
| Public contact               | Kajsa Larsson, Cinclus Pharma AG, +46 706750128, kajsa.larsson@cincluspharma.com |
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Notes:

**Paediatric regulatory details**

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 30 May 2023       |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 01 September 2022 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 01 September 2022 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

Determine the safety and tolerability of X842 after single and multiple oral dose administration in healthy subjects

Protection of trial subjects:

This study was performed in accordance with the protocol and ethical principles that have their origin in the Declaration of Helsinki (version 2013, 7th revision) and are consistent with ICH/GCP E6 (R2), EU Clinical Trials Directive, and applicable local regulatory requirements. Before performing any study related procedures, the ICF was signed and personally dated by the patient (or their legally acceptable representative and/or witness, as applicable) and by the Investigator.

Background therapy: -

Evidence for comparator: -

|   |                |
|---|----------------|
| Actual start date of recruitment                          | 11 August 2021 |
| Long term follow-up planned                               | No             |
| Independent data monitoring committee (IDMC) involvement? | Yes            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | United States: 2 |
| Country: Number of subjects enrolled | Ukraine: 10      |
| Country: Number of subjects enrolled | Bulgaria: 87     |
| Country: Number of subjects enrolled | Czechia: 1       |
| Country: Number of subjects enrolled | Georgia: 77      |
| Country: Number of subjects enrolled | Hungary: 17      |
| Country: Number of subjects enrolled | Poland: 51       |
| Country: Number of subjects enrolled | Serbia: 3        |
| Worldwide total number of subjects   | 248              |
| EEA total number of subjects         | 156              |

Notes:

### Subjects enrolled per age group

|          |   |
|----------|---|
| In utero | 0 |
|----------|---|

|   |     |
|---|-----|
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 197 |
| From 65 to 84 years                       | 51  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

This study was conducted at 36 centers which included 248 patients across 08 countries. The trial began on 11 Aug 2021 (first patient enrolled) and was completed on 01 Sep 2022 (Last patient completed).

### Pre-assignment

Screening details:

The pre-treatment assessments were performed during the screening period (Day -7 to Day 0) prior to the first dose preferably. All the study assessments were performed as per the schedule of assessments.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Double blind                   |
| Roles blinded                | Subject, Investigator          |

Blinding implementation details:

Due to tool limitations the double-blind period and open-label arms were presented here under the overall study period.

### Arms

|                              |                                      |
|------------------------------|--------------------------------------|
| Are arms mutually exclusive? | Yes                                  |
| <b>Arm title</b>             | X842 25 mg BID (Double-blind Period) |

Arm description:

Patients received 2 tablets (X842 25 mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning and 2 tablets (X842 25 mg+ X842 dummy) in the evening.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | X842         |
| Investigational medicinal product code | X842         |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Patients received 2 tablets (X842 25 mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 25 mg + X842 dummy) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.

|  |                    |
|--|--------------------|
| Investigational medicinal product name | Lansoprazole dummy |
| Investigational medicinal product code | Lansoprazole dummy |
| Other name                             |                    |
| Pharmaceutical forms                   | Capsule            |
| Routes of administration               | Oral use           |

Dosage and administration details:

Patients received 2 tablets (X842 25 mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 25 mg + X842 dummy) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.

|  |            |
|--|------------|
| Investigational medicinal product name | X842 dummy |
| Investigational medicinal product code | X842 dummy |
| Other name                             |            |
| Pharmaceutical forms                   | Tablet     |
| Routes of administration               | Oral use   |

Dosage and administration details:

Patients received 2 tablets (X842 25 mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 25 mg + X842 dummy) in the evening during 4-week double-blind

treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.

|   |                                      |
|---|--------------------------------------|
| <b>Arm title</b>  | X842 50 mg BID (Double-blind Period) |
| Arm description:<br>Patients received 2 tablets (X842 50 mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning and 2 tablets (X842 50 mg+ X842 dummy) in the evening.  |                                      |
| Arm type  | Experimental                         |
| Investigational medicinal product name  | X842                                 |
| Investigational medicinal product code  | X842                                 |
| Other name  | X842                                 |
| Pharmaceutical forms  | Tablet                               |
| Routes of administration  | Other use                            |
| Dosage and administration details:<br>Patients received 2 tablets (X842 50 mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 50 mg + X842 dummy) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.   |                                      |
| Investigational medicinal product name  | Lansoprazole dummy                   |
| Investigational medicinal product code  | Lansoprazole dummy                   |
| Other name  |                                      |
| Pharmaceutical forms  | Capsule                              |
| Routes of administration  | Oral use                             |
| Dosage and administration details:<br>Patients received 2 tablets (X842 50 mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 50 mg + X842 dummy) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.   |                                      |
| Investigational medicinal product name  | X842 dummy                           |
| Investigational medicinal product code  | X842 dummy                           |
| Other name  |                                      |
| Pharmaceutical forms  | Tablet                               |
| Routes of administration  | Oral use                             |
| Dosage and administration details:<br>Patients received 2 tablets (X842 50 mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 50 mg + X842 dummy) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.   |                                      |
| <b>Arm title</b>  | X842 75 mg BID (Double-blind Period) |
| Arm description:<br>Patients received 2 tablets (X842 50 mg + X842 25 mg) and 1 capsule (Lansoprazole dummy) in the morning and 2 tablets (X842 50 mg+ X842 25 mg) in the evening.  |                                      |
| Arm type  | Experimental                         |
| Investigational medicinal product name  | Lansoprazole dummy                   |
| Investigational medicinal product code  | Lansoprazole dummy                   |
| Other name  |                                      |
| Pharmaceutical forms  | Capsule                              |
| Routes of administration  | Oral use                             |
| Dosage and administration details:<br>Patients received 2 tablets (X842 50 mg + X842 25 mg) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 50 mg+ X842 25 dummy) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks. |                                      |
| Investigational medicinal product name  | X842                                 |
| Investigational medicinal product code  | X842                                 |
| Other name  |                                      |

|                          |          |
|--------------------------|----------|
| Pharmaceutical forms     | Tablet   |
| Routes of administration | Oral use |

Dosage and administration details:

Patients received 2 tablets (X842 50 mg + X842 25 mg) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 50 mg+ X842 25 dummy) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.

|                  |                                       |
|------------------|---------------------------------------|
| <b>Arm title</b> | X842 100 mg BID (Double-blind Period) |
|------------------|---------------------------------------|

Arm description:

Patients received 2 tablets (X842 50 mg×2) and 1 capsule (Lansoprazole dummy) in the morning and 2 tablets (X842 50 mg×2) in the evening.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | Lansoprazole dummy |
| Investigational medicinal product code | Lansoprazole dummy |
| Other name                             |                    |
| Pharmaceutical forms                   | Capsule            |
| Routes of administration               | Other use          |

Dosage and administration details:

Patients received 2 tablets (X842 50 mg×2) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 50 mg×2) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.

|  |          |
|--|----------|
| Investigational medicinal product name | X842     |
| Investigational medicinal product code | X842     |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

Patients received 2 tablets (X842 50 mg×2) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 50 mg×2) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.

|                  |                                  |
|------------------|----------------------------------|
| <b>Arm title</b> | Lansoprazole (Open-label Period) |
|------------------|----------------------------------|

Arm description:

Patients received 2 tablets (X842 dummy×2) and 1 capsule (Lansoprazole 30 mg) in the morning, and 2 tablets (X842 dummy×2) in the evening

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Lansoprazole      |
| Investigational medicinal product code | Lansoprazole      |
| Other name                             |                   |
| Pharmaceutical forms                   | Capsule           |
| Routes of administration               | Oral use          |

Dosage and administration details:

Patients received 2 tablets (X842 dummy×2) and 1 capsule (Lansoprazole 30 mg) in the morning, and 2 tablets (X842 dummy×2) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.

|  |            |
|--|------------|
| Investigational medicinal product name | X842 dummy |
| Investigational medicinal product code | X842 dummy |
| Other name                             |            |
| Pharmaceutical forms                   | Tablet     |
| Routes of administration               | Oral use   |

Dosage and administration details:

Patients received 2 tablets (X842 dummy×2) and 1 capsule (Lansoprazole 30 mg) in the morning, and 2 tablets (X842 dummy×2) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.

| Number of subjects in period 1 | X842 25 mg BID<br>(Double-blind<br>Period) | X842 50 mg BID<br>(Double-blind<br>Period) | X842 75 mg BID<br>(Double-blind<br>Period) |
|--------------------------------|--|--|--|
| Started                        | 51   | 48   | 52   |
| Completed                      | 45   | 45   | 50   |
| Not completed                  | 6  | 3  | 2  |
| Consent withdrawn by subject   | 5  | 2  | 2  |
| Adverse event, non-fatal       | -  | -  | -  |
| Other                          | 1  | -  | -  |
| Randomized by mistake          | -  | 1  | -  |
| Protocol deviation             | -  | -  | -  |

| Number of subjects in period 1 | X842 100 mg BID<br>(Double-blind<br>Period) | Lansoprazole (Open-<br>label Period) |
|--------------------------------|---|--------------------------------------|
| Started                        | 47  | 50                                   |
| Completed                      | 41  | 47                                   |
| Not completed                  | 6   | 3                                    |
| Consent withdrawn by subject   | 4   | 2                                    |
| Adverse event, non-fatal       | 1   | 1                                    |
| Other                          | -   | -                                    |
| Randomized by mistake          | -   | -                                    |
| Protocol deviation             | 1   | -                                    |

## Baseline characteristics

### Reporting groups

|  |                                       |
|--|---------------------------------------|
| Reporting group title  | X842 25 mg BID (Double-blind Period)  |
| Reporting group description:<br>Patients received 2 tablets (X842 25 mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning and 2 tablets (X842 25 mg+ X842 dummy) in the evening. |                                       |
| Reporting group title  | X842 50 mg BID (Double-blind Period)  |
| Reporting group description:<br>Patients received 2 tablets (X842 50 mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning and 2 tablets (X842 50 mg+ X842 dummy) in the evening. |                                       |
| Reporting group title  | X842 75 mg BID (Double-blind Period)  |
| Reporting group description:<br>Patients received 2 tablets (X842 50 mg + X842 25 mg) and 1 capsule (Lansoprazole dummy) in the morning and 2 tablets (X842 50 mg+ X842 25 mg) in the evening. |                                       |
| Reporting group title  | X842 100 mg BID (Double-blind Period) |
| Reporting group description:<br>Patients received 2 tablets (X842 50 mg×2) and 1 capsule (Lansoprazole dummy) in the morning and 2 tablets (X842 50 mg×2) in the evening.                      |                                       |
| Reporting group title  | Lansoprazole (Open-label Period)      |
| Reporting group description:<br>Patients received 2 tablets (X842 dummy×2) and 1 capsule (Lansoprazole 30 mg) in the morning, and 2 tablets (X842 dummy×2) in the evening                      |                                       |

| Reporting group values                                | X842 25 mg BID<br>(Double-blind<br>Period) | X842 50 mg BID<br>(Double-blind<br>Period) | X842 75 mg BID<br>(Double-blind<br>Period) |
|---|--|--|--|
| Number of subjects                                    | 51   | 48   | 52   |
| Age categorical<br>Units: Subjects                    |  |  |  |
| In utero  | 0  | 0  | 0  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0  | 0  | 0  |
| Newborns (0-27 days)                                  | 0  | 0  | 0  |
| Infants and toddlers (28 days-23<br>months)           | 0  | 0  | 0  |
| Children (2-11 years)                                 | 0  | 0  | 0  |
| Adolescents (12-17 years)                             | 0  | 0  | 0  |
| Adults (18-64 years)                                  | 42   | 41   | 45   |
| From 65-84 years                                      | 9  | 7  | 7  |
| 85 years and over                                     | 0  | 0  | 0  |
| Age continuous<br>Units: years                        |  |  |  |
| arithmetic mean                                       | 48.7                                       | 45.3                                       | 48.7                                       |
| standard deviation                                    | ± 15.99                                    | ± 14.11                                    | ± 14.05                                    |
| Gender categorical<br>Units: Subjects                 |  |  |  |
| Female  | 18   | 19   | 22   |
| Male  | 33   | 29   | 30   |

| Reporting group values | X842 100 mg BID<br>(Double-blind<br>Period) | Lansoprazole (Open-<br>label Period) | Total |
|------------------------|---|--------------------------------------|-------|
|------------------------|---|--------------------------------------|-------|



|   |         |         |     |
|---|---------|---------|-----|
| Number of subjects                                    | 47      | 50      | 248 |
| Age categorical                                       |         |         |     |
| Units: Subjects                                       |         |         |     |
| In utero  | 0       | 0       | 0   |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0       | 0       | 0   |
| Newborns (0-27 days)                                  | 0       | 0       | 0   |
| Infants and toddlers (28 days-23<br>months)           | 0       | 0       | 0   |
| Children (2-11 years)                                 | 0       | 0       | 0   |
| Adolescents (12-17 years)                             | 0       | 0       | 0   |
| Adults (18-64 years)                                  | 31      | 38      | 197 |
| From 65-84 years                                      | 16      | 12      | 51  |
| 85 years and over                                     | 0       | 0       | 0   |
| Age continuous  |         |         |     |
| Units: years  |         |         |     |
| arithmetic mean                                       | 54.8    | 49.1    |     |
| standard deviation                                    | ± 13.26 | ± 15.41 | -   |
| Gender categorical                                    |         |         |     |
| Units: Subjects                                       |         |         |     |
| Female  | 17      | 20      | 96  |
| Male  | 30      | 30      | 152 |

## End points

### End points reporting groups

|  |                                       |
|--|---------------------------------------|
| Reporting group title  | X842 25 mg BID (Double-blind Period)  |
| Reporting group description:<br>Patients received 2 tablets (X842 25 mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning and 2 tablets (X842 25 mg+ X842 dummy) in the evening. |                                       |
| Reporting group title  | X842 50 mg BID (Double-blind Period)  |
| Reporting group description:<br>Patients received 2 tablets (X842 50 mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning and 2 tablets (X842 50 mg+ X842 dummy) in the evening. |                                       |
| Reporting group title  | X842 75 mg BID (Double-blind Period)  |
| Reporting group description:<br>Patients received 2 tablets (X842 50 mg + X842 25 mg) and 1 capsule (Lansoprazole dummy) in the morning and 2 tablets (X842 50 mg+ X842 25 mg) in the evening. |                                       |
| Reporting group title  | X842 100 mg BID (Double-blind Period) |
| Reporting group description:<br>Patients received 2 tablets (X842 50 mg×2) and 1 capsule (Lansoprazole dummy) in the morning and 2 tablets (X842 50 mg×2) in the evening.                      |                                       |
| Reporting group title  | Lansoprazole (Open-label Period)      |
| Reporting group description:<br>Patients received 2 tablets (X842 dummy×2) and 1 capsule (Lansoprazole 30 mg) in the morning, and 2 tablets (X842 dummy×2) in the evening                      |                                       |

### Primary: Number of Patients With Esophageal Mucosa Healing

|  |  |
|--|--|
| End point title  | Number of Patients With Esophageal Mucosa Healing <sup>[1]</sup> |
| End point description:<br>The healing of erosive esophagitis due to gastro-esophageal reflux disease (GERD) was assessed. It supported the dose selection LG, through the assessment of healing of erosive esophagitis due to GERD based on endoscopic assessment after 4 weeks of treatment. The dose that would lead to having 85% of the patients have esophageal mucosa healing after 4 weeks of treatment. The full analysis set (FAS) consisted of all patients who had been randomized and received at least 1 dose of study drug. FAS erosive is a subset of FAS consisted of patients who had been classified as erosive (Grade A, B, C or D) as screening according to the central reading or imputed by local reading if missing. |  |
| End point type   | Primary  |
| End point timeframe:<br>Week 4   |  |

#### Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There were no statistical analysis performed for this endpoint.

| End point values            | X842 25 mg BID (Double-blind Period) | X842 50 mg BID (Double-blind Period) | X842 75 mg BID (Double-blind Period) | X842 100 mg BID (Double-blind Period) |
|-----------------------------|--------------------------------------|--------------------------------------|--------------------------------------|---------------------------------------|
| Subject group type          | Reporting group                      | Reporting group                      | Reporting group                      | Reporting group                       |
| Number of subjects analysed | 38                                   | 37                                   | 41                                   | 33                                    |
| Units: Participants         | 28                                   | 28                                   | 32                                   | 18                                    |

|                  |              |  |  |  |
|------------------|--------------|--|--|--|
| End point values | Lansoprazole |  |  |  |
|------------------|--------------|--|--|--|

|                             |                     |  |  |  |
|-----------------------------|---------------------|--|--|--|
|                             | (Open-label Period) |  |  |  |
| Subject group type          | Reporting group     |  |  |  |
| Number of subjects analysed | 33                  |  |  |  |
| Units: Participants         | 20                  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Patients With Adverse Events (AEs)

|                 |  |
|-----------------|--|
| End point title | Number of Patients With Adverse Events (AEs) |
|-----------------|--|

End point description:

Safety and tolerability of 4 doses of LG and Lansoprazole were evaluated, where LAN served as the active comparator. TEAE-Treatment-emergent adverse event, ADR-Adverse drug reaction, SAE-Serious adverse event, and AESI-Adverse events of special interest. The safety analysis set consisted of all patients who had been randomized and received at least 1 dose of study drug. Patients were analyzed according to the treatment actually received.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Screening (Day -7 to Day 0) until Week 8

| End point values                          | X842 25 mg<br>BID (Double-blind Period) | X842 50 mg<br>BID (Double-blind Period) | X842 75 mg<br>BID (Double-blind Period) | X842 100 mg<br>BID (Double-blind Period) |
|---|---|---|---|--|
| Subject group type                        | Reporting group                         | Reporting group                         | Reporting group                         | Reporting group                          |
| Number of subjects analysed               | 51                                      | 48                                      | 52                                      | 47                                       |
| Units: Participants                       |   |   |   |  |
| Any AE                                    | 15                                      | 10                                      | 12                                      | 11                                       |
| Any TEAE                                  | 14                                      | 10                                      | 12                                      | 11                                       |
| Any severe TEAE                           | 1                                       | 0                                       | 0                                       | 0  |
| Any treatment related TEAE (ADR)          | 4                                       | 2                                       | 0                                       | 2  |
| Any TEAE leading to study discontinuation | 1                                       | 0                                       | 0                                       | 1  |
| Any SAE                                   | 1                                       | 0                                       | 1                                       | 0  |
| Any Serious TEAE                          | 1                                       | 0                                       | 1                                       | 0  |
| Any treatment emergent AESI               | 0                                       | 0                                       | 0                                       | 0  |

| End point values            | Lansoprazole<br>(Open-label Period) |  |  |  |
|-----------------------------|-------------------------------------|--|--|--|
| Subject group type          | Reporting group                     |  |  |  |
| Number of subjects analysed | 50                                  |  |  |  |
| Units: Participants         |                                     |  |  |  |
| Any AE                      | 10                                  |  |  |  |
| Any TEAE                    | 10                                  |  |  |  |
| Any severe TEAE             | 0                                   |  |  |  |

|   |   |  |  |  |
|---|---|--|--|--|
| Any treatment related TEAE (ADR)          | 2 |  |  |  |
| Any TEAE leading to study discontinuation | 0 |  |  |  |
| Any SAE                                   | 0 |  |  |  |
| Any Serious TEAE                          | 0 |  |  |  |
| Any treatment emergent AESI               | 0 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Heartburn-Free 24-hour Days

|  |   |
|--|---|
| End point title  | Percentage of Heartburn-Free 24-hour Days |
| End point description:   |   |
| Heartburn-free in a 24-hour day was defined as a day where the patient reported having no burning feeling or pain behind the breast or in the center of the upper stomach (score of 0) for both morning and evening. The percentage of heartburn-free 24-hour days based on eDiary (Reflux Symptom Questionnaire electronic Diary: RESQ-eDiary) was evaluated. The reflux-related symptom pattern was evaluated during the initial 4 weeks of treatment with four dose levels of LG and with Lansoprazole, and the symptom pattern during the subsequent additional 4 weeks (Weeks 5-8) of open-label treatment with Lansoprazole. Modified RESQ-eDiary was a validated self-reported questionnaire electronic symptom diary. mRESQ-eD has 3 domains [i.e. Heartburn (min-max: 0-10), Other GERD signs/symptoms (min-max: 0-15) and Regurgitations/Reflux (min-max: 0-8)]. The FAS consisted of all patients who had been randomized and received at least 1 dose of study drug. |   |
| End point type   | Secondary                                 |
| End point timeframe:   |   |
| Weeks 1 and 8  |   |

| End point values                     | X842 25 mg BID (Double-blind Period) | X842 50 mg BID (Double-blind Period) | X842 75 mg BID (Double-blind Period) | X842 100 mg BID (Double-blind Period) |
|--------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|---------------------------------------|
| Subject group type                   | Reporting group                      | Reporting group                      | Reporting group                      | Reporting group                       |
| Number of subjects analysed          | 51                                   | 48                                   | 52                                   | 47                                    |
| Units: Percentage of days            |                                      |                                      |                                      |                                       |
| arithmetic mean (standard deviation) |                                      |                                      |                                      |                                       |
| Week 1 (n=48, 46, 51, 46, 48)        | 27.0 (± 5.80)                        | 25.1 (± 5.91)                        | 29.2 (± 5.56)                        | 26.1 (± 5.86)                         |
| Week 8 (n=31, 34, 34, 29, 32)        | 82.4 (± 6.59)                        | 73.8 (± 6.51)                        | 78.6 (± 6.19)                        | 72.2 (± 6.78)                         |

| End point values                     | Lansoprazole (Open-label Period) |  |  |  |
|--------------------------------------|----------------------------------|--|--|--|
| Subject group type                   | Reporting group                  |  |  |  |
| Number of subjects analysed          | 50                               |  |  |  |
| Units: Percentage of days            |                                  |  |  |  |
| arithmetic mean (standard deviation) |                                  |  |  |  |
| Week 1 (n=48, 46, 51, 46, 48)        | 19.1 (± 5.68)                    |  |  |  |
| Week 8 (n=31, 34, 34, 29, 32)        | 59.2 (± 6.48)                    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of at Most-mild Heartburn 24-hour Days

|                 |   |
|-----------------|---|
| End point title | Percentage of at Most-mild Heartburn 24-hour Days |
|-----------------|---|

End point description:

Heartburn with at most mild symptoms in a 24-hour day was defined as a day where the patient reported having either no symptoms, very mild symptoms or mild burning feeling or pain behind the breast or in the center of the upper stomach (score between 0-2) for both morning and evening. The FAS consisted of all patients who had been randomized and received at least 1 dose of study drug.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 1 and 8

| End point values                     | X842 25 mg<br>BID (Double-<br>blind Period) | X842 50 mg<br>BID (Double-<br>blind Period) | X842 75 mg<br>BID (Double-<br>blind Period) | X842 100 mg<br>BID (Double-<br>blind Period) |
|--------------------------------------|---|---|---|--|
| Subject group type                   | Reporting group                             | Reporting group                             | Reporting group                             | Reporting group                              |
| Number of subjects analysed          | 51  | 48  | 52  | 47   |
| Units: Percentage of days            |   |   |   |  |
| arithmetic mean (standard deviation) |   |   |   |  |
| Week 1 (n=48, 46, 51, 46, 48)        | 75.3 (± 3.78)                               | 67.9 (± 3.85)                               | 79.4 (± 3.62)                               | 69.7 (± 3.81)                                |
| Week 8 (n=31, 34, 34, 29, 32)        | 98.5 (± 4.34)                               | 96.5 (± 4.27)                               | 95.8 (± 4.08)                               | 97.1 (± 4.46)                                |

| End point values                     | Lansoprazole<br>(Open-label<br>Period) |  |  |  |
|--------------------------------------|--|--|--|--|
| Subject group type                   | Reporting group                        |  |  |  |
| Number of subjects analysed          | 50                                     |  |  |  |
| Units: Percentage of days            |  |  |  |  |
| arithmetic mean (standard deviation) |  |  |  |  |
| Week 1 (n=48, 46, 51, 46, 48)        | 63.1 (± 3.70)                          |  |  |  |
| Week 8 (n=31, 34, 34, 29, 32)        | 92.2 (± 4.26)                          |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Investigator Assessment of Symptoms by Frequency and Severity

|  |   |
|--|---|
| End point title  | Investigator Assessment of Symptoms by Frequency and Severity |
| End point description:   |   |
| Investigator assessed the severity and frequency (FRQ) of patients' heartburn (HB), regurgitation/reflux (R/R) and dysphagia (DYS) in the 7 days prior to visit. Assessment included both severity grade (for severity, items were coded: none, mild, moderate, severe where none represented no complaints, severe represented incapacitating symptoms) and the FRQ (for FRQ, 7-graded Likert scale was used, ranging from none of the time to all of the time) of symptoms. Symptoms were scored as follows: none (no complaints), mild (aware of symptom, but easily tolerated), moderate (discomforting symptom, sufficient to cause interference with normal daily activities and/or sleep), severe (incapacitating symptom, with inability to perform normal daily activities and/or sleep). For FRQ- All of the time and None of the time, and for symptoms- none and severe data has been presented. The FAS consisted of all patients who had been randomized and received at least 1 dose of study drug. |   |
| WK- week   |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Weeks 1 and 8  |   |

| End point values                                | X842 25 mg BID (Double-blind Period) | X842 50 mg BID (Double-blind Period) | X842 75 mg BID (Double-blind Period) | X842 100 mg BID (Double-blind Period) |
|---|--------------------------------------|--------------------------------------|--------------------------------------|---------------------------------------|
| Subject group type                              | Reporting group                      | Reporting group                      | Reporting group                      | Reporting group                       |
| Number of subjects analysed                     | 51                                   | 48                                   | 52                                   | 47                                    |
| Units: Participants                             |                                      |                                      |                                      |                                       |
| WK1 (DYS) FRQ AT (n=50, 46, 50, 45, 47)         | 0                                    | 2                                    | 0                                    | 1                                     |
| WK1 (DYS) FRQ NT (n=50, 46, 50, 45, 47)         | 14                                   | 10                                   | 13                                   | 13                                    |
| WK8 (DYS) FRQ AT (n=48, 46, 50, 42, 48)         | 0                                    | 0                                    | 0                                    | 1                                     |
| WK8 (DYS) FRQ NT (n=48, 46, 50, 42, 48)         | 42                                   | 37                                   | 43                                   | 34                                    |
| WK1 (HB) FRQ AT (n=50, 46, 50, 45, 47)          | 4                                    | 0                                    | 3                                    | 3                                     |
| WK1 (HB) FRQ NT (n=50, 46, 50, 45, 47)          | 1                                    | 0                                    | 4                                    | 4                                     |
| WK8 (HB) FRQ AT (n=48, 46, 50, 42, 48)          | 0                                    | 0                                    | 0                                    | 0                                     |
| WK8 (HB) FRQ NT (n=48, 46, 50, 42, 48)          | 38                                   | 37                                   | 43                                   | 33                                    |
| WK1 (R/R) FRQ AT (n=50, 46, 50, 45, 47)         | 1                                    | 0                                    | 2                                    | 1                                     |
| WK1 (R/R) FRQ NT (n=50, 46, 50, 45, 47)         | 1                                    | 2                                    | 4                                    | 4                                     |
| WK8 (R/R) FRQ AT (n=48, 46, 50, 42, 48)         | 0                                    | 0                                    | 0                                    | 1                                     |
| WK8 (R/R) FRQ NT (n=48, 46, 50, 42, 48)         | 41                                   | 36                                   | 41                                   | 32                                    |
| WK1 (DYS) Symptom-None (n=50, 46, 50, 45, 47)   | 14                                   | 12                                   | 13                                   | 15                                    |
| WK1 (DYS) Symptom-Severe (n=50, 46, 50, 45, 47) | 1                                    | 2                                    | 2                                    | 2                                     |
| WK8 (DYS) Symptom-None (n=48, 46, 50, 42, 48)   | 42                                   | 37                                   | 43                                   | 35                                    |
| WK8 (DYS) Symptom-Severe (n=48, 46, 50, 42, 48) | 0                                    | 0                                    | 0                                    | 0                                     |

|   |    |    |    |    |
|---|----|----|----|----|
| WK1 (HB) Symptom-None (n=50, 46, 50, 45, 47)    | 1  | 0  | 4  | 5  |
| WK1 (HB) Symptom-Severe (n=50, 46, 50, 45, 47)  | 5  | 1  | 4  | 2  |
| WK8 (HB) Symptom-None (n=48, 46, 50, 42, 48)    | 38 | 37 | 44 | 33 |
| WK8 (HB) Symptom-Severe (n=48, 46, 50, 42, 48)  | 1  | 0  | 1  | 0  |
| WK1 (R/R) Symptom-None (n=50, 46, 50, 45, 47)   | 1  | 3  | 6  | 5  |
| WK1 (R/R) Symptom-Severe (n=50, 46, 50, 45, 47) | 3  | 3  | 5  | 4  |
| WK8 (R/R) Symptom-None (n=48, 46, 50, 42, 48)   | 41 | 36 | 41 | 33 |
| WK8 (R/R) Symptom-Severe (n=48, 46, 50, 42, 48) | 0  | 0  | 0  | 0  |

| End point values                                | Lansoprazole<br>(Open-label<br>Period) |  |  |  |
|---|--|--|--|--|
| Subject group type                              | Reporting group                        |  |  |  |
| Number of subjects analysed                     | 50                                     |  |  |  |
| Units: Participants                             |  |  |  |  |
| WK1 (DYS) FRQ AT (n=50, 46, 50, 45, 47)         | 0                                      |  |  |  |
| WK1 (DYS) FRQ NT (n=50, 46, 50, 45, 47)         | 11                                     |  |  |  |
| WK8 (DYS) FRQ AT (n=48, 46, 50, 42, 48)         | 0                                      |  |  |  |
| WK8 (DYS) FRQ NT (n=48, 46, 50, 42, 48)         | 40                                     |  |  |  |
| WK1 (HB) FRQ AT (n=50, 46, 50, 45, 47)          | 3                                      |  |  |  |
| WK1 (HB) FRQ NT (n=50, 46, 50, 45, 47)          | 1                                      |  |  |  |
| WK8 (HB) FRQ AT (n=48, 46, 50, 42, 48)          | 0                                      |  |  |  |
| WK8 (HB) FRQ NT (n=48, 46, 50, 42, 48)          | 36                                     |  |  |  |
| WK1 (R/R) FRQ AT (n=50, 46, 50, 45, 47)         | 0                                      |  |  |  |
| WK1 (R/R) FRQ NT (n=50, 46, 50, 45, 47)         | 3                                      |  |  |  |
| WK8 (R/R) FRQ AT (n=48, 46, 50, 42, 48)         | 0                                      |  |  |  |
| WK8 (R/R) FRQ NT (n=48, 46, 50, 42, 48)         | 39                                     |  |  |  |
| WK1 (DYS) Symptom-None (n=50, 46, 50, 45, 47)   | 12                                     |  |  |  |
| WK1 (DYS) Symptom-Severe (n=50, 46, 50, 45, 47) | 1                                      |  |  |  |
| WK8 (DYS) Symptom-None (n=48, 46, 50, 42, 48)   | 41                                     |  |  |  |
| WK8 (DYS) Symptom-Severe (n=48, 46, 50, 42, 48) | 0                                      |  |  |  |
| WK1 (HB) Symptom-None (n=50, 46, 50, 45, 47)    | 1                                      |  |  |  |

|   |    |  |  |  |
|---|----|--|--|--|
| WK1 (HB) Symptom-Severe (n=50, 46, 50, 45, 47)  | 3  |  |  |  |
| WK8 (HB) Symptom-None (n=48, 46, 50, 42, 48)    | 38 |  |  |  |
| WK8 (HB) Symptom-Severe (n=48, 46, 50, 42, 48)  | 0  |  |  |  |
| WK1 (R/R) Symptom-None (n=50, 46, 50, 45, 47)   | 3  |  |  |  |
| WK1 (R/R) Symptom-Severe (n=50, 46, 50, 45, 47) | 2  |  |  |  |
| WK8 (R/R) Symptom-None (n=48, 46, 50, 42, 48)   | 41 |  |  |  |
| WK8 (R/R) Symptom-Severe (n=48, 46, 50, 42, 48) | 1  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Quality of Life in Reflux and Dyspepsia (QOLRAD) Score

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Quality of Life in Reflux and Dyspepsia (QOLRAD) Score |
|-----------------|--|

End point description:

The reflux-related symptom pattern was evaluated during the initial 4 weeks treatment with four dose levels of X842 and with Lansoprazole, and the symptom pattern during the subsequent additional 4 weeks open-label treatment with Lansoprazole 30 mg QD. The heartburn version of the Quality of Life in Reflux and Dyspepsia (QOLRAD) is a disease specific instrument and contained 25 questions addressing concerns associated with gastrointestinal symptoms. The questions were rated on a seven-grade (1-7) Likert scale, where a score of 1 represented low quality of life, and as the score increased, the patient's condition was considered better. The questions were categorized into 5 domains: emotional distress, sleep disturbance (SD), vitality, food/drink problems, and physical/social (P/S) functioning. The score ranges from 1 to 175, higher scores mean a better outcome. The FAS consisted of all patients who had been randomized and received at least 1 dose of study drug.

WK- week

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 1, and 8

| End point values                                 | X842 25 mg BID (Double-blind Period) | X842 50 mg BID (Double-blind Period) | X842 75 mg BID (Double-blind Period) | X842 100 mg BID (Double-blind Period) |
|--|--------------------------------------|--------------------------------------|--------------------------------------|---------------------------------------|
| Subject group type                               | Reporting group                      | Reporting group                      | Reporting group                      | Reporting group                       |
| Number of subjects analysed                      | 51                                   | 48                                   | 52                                   | 47                                    |
| Units: Scores on a scale                         |                                      |                                      |                                      |                                       |
| arithmetic mean (standard deviation)             |                                      |                                      |                                      |                                       |
| WK1 Emotional Distress Score (n=40,40,41,34,41)  | 1.69 (± 0.247)                       | 1.55 (± 0.251)                       | 1.14 (± 0.233)                       | 1.54 (± 0.255)                        |
| WK8 Emotional Distress Score (n=27,24,27,22,23)  | 2.76 (± 0.265)                       | 2.51 (± 0.275)                       | 1.84 (± 0.253)                       | 2.00 (± 0.278)                        |
| WK1 Food/Drink Problems Score (n=40,40,41,34,41) | 1.84 (± 0.229)                       | 1.62 (± 0.232)                       | 1.32 (± 0.217)                       | 1.65 (± 0.238)                        |



|   |                |                |                |                |
|---|----------------|----------------|----------------|----------------|
| WK8 Food/Drink Problems Score (n= 27,24,27,22,23) | 3.08 (± 0.249) | 2.97 (± 0.259) | 2.34 (± 0.240) | 2.28 (± 0.264) |
| WK1 P/S Functioning Score (n= 40,40,41,34,41)     | 1.26 (± 0.247) | 1.32 (± 0.252) | 1.02 (± 0.233) | 1.19 (± 0.255) |
| WK8 P/S Functioning Score (n= 27,24,27,22,23)     | 2.06 (± 0.262) | 2.26 (± 0.271) | 1.57 (± 0.249) | 1.60 (± 0.274) |
| WK1 SD Score (n= 40,40,41,34,41)                  | 1.60 (± 0.250) | 1.45 (± 0.255) | 1.08 (± 0.236) | 1.49 (± 0.258) |
| WK8 SD Score (n= 27,24,27,22,23)                  | 2.78 (± 0.266) | 2.48 (± 0.276) | 1.89 (± 0.254) | 1.91 (± 0.279) |
| WK1 Vitality Score (n= 40,40,41,34,41)            | 1.55 (± 0.237) | 1.51 (± 0.240) | 1.42 (± 0.224) | 1.50 (± 0.246) |
| WK8 Vitality Score (n= 27,24,27,22,23)            | 2.84 (± 0.257) | 2.79 (± 0.268) | 2.25 (± 0.247) | 2.21 (± 0.272) |

| End point values                                  | Lansoprazole<br>(Open-label<br>Period) |  |  |  |
|---|--|--|--|--|
| Subject group type                                | Reporting group                        |  |  |  |
| Number of subjects analysed                       | 50                                     |  |  |  |
| Units: Scores on a scale                          |  |  |  |  |
| arithmetic mean (standard deviation)              |  |  |  |  |
| WK1 Emotional Distress Score (n= 40,40,41,34,41)  | 1.34 (± 0.241)                         |  |  |  |
| WK8 Emotional Distress Score (n= 27,24,27,22,23)  | 2.19 (± 0.269)                         |  |  |  |
| WK1 Food/Drink Problems Score (n= 40,40,41,34,41) | 1.40 (± 0.223)                         |  |  |  |
| WK8 Food/Drink Problems Score (n= 27,24,27,22,23) | 2.56 (± 0.256)                         |  |  |  |
| WK1 P/S Functioning Score (n= 40,40,41,34,41)     | 0.97 (± 0.241)                         |  |  |  |
| WK8 P/S Functioning Score (n= 27,24,27,22,23)     | 1.71 (± 0.265)                         |  |  |  |
| WK1 SD Score (n= 40,40,41,34,41)                  | 1.54 (± 0.244)                         |  |  |  |
| WK8 SD Score (n= 27,24,27,22,23)                  | 2.37 (± 0.270)                         |  |  |  |
| WK1 Vitality Score (n= 40,40,41,34,41)            | 1.21 (± 0.231)                         |  |  |  |
| WK8 Vitality Score (n= 27,24,27,22,23)            | 2.19 (± 0.264)                         |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From Screening (Day -7 to Day 0) until Week 8

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |    |
|--------------------|----|
| Dictionary version | 24 |
|--------------------|----|

### Reporting groups

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | X842 25 mg BID (Double-blind Period) |
|-----------------------|--------------------------------------|

Reporting group description:

Patients received 2 tablets (X842 25mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 25 mg + X842 dummy) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | X842 50 mg BID (Double-blind Period) |
|-----------------------|--------------------------------------|

Reporting group description:

Patients received 2 tablets (X842 50 mg + X842 dummy) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 50 mg + X842 dummy) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.

|                       |                                  |
|-----------------------|----------------------------------|
| Reporting group title | Lansoprazole (Open-label Period) |
|-----------------------|----------------------------------|

Reporting group description:

Patients received 2 tablets (X842 dummy×2) and 1 capsule (Lansoprazole 30 mg) in the morning, and 2 tablets (X842 dummy×2) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | X842 100 mg (Double-blind Period) |
|-----------------------|-----------------------------------|

Reporting group description:

Patients received 2 tablets (X842 50 mg×2) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 50 mg×2) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.

|                       |                                  |
|-----------------------|----------------------------------|
| Reporting group title | X842 75 mg (Double-blind Period) |
|-----------------------|----------------------------------|

Reporting group description:

Patients received 2 tablets (X842 50 mg + X842 25 mg) and 1 capsule (Lansoprazole dummy) in the morning, and 2 tablets (X842 50 mg + X842 25 mg) in the evening during 4-week double-blind treatment. Thereafter, patients received 1 capsule of Lansoprazole 30 mg QD for 4 weeks.

| Serious adverse events                            | X842 25 mg BID (Double-blind Period) | X842 50 mg BID (Double-blind Period) | Lansoprazole (Open-label Period) |
|---|--------------------------------------|--------------------------------------|----------------------------------|
| Total subjects affected by serious adverse events |                                      |                                      |                                  |
| subjects affected / exposed                       | 1 / 51 (1.96%)                       | 0 / 48 (0.00%)                       | 0 / 50 (0.00%)                   |
| number of deaths (all causes)                     | 0                                    | 0                                    | 0                                |
| number of deaths resulting from adverse events    | 0                                    | 0                                    | 0                                |
| Respiratory, thoracic and mediastinal disorders   |                                      |                                      |                                  |
| Laryngospasm                                      |                                      |                                      |                                  |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 51 (0.00%) | 0 / 48 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| Cholecystitis                                   |                |                |                |
| subjects affected / exposed                     | 1 / 51 (1.96%) | 0 / 48 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                     | X842 100 mg<br>(Double-blind<br>Period) | X842 75 mg<br>(Double-blind<br>Period) |  |
|---|---|--|--|
| Total subjects affected by serious adverse events |   |  |  |
| subjects affected / exposed                       | 0 / 47 (0.00%)                          | 1 / 52 (1.92%)                         |  |
| number of deaths (all causes)                     | 0                                       | 0                                      |  |
| number of deaths resulting from adverse events    | 0                                       | 0                                      |  |
| Respiratory, thoracic and mediastinal disorders   |   |  |  |
| Laryngospasm                                      |   |  |  |
| subjects affected / exposed                       | 0 / 47 (0.00%)                          | 1 / 52 (1.92%)                         |  |
| occurrences causally related to treatment / all   | 0 / 0                                   | 1 / 1                                  |  |
| deaths causally related to treatment / all        | 0 / 0                                   | 0 / 0                                  |  |
| Hepatobiliary disorders                           |   |  |  |
| Cholecystitis                                     |   |  |  |
| subjects affected / exposed                       | 0 / 47 (0.00%)                          | 0 / 52 (0.00%)                         |  |
| occurrences causally related to treatment / all   | 0 / 0                                   | 0 / 0                                  |  |
| deaths causally related to treatment / all        | 0 / 0                                   | 0 / 0                                  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                     | X842 25 mg BID<br>(Double-blind<br>Period) | X842 50 mg BID<br>(Double-blind<br>Period) | Lansoprazole (Open-<br>label Period) |
|---|--|--|--------------------------------------|
| Total subjects affected by non-serious adverse events |  |  |                                      |
| subjects affected / exposed                           | 14 / 51 (27.45%)                           | 10 / 48 (20.83%)                           | 10 / 50 (20.00%)                     |
| Vascular disorders                                    |  |  |                                      |
| Hypertension  |  |  |                                      |
| subjects affected / exposed                           | 0 / 51 (0.00%)                             | 0 / 48 (0.00%)                             | 1 / 50 (2.00%)                       |
| occurrences (all)                                     | 0  | 0  | 1                                    |

|  |                |                |                |
|--|----------------|----------------|----------------|
| General disorders and administration site conditions |                |                |                |
| Peripheral swelling                                  |                |                |                |
| subjects affected / exposed                          | 0 / 51 (0.00%) | 1 / 48 (2.08%) | 0 / 50 (0.00%) |
| occurrences (all)                                    | 0              | 1              | 0              |
| Mucosal dryness                                      |                |                |                |
| subjects affected / exposed                          | 0 / 51 (0.00%) | 1 / 48 (2.08%) | 0 / 50 (0.00%) |
| occurrences (all)                                    | 0              | 1              | 0              |
| Hepatobiliary disorders                              |                |                |                |
| subjects affected / exposed                          | 1 / 51 (1.96%) | 0 / 48 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                                    | 1              | 0              | 0              |
| Fatigue  |                |                |                |
| subjects affected / exposed                          | 0 / 51 (0.00%) | 0 / 48 (0.00%) | 1 / 50 (2.00%) |
| occurrences (all)                                    | 0              | 0              | 1              |
| Chest pain   |                |                |                |
| subjects affected / exposed                          | 1 / 51 (1.96%) | 0 / 48 (0.00%) | 1 / 50 (2.00%) |
| occurrences (all)                                    | 1              | 0              | 1              |
| Respiratory, thoracic and mediastinal disorders      |                |                |                |
| Cough  |                |                |                |
| subjects affected / exposed                          | 1 / 51 (1.96%) | 0 / 48 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                                    | 1              | 0              | 0              |
| Laryngospasm   |                |                |                |
| subjects affected / exposed                          | 0 / 51 (0.00%) | 0 / 48 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                                    | 0              | 0              | 0              |
| Investigations                                       |                |                |                |
| Aspartate aminotransferase increased                 |                |                |                |
| subjects affected / exposed                          | 0 / 51 (0.00%) | 0 / 48 (0.00%) | 1 / 50 (2.00%) |
| occurrences (all)                                    | 0              | 0              | 1              |
| Activated partial thromboplastin time prolonged      |                |                |                |
| subjects affected / exposed                          | 0 / 51 (0.00%) | 0 / 48 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                                    | 0              | 0              | 0              |
| Alanine aminotransferase increased                   |                |                |                |
| subjects affected / exposed                          | 0 / 51 (0.00%) | 0 / 48 (0.00%) | 1 / 50 (2.00%) |
| occurrences (all)                                    | 0              | 0              | 1              |
| Electrocardiogram QT prolonged                       |                |                |                |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 51 (0.00%)<br>0 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| SARS-CoV-2 test positive<br>subjects affected / exposed<br>occurrences (all)            | 0 / 51 (0.00%)<br>0 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Injury, poisoning and procedural complications  |                     |                     |                     |
| Hand fracture<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 51 (0.00%)<br>0 | 0 / 48 (0.00%)<br>0 | 1 / 50 (2.00%)<br>1 |
| Limb injury<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 51 (1.96%)<br>1 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Cardiac disorders   |                     |                     |                     |
| Atrioventricular block first degree<br>subjects affected / exposed<br>occurrences (all) | 1 / 51 (1.96%)<br>1 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 51 (0.00%)<br>0 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Ventricular extrasystoles<br>subjects affected / exposed<br>occurrences (all)           | 0 / 51 (0.00%)<br>0 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Nervous system disorders  |                     |                     |                     |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 51 (0.00%)<br>0 | 1 / 48 (2.08%)<br>9 | 0 / 50 (0.00%)<br>0 |
| Headache<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 51 (1.96%)<br>1 | 3 / 48 (6.25%)<br>3 | 1 / 50 (2.00%)<br>1 |
| Blood and lymphatic system disorders  |                     |                     |                     |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 51 (1.96%)<br>1 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 51 (0.00%)<br>0 | 0 / 48 (0.00%)<br>0 | 1 / 50 (2.00%)<br>1 |

|                                |                |                |                |
|--------------------------------|----------------|----------------|----------------|
| Gastrointestinal disorders     |                |                |                |
| Abdominal discomfort           |                |                |                |
| subjects affected / exposed    | 0 / 51 (0.00%) | 1 / 48 (2.08%) | 0 / 50 (0.00%) |
| occurrences (all)              | 0              | 2              | 0              |
| Constipation                   |                |                |                |
| subjects affected / exposed    | 2 / 51 (3.92%) | 1 / 48 (2.08%) | 0 / 50 (0.00%) |
| occurrences (all)              | 2              | 1              | 0              |
| Abdominal pain upper           |                |                |                |
| subjects affected / exposed    | 0 / 51 (0.00%) | 1 / 48 (2.08%) | 0 / 50 (0.00%) |
| occurrences (all)              | 0              | 1              | 0              |
| Abdominal pain                 |                |                |                |
| subjects affected / exposed    | 1 / 51 (1.96%) | 0 / 48 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)              | 1              | 0              | 0              |
| Abdominal distension           |                |                |                |
| subjects affected / exposed    | 0 / 51 (0.00%) | 1 / 48 (2.08%) | 0 / 50 (0.00%) |
| occurrences (all)              | 0              | 2              | 0              |
| Diarrhoea                      |                |                |                |
| subjects affected / exposed    | 2 / 51 (3.92%) | 0 / 48 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)              | 2              | 0              | 0              |
| Dyspepsia                      |                |                |                |
| subjects affected / exposed    | 0 / 51 (0.00%) | 1 / 48 (2.08%) | 0 / 50 (0.00%) |
| occurrences (all)              | 0              | 1              | 0              |
| Dysphagia                      |                |                |                |
| subjects affected / exposed    | 1 / 51 (1.96%) | 1 / 48 (2.08%) | 0 / 50 (0.00%) |
| occurrences (all)              | 1              | 1              | 0              |
| Nausea                         |                |                |                |
| subjects affected / exposed    | 1 / 51 (1.96%) | 0 / 48 (0.00%) | 4 / 50 (8.00%) |
| occurrences (all)              | 1              | 0              | 4              |
| Hyperchlorhydria               |                |                |                |
| subjects affected / exposed    | 0 / 51 (0.00%) | 0 / 48 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)              | 0              | 0              | 0              |
| Gastrointestinal hypermotility |                |                |                |
| subjects affected / exposed    | 1 / 51 (1.96%) | 0 / 48 (0.00%) | 1 / 50 (2.00%) |
| occurrences (all)              | 1              | 0              | 1              |
| Eructation                     |                |                |                |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                      | 0 / 51 (0.00%)<br>0 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Oesophageal pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 51 (0.00%)<br>0 | 1 / 48 (2.08%)<br>2 | 0 / 50 (0.00%)<br>0 |
| Regurgitation<br>subjects affected / exposed<br>occurrences (all)     | 0 / 51 (0.00%)<br>0 | 2 / 48 (4.17%)<br>3 | 0 / 50 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders                                |                     |                     |                     |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)          | 0 / 51 (0.00%)<br>0 | 1 / 48 (2.08%)<br>1 | 0 / 50 (0.00%)<br>0 |
| Purpura<br>subjects affected / exposed<br>occurrences (all)           | 0 / 51 (0.00%)<br>0 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Rash<br>subjects affected / exposed<br>occurrences (all)              | 1 / 51 (1.96%)<br>1 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders                       |                     |                     |                     |
| Back pain<br>subjects affected / exposed<br>occurrences (all)         | 0 / 51 (0.00%)<br>0 | 0 / 48 (0.00%)<br>0 | 1 / 50 (2.00%)<br>1 |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all) | 0 / 51 (0.00%)<br>0 | 0 / 48 (0.00%)<br>0 | 1 / 50 (2.00%)<br>1 |
| Infections and infestations   |                     |                     |                     |
| COVID-19<br>subjects affected / exposed<br>occurrences (all)          | 1 / 51 (1.96%)<br>1 | 2 / 48 (4.17%)<br>2 | 2 / 50 (4.00%)<br>2 |
| Laryngitis<br>subjects affected / exposed<br>occurrences (all)        | 0 / 51 (0.00%)<br>0 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)   | 1 / 51 (1.96%)<br>1 | 2 / 48 (4.17%)<br>2 | 0 / 50 (0.00%)<br>0 |
| Pharyngitis   |                     |                     |                     |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 51 (0.00%)<br>0 | 0 / 48 (0.00%)<br>0 | 1 / 50 (2.00%)<br>1 |
| Rhinitis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 51 (0.00%)<br>0 | 1 / 48 (2.08%)<br>1 | 0 / 50 (0.00%)<br>0 |
| Tonsillitis<br>subjects affected / exposed<br>occurrences (all)   | 1 / 51 (1.96%)<br>1 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 51 (1.96%)<br>1 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Metabolism and nutrition disorders<br>Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 51 (0.00%)<br>0 | 0 / 48 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |

| <b>Non-serious adverse events</b>  | X842 100 mg<br>(Double-blind<br>Period) | X842 75 mg<br>(Double-blind<br>Period) |  |
|--|---|--|--|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed  | 11 / 47 (23.40%)                        | 12 / 52 (23.08%)                       |  |
| Vascular disorders<br>Hypertension<br>subjects affected / exposed<br>occurrences (all)   | 0 / 47 (0.00%)<br>0                     | 0 / 52 (0.00%)<br>0                    |  |
| General disorders and administration<br>site conditions<br>Peripheral swelling<br>subjects affected / exposed<br>occurrences (all) | 0 / 47 (0.00%)<br>0                     | 0 / 52 (0.00%)<br>0                    |  |
| Mucosal dryness<br>subjects affected / exposed<br>occurrences (all)  | 0 / 47 (0.00%)<br>0                     | 0 / 52 (0.00%)<br>0                    |  |
| Hepatobiliary disorders<br>subjects affected / exposed<br>occurrences (all)  | 0 / 47 (0.00%)<br>0                     | 0 / 52 (0.00%)<br>0                    |  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)  | 0 / 47 (0.00%)<br>0                     | 0 / 52 (0.00%)<br>0                    |  |



|   |  |   |  |
|---|--|---|--|
| Chest pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 47 (0.00%)<br>0  | 0 / 52 (0.00%)<br>0   |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Laryngospasm<br>subjects affected / exposed<br>occurrences (all)  | 0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0   | 0 / 52 (0.00%)<br>0<br><br>1 / 52 (1.92%)<br>1  |  |
| Investigations<br>Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)<br><br>Activated partial thromboplastin time prolonged<br>subjects affected / exposed<br>occurrences (all)<br><br>Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)<br><br>Electrocardiogram QT prolonged<br>subjects affected / exposed<br>occurrences (all)<br><br>SARS-CoV-2 test positive<br>subjects affected / exposed<br>occurrences (all) | 0 / 47 (0.00%)<br>0<br><br>1 / 47 (2.13%)<br>1<br><br>0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0<br><br>0 / 52 (0.00%)<br>0<br><br>0 / 52 (0.00%)<br>0<br><br>1 / 52 (1.92%)<br>1<br><br>1 / 52 (1.92%)<br>1 |  |
| Injury, poisoning and procedural complications<br>Hand fracture<br>subjects affected / exposed<br>occurrences (all)<br><br>Limb injury<br>subjects affected / exposed<br>occurrences (all)  | 0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0   | 0 / 52 (0.00%)<br>0<br><br>0 / 52 (0.00%)<br>0  |  |
| Cardiac disorders   |  |   |  |

|  |   |   |  |
|--|---|---|--|
| Atrioventricular block first degree<br>subjects affected / exposed<br>occurrences (all)  | 0 / 47 (0.00%)<br>0   | 0 / 52 (0.00%)<br>0   |  |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)  | 0 / 47 (0.00%)<br>0   | 1 / 52 (1.92%)<br>1   |  |
| Ventricular extrasystoles<br>subjects affected / exposed<br>occurrences (all)  | 0 / 47 (0.00%)<br>0   | 1 / 52 (1.92%)<br>1   |  |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)<br><br>Headache<br>subjects affected / exposed<br>occurrences (all)  | 0 / 47 (0.00%)<br>0<br><br>1 / 47 (2.13%)<br>1  | 0 / 52 (0.00%)<br>0<br><br>1 / 52 (1.92%)<br>1  |  |
| Blood and lymphatic system disorders<br>Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)<br><br>Anaemia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0  | 1 / 52 (1.92%)<br>1<br><br>0 / 52 (0.00%)<br>0  |  |
| Gastrointestinal disorders<br>Abdominal discomfort<br>subjects affected / exposed<br>occurrences (all)<br><br>Constipation<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal distension | 0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0<br><br>0 | 0 / 52 (0.00%)<br>0<br><br>2 / 52 (3.85%)<br>2<br><br>0 / 52 (0.00%)<br>0<br><br>0 / 52 (0.00%)<br>0<br><br>0 |  |

|  |                |                |  |
|--|----------------|----------------|--|
| subjects affected / exposed            | 0 / 47 (0.00%) | 0 / 52 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Diarrhoea                              |                |                |  |
| subjects affected / exposed            | 0 / 47 (0.00%) | 1 / 52 (1.92%) |  |
| occurrences (all)                      | 0              | 1              |  |
| Dyspepsia                              |                |                |  |
| subjects affected / exposed            | 0 / 47 (0.00%) | 0 / 52 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Dysphagia                              |                |                |  |
| subjects affected / exposed            | 1 / 47 (2.13%) | 0 / 52 (0.00%) |  |
| occurrences (all)                      | 1              | 0              |  |
| Nausea                                 |                |                |  |
| subjects affected / exposed            | 0 / 47 (0.00%) | 0 / 52 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Hyperchlorhydria                       |                |                |  |
| subjects affected / exposed            | 1 / 47 (2.13%) | 0 / 52 (0.00%) |  |
| occurrences (all)                      | 1              | 0              |  |
| Gastrointestinal hypermotility         |                |                |  |
| subjects affected / exposed            | 0 / 47 (0.00%) | 0 / 52 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Eructation                             |                |                |  |
| subjects affected / exposed            | 2 / 47 (4.26%) | 0 / 52 (0.00%) |  |
| occurrences (all)                      | 2              | 0              |  |
| Oesophageal pain                       |                |                |  |
| subjects affected / exposed            | 1 / 47 (2.13%) | 0 / 52 (0.00%) |  |
| occurrences (all)                      | 1              | 0              |  |
| Regurgitation                          |                |                |  |
| subjects affected / exposed            | 2 / 47 (4.26%) | 0 / 52 (0.00%) |  |
| occurrences (all)                      | 2              | 0              |  |
| Skin and subcutaneous tissue disorders |                |                |  |
| Alopecia                               |                |                |  |
| subjects affected / exposed            | 0 / 47 (0.00%) | 0 / 52 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Purpura                                |                |                |  |
| subjects affected / exposed            | 0 / 47 (0.00%) | 1 / 52 (1.92%) |  |
| occurrences (all)                      | 0              | 1              |  |

|   |   |  |  |
|---|---|--|--|
| Rash<br>subjects affected / exposed<br>occurrences (all)  | 0 / 47 (0.00%)<br>0   | 0 / 52 (0.00%)<br>0  |  |
| Musculoskeletal and connective tissue disorders<br>Back pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all)   | <br>0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0  | <br>0 / 52 (0.00%)<br>0<br><br>0 / 52 (0.00%)<br>0   |  |
| Infections and infestations<br>COVID-19<br>subjects affected / exposed<br>occurrences (all)<br><br>Laryngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Pharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Rhinitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Tonsillitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | <br>4 / 47 (8.51%)<br>4<br><br>1 / 47 (2.13%)<br>1<br><br>1 / 47 (2.13%)<br>1<br><br>0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0<br><br>0 / 47 (0.00%)<br>0 | <br>1 / 52 (1.92%)<br>1<br><br>0 / 52 (0.00%)<br>0<br><br>0 / 52 (0.00%)<br>0<br><br>0 / 52 (0.00%)<br>0<br><br>0 / 52 (0.00%)<br>0<br><br>1 / 52 (1.92%)<br>1 |  |
| Metabolism and nutrition disorders<br>Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)   | <br>1 / 47 (2.13%)<br>1   | <br>0 / 52 (0.00%)<br>0  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 19 July 2019     | Amendment 1: Inclusion criteria- lansoprazole was excluded from the primary treatment. Change in 5 days to 7 days was done based on extension of screening period. Reflux Related Symptoms Assessed Based on PRO- Modified RESQeDiary added for clarity and "every 12-hours" was added to be more specific in reporting time. Reflux Related Symptoms Assessed by Investigator-Text updated to define frequency of symptoms on 7-graded Likert scale. |
| 25 February 2022 | Amendment 2: Study Population- Text updated to clarify criteria for patients identified during their routine endoscopy and for patients invited for screening endoscopy based on their past medical history.  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported