

**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	v2 (current)
This version publication date	15 December 2023
First version publication date	15 September 2023
Version creation reason	• Changes to summary attachments changes added

Trial information**Trial identification**

Sponsor protocol code	CX842A2201
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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
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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
Arm title	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.

Arm title	X842 50 mg BID (Double-blind Period)
Arm 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.	
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: 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: 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: 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.	
Arm title	X842 75 mg BID (Double-blind Period)
Arm 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.	
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: 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.

Arm title	X842 100 mg BID (Double-blind Period)
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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.

Arm title	Lansoprazole (Open-label Period)
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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 (Double-blind Period)	X842 50 mg BID (Double-blind Period)	X842 75 mg BID (Double-blind 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 (Double-blind Period)	Lansoprazole (Open- 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:	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:	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:	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:	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:	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 (Double-blind Period)	X842 50 mg BID (Double-blind Period)	X842 75 mg BID (Double-blind Period)
Number of subjects	51	48	52
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 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			
Units: years			
arithmetic mean	48.7	45.3	48.7
standard deviation	± 15.99	± 14.11	± 14.05
Gender categorical			
Units: Subjects			
Female	18	19	22
Male	33	29	30

Reporting group values	X842 100 mg BID (Double-blind Period)	Lansoprazole (Open- label Period)	Total
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Number of subjects	47	50	248
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 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: 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: 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: 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: 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: 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 ^[1]
End point description: 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: 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 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				
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 (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:	
<p>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.</p>	
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
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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
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End point timeframe:

Week 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)	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 (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)	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
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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
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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 (Open-label 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
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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
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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 (Open-label 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24
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Reporting groups

Reporting group title	X842 25 mg BID (Double-blind Period)
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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)
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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	X842 75 mg (Double-blind Period)
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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.

Reporting group title	X842 100 mg (Double-blind Period)
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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	Lansoprazole (Open-label Period)
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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.

Serious adverse events	X842 25 mg BID (Double-blind Period)	X842 50 mg BID (Double-blind Period)	X842 75 mg (Double-blind Period)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	1 / 52 (1.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 52 (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

Respiratory, thoracic and mediastinal disorders			
Laryngospasm			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	X842 100 mg (Double-blind Period)	Lansoprazole (Open-label Period)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Laryngospasm			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (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 %

Non-serious adverse events	X842 25 mg BID (Double-blind Period)	X842 50 mg BID (Double-blind Period)	X842 75 mg (Double-blind Period)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 51 (27.45%)	10 / 48 (20.83%)	12 / 52 (23.08%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Mucosal dryness			

subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Laryngospasm			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			

subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	1 / 52 (1.92%) 1
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Atrioventricular block first degree			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 52 (0.00%)
occurrences (all)	0	9	0
Headache			
subjects affected / exposed	1 / 51 (1.96%)	3 / 48 (6.25%)	1 / 52 (1.92%)
occurrences (all)	1	3	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	1 / 52 (1.92%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	2 / 51 (3.92%)	1 / 48 (2.08%)	2 / 52 (3.85%)
occurrences (all)	2	1	2
Abdominal distension			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 52 (0.00%)
occurrences (all)	0	2	0
Abdominal discomfort			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 52 (0.00%)
occurrences (all)	0	2	0
Dyspepsia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	0 / 52 (0.00%)
occurrences (all)	1	1	0
Eructation			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal hypermotility			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Hyperchlorhydria			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Oesophageal pain			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 52 (0.00%)
occurrences (all)	0	2	0
Diarrhoea			

subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2	0 / 48 (0.00%) 0	1 / 52 (1.92%) 1
Regurgitation subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	2 / 48 (4.17%) 3	0 / 52 (0.00%) 0
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 48 (0.00%) 0	0 / 52 (0.00%) 0
Purpura subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	1 / 52 (1.92%) 1
Alopecia subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 48 (2.08%) 1	0 / 52 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Pain in extremity subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	0 / 52 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	0 / 52 (0.00%) 0
Infections and infestations			
Laryngitis subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	0 / 52 (0.00%) 0
COVID-19 subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	2 / 48 (4.17%) 2	1 / 52 (1.92%) 1
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	2 / 48 (4.17%) 2	0 / 52 (0.00%) 0
Pharyngitis subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	0 / 52 (0.00%) 0
Rhinitis			

subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 48 (2.08%) 1	0 / 52 (0.00%) 0
Tonsillitis subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 48 (0.00%) 0	0 / 52 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 48 (0.00%) 0	1 / 52 (1.92%) 1
Metabolism and nutrition disorders Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	0 / 52 (0.00%) 0

Non-serious adverse events	X842 100 mg (Double-blind Period)	Lansoprazole (Open- label Period)	
Total subjects affected by non-serious adverse events subjects affected / exposed	11 / 47 (23.40%)	10 / 50 (20.00%)	
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 50 (2.00%) 1	
General disorders and administration site conditions Mucosal dryness subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Peripheral swelling subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Hepatobiliary disorders subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Fatigue subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 50 (2.00%) 1	
Chest pain subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 50 (2.00%) 1	

Respiratory, thoracic and mediastinal disorders			
Laryngospasm			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Limb injury			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Atrioventricular block first degree			

subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Ventricular extrasystoles subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	1 / 50 (2.00%) 1	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 50 (2.00%) 1	
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Abdominal distension subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Dyspepsia			

subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Dysphagia			
subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 50 (0.00%) 0	
Eructation			
subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2	0 / 50 (0.00%) 0	
Gastrointestinal hypermotility			
subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	1 / 50 (2.00%) 1	
Hyperchlorhydria			
subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 50 (0.00%) 0	
Nausea			
subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	4 / 50 (8.00%) 4	
Oesophageal pain			
subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 50 (0.00%) 0	
Diarrhoea			
subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Regurgitation			
subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2	0 / 50 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Purpura			
subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	
Alopecia			
subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0	0 / 50 (0.00%) 0	

Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Infections and infestations			
Laryngitis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
COVID-19			
subjects affected / exposed	4 / 47 (8.51%)	2 / 50 (4.00%)	
occurrences (all)	4	2	
Nasopharyngitis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Tonsillitis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Hypophosphataemia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	
occurrences (all)	1	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:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported