Clinical trial results:
A randomized, participant- and investigator-blinded, placebo-controlled study to investigate efficacy, safety and tolerability of LTP001 in participants with pulmonary arterial hypertension

Summary

EudraCT number	2021-000670-28
Trial protocol	DE NL ES
Global end of trial date	25 April 2024

Results information

Result version number	v1
This version publication date	03 April 2025
First version publication date	03 April 2025

Trial information

Trial identification

Sponsor protocol code	CLTP001A12201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05135000
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com

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	25 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 April 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the efficacy of LTP001 in participants with pulmonary arterial hypertension (PAH). Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 June 2022
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 Kingdom: 7
Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Spain: 11
Worldwide total number of subjects	47
EEA total number of subjects	34

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)	43
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 56 participants were screened for the study. Out of these, 47 participants were randomized.

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, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	LTP001

Arm description:

Participants received LTP001, 6 mg, oral capsules, once daily in the morning for approximately 24 weeks

Arm type	Experimental
Investigational medicinal product name	LTP001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LTP001, 6 mg, once daily in the morning for approximately 24 weeks

Arm title	Placebo

Arm description:

Participants received LTP001 placebo capsules matching LTP001 orally once daily in the morning for approximately 24 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LTP001-matching placebo, once daily, in the morning for approximately 24 weeks

Number of subjects in period 1	LTP001	Placebo
Started	35	12
Completed	26	9
Not completed	9	3
Adverse event, non-fatal	2	-

Study Terminated by Sponsor	6	3
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	LTP001
Reporting group description:	
Participants received LTP001, 6 mg, oral capsules, once daily in the morning for approximately 24 weeks	
Reporting group title	Placebo
Reporting group description:	
Participants received LTP001 placebo capsules matching LTP001 orally once daily in the morning for approximately 24 weeks	

Reporting group values	LTP001	Placebo	Total
Number of subjects	35	12	47
Age Categorical Units: Participants			
18 - <65	32	11	43
65 - <85	3	1	4
Age Continuous Units: Years			
arithmetic mean	45.3	45.3	
standard deviation	± 13.03	± 13.78	-
Sex: Female, Male Units: Participants			
Female	29	10	39
Male	6	2	8
Race/Ethnicity, Customized Units: Subjects			
White	32	11	43
American Indian or Alaska	2	0	2
Asian	1	1	2

End points

End points reporting groups

Reporting group title	LTP001
Reporting group description:	
Participants received LTP001, 6 mg, oral capsules, once daily in the morning for approximately 24 weeks	
Reporting group title	Placebo
Reporting group description:	
Participants received LTP001 placebo capsules matching LTP001 orally once daily in the morning for approximately 24 weeks	

Primary: Change From Baseline in Right Heard Catheterization Pulmonary Vascular Resistance (PVR) at Week 25

End point title	Change From Baseline in Right Heard Catheterization Pulmonary Vascular Resistance (PVR) at Week 25[1]
End point description:	
PVR was defined as the resistance against blood flow from the pulmonary artery to the left atrium measured in dyn.s.cm-5	
End point type	Primary
End point timeframe:	
Baseline, Week 25	

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: Descriptive statistics are reported.

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	8		
Units: dynes.sec.cm^-5				
arithmetic mean (standard deviation)	-1.175 (± 254.0792)	-49.685 (± 181.3745)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Six Minute Walk Distance (6MWD)

End point title	Change From Baseline in Six Minute Walk Distance (6MWD)
End point description:	
6MWD test measures the distance that a patient can walk on a flat, hard surface in a period of 6 minutes	
End point type	Secondary
End point timeframe:	
Baseline, Weeks 13 and 25	

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	10		
Units: meters				
arithmetic mean (standard deviation)				
Week 13 n=30,10	3.2 (± 42.45)	7.4 (± 29.34)		
Week 25 n=28,10	10.4 (± 44.36)	21.0 (± 32.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Right Atrium (RA) Pressures at Week 25

End point title	Change From Baseline in Right Atrium (RA) Pressures at Week 25

End point description:

The Right Heart Catheterization (RHC) assessment was performed to assess several hemodynamic variables in pulmonary hypertension, including RA pressures.

End point type	Secondary

End point timeframe:

Baseline, Week 25

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	9		
Units: mmHg				
arithmetic mean (standard deviation)	-0.4 (± 4.40)	-0.6 (± 0.73)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pulmonary Capillary Wedge Pressure at Week 25

End point title	Change From Baseline in Pulmonary Capillary Wedge Pressure at Week 25

End point description:

Right heart catheterization (RHC) assessment was performed to assess several hemodynamic variables in pulmonary hypertension, including pulmonary capillary wedge pressure (PCWP).

End point type	Secondary

End point timeframe:

Baseline, Week 25

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	9		
Units: mmHg				
arithmetic mean (standard deviation)	0.2 (± 3.66)	0.9 (± 2.26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean Pulmonary Artery Pressure at Week 25

End point title	Change From Baseline in Mean Pulmonary Artery Pressure at Week 25

End point description:

Right heart catheterization (RHC) assessment was performed to assess several hemodynamic variables in pulmonary hypertension, including pulmonary artery pressure.

End point type	Secondary

End point timeframe:

Baseline, Week 25

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	9		
Units: mmHg				
arithmetic mean (standard deviation)	0.4 (± 8.55)	-0.6 (± 5.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Average Cardiac Output (CO) at Week 25

End point title	Change From Baseline in Average Cardiac Output (CO) at Week 25

End point description:

Right heart catheterization (RHC) assessment was performed to assess several hemodynamic variables in pulmonary hypertension, including cardiac output (CO).

End point type	Secondary

End point timeframe:

Baseline, Week 25

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	8		
Units: liters per minute				
arithmetic mean (standard deviation)	0.067 (± 1.0772)	0.493 (± 0.9075)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fractional Area Change (FAC)

End point title	Change From Baseline in Fractional Area Change (FAC)

End point description:

Key right ventricular (RV) function endpoints such as RV fractional area change (RV FAC) were assessed with echocardiography.

End point type	Secondary

End point timeframe:

Baseline, Weeks 5, 13, and 25

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	10		
Units: percent				
arithmetic mean (standard deviation)				
Week 5 n=31,9	0.35 (± 6.944)	0.92 (± 5.622)		
Week 13 n=29,10	-1.19 (± 6.424)	2.62 (± 4.417)		
Week 25 n=26,8	-1.85 (± 5.412)	-1.45 (± 7.532)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Peak Velocity of Excursion (RV S')

End point title	Change From Baseline in Peak Velocity of Excursion (RV S')

End point description:

Key right ventricular (RV) function per echocardiography. The terms Tricuspid Annular Systolic Velocity (TASV) and Peak Velocity of Excursion (RV S') are synonymous in echocardiography to describe the peak systolic velocity of the lateral tricuspid annulus. Including both TASV and RV S' as separate

secondary endpoints was an oversight in the protocol as the data, calculation, and analyses for both (TASV and RV S') are identical. Therefore, the TASV nomenclature is used in this results disclosure

End point type	Secondary

End point timeframe:

Baseline, weeks 5, 13, and 25

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: centimeters per second				
arithmetic mean (standard deviation)	()	()		

Notes:

[2] - TASV and RV S' are synonymous. Data are reported in the TASV endpoint.

[3] - TASV and RV S' are synonymous. Data are reported in the TASV endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Tricuspid Annular Plane Systolic Excursion (TAPSE)

End point title	Change From Baseline in Tricuspid Annular Plane Systolic Excursion (TAPSE)

End point description:

Key right ventricular (RV) function endpoints such as tricuspid annular plane systolic excursion (TAPSE) were assessed with echocardiography.

End point type	Secondary

End point timeframe:

Baseline, Weeks 5, 13, and 25

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	11		
Units: centimeters				
arithmetic mean (standard deviation)				
Week 5 n=33,11	0.061 (± 0.3181)	0.042 (± 0.3383)		
Week 13 n=31,11	-0.026 (± 0.2594)	0.100 (± 0.2933)		
Week 25 n=27,9	0.015 (± 0.3697)	-0.067 (± 0.2121)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Tricuspid Annular Systolic Velocity (TASV)

End point title	Change From Baseline in Tricuspid Annular Systolic Velocity (TASV)

End point description:

Key right ventricular (RV) function endpoints such as tricuspid annular systolic velocity (TASV) were assessed with echocardiography.

End point type	Secondary

End point timeframe:

Baseline, weeks 5, 13 and 25

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	11		
Units: centimeters per second				
arithmetic mean (standard deviation)				
Week 5 n=33,11	0.2 (± 2.14)	-0.4 (± 1.50)		
Week 13 n=32,11	-0.2 (± 2.38)	-0.5 (± 1.63)		
Week 25 n=26,9	0.4 (± 2.28)	-1.0 (± 3.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EmPHasis-10

End point title	Change From Baseline in EmPHasis-10

End point description:

emPHasis-10 is a questionnaire with 10 questions designed to determine how pulmonary hypertension affects a participant's life. Each item is scored on a scale of 0 to 5, with a total score ranging from 0 to 50. A higher score indicates worse quality of life.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13 and 25

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	9		
Units: score				
arithmetic mean (standard deviation)				
Week 13 n=21,9	-1.490 (± 5.7108)	-3.622 (± 3.1712)		
Week 25 n=17,9	-4.972 (± 8.7643)	-3.000 (± 4.2961)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pulmonary Arterial Hypertension—Symptoms and Impact (PAH-SYMPACT)

End point title	Change From Baseline in Pulmonary Arterial Hypertension—Symptoms and Impact (PAH-SYMPACT)

End point description:

PAH-SYMPACT is a questionnaire used to assess pulmonary arterial hypertension symptoms and their impact. Individual item scores range from 0 to 4. Total score is calculated as the sum of the scores for the individual items divided by the number of items. A higher score indicates more severe symptoms/impacts.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13 and 25

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	4		
Units: score				
arithmetic mean (standard deviation)				
Week 13	-1.452 (± 6.3897)	-3.545 (± 3.2693)		
Week 25	-0.680 (± 5.7304)	-4.220 (± 6.1990)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Blood Concentrations (Cmax) for LTP001

End point title	Maximum Observed Blood Concentrations (Cmax) for LTP001

End point description:

The maximum (peak) observed blood drug concentration after single dose administration.

End point type	Secondary

End point timeframe:

Day 1 and Week 25 at 15, 45, and 120 minutes post-dose

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	0[4]		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1	38.6 (± 58.2)	()		
Week 25	39.2 (± 54.7)	()		

Notes:

[4] - Not analyzed in the placebo group.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Blood Concentrations (Tmax) of LTP001

End point title	Time to Reach Maximum Blood Concentrations (Tmax) of LTP001

End point description:

The time to reach maximum (peak) blood drug concentration after single dose administration.

End point type	Secondary

End point timeframe:

Day 1 and Week 25 at 15, 45, and 120 minutes post-dose

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	0[5]		
Units: hours				
geometric mean (geometric coefficient of variation)				
Day 1	1.05 (± 56.6)	()		
Week 25	0.979 (± 68.8)	()		

Notes:

[5] - Not analyzed in the placebo group.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in N-terminal Fragment of the Prohormone B-type Natriuretic Peptide (NT-ProBNP)

End point title	Change From Baseline in N-terminal Fragment of the Prohormone B-type Natriuretic Peptide (NT-ProBNP)

End point description:

NT-proBNP is a blood biomarker to assess right ventricular distress.

End point type	Secondary

End point timeframe:

Baseline to Week 29

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	11		
Units: picomoles per liter				
arithmetic mean (standard deviation)	4.609 (± 52.9047)	-7.918 (± 21.9731)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Clinical Worsening

End point title	Time to Clinical Worsening

End point description:

Time to any of the following:
- Death
- Hospital stay greater than 24 hours due to worsening of pulmonary arterial hypertension
- Worsening of PAH resulting in need for lung transplantation or balloon atrial septostomy
- Initiation of parenteral prostanoid therapy, initiation of oxygen therapy, initiation of any other pulmonary arterial hypertension-specific therapies or need for increase of diuretics for more than 4 weeks due to worsening of pulmonary arterial hypertension
- Significant drop in six minute walk distance

End point type	Secondary

End point timeframe:

Baseline up to approximately 30 weeks

End point values	LTP001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	12		
Units: days				
median (confidence interval 95%)	211.0 (174.0 to 999)	175.0 (174.0 to 999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	LTP001 v Placebo

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6843
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.7
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.2
upper limit	2.8

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of 241 days.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	LTP001 6 mg

Reporting group description:

LTP001 6 mg

Reporting group title	Total

Reporting group description:

Total

Reporting group title	Placebo

Reporting group description:

Placebo

Serious adverse events	LTP001 6 mg	Total	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 35 (14.29%)	7 / 47 (14.89%)	2 / 12 (16.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Right ventricular failure			
subjects affected / exposed	1 / 35 (2.86%)	1 / 47 (2.13%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 35 (2.86%)	1 / 47 (2.13%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 35 (2.86%)	1 / 47 (2.13%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal pain upper			
subjects affected / exposed	0 / 35 (0.00%)	1 / 47 (2.13%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 35 (2.86%)	1 / 47 (2.13%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 35 (2.86%)	1 / 47 (2.13%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	1 / 35 (2.86%)	1 / 47 (2.13%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Catheter site cellulitis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 47 (2.13%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 35 (2.86%)	1 / 47 (2.13%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 35 (2.86%)	1 / 47 (2.13%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	LTP001 6 mg	Total	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 35 (57.14%)	27 / 47 (57.45%)	7 / 12 (58.33%)
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 35 (5.71%)	2 / 47 (4.26%)	0 / 12 (0.00%)
occurrences (all)	4	4	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	3 / 35 (8.57%)	4 / 47 (8.51%)	1 / 12 (8.33%)
occurrences (all)	3	4	1
Tachycardia			
subjects affected / exposed	0 / 35 (0.00%)	1 / 47 (2.13%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Nervous system disorders			
Presyncope			
subjects affected / exposed	2 / 35 (5.71%)	3 / 47 (6.38%)	1 / 12 (8.33%)
occurrences (all)	2	3	1
Headache			
subjects affected / exposed	6 / 35 (17.14%)	6 / 47 (12.77%)	0 / 12 (0.00%)
occurrences (all)	8	8	0
Dizziness			
subjects affected / exposed	0 / 35 (0.00%)	1 / 47 (2.13%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 35 (0.00%)	1 / 47 (2.13%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	2 / 35 (5.71%)	2 / 47 (4.26%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Influenza like illness			
subjects affected / exposed	1 / 35 (2.86%)	2 / 47 (4.26%)	1 / 12 (8.33%)
occurrences (all)	1	2	1
Fatigue			

subjects affected / exposed	2 / 35 (5.71%)	3 / 47 (6.38%)	1 / 12 (8.33%)
occurrences (all)	2	3	1
Chest discomfort			
subjects affected / exposed	0 / 35 (0.00%)	1 / 47 (2.13%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Asthenia			
subjects affected / exposed	2 / 35 (5.71%)	2 / 47 (4.26%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 35 (2.86%)	2 / 47 (4.26%)	1 / 12 (8.33%)
occurrences (all)	1	2	1
Nausea			
subjects affected / exposed	4 / 35 (11.43%)	5 / 47 (10.64%)	1 / 12 (8.33%)
occurrences (all)	4	5	1
Diarrhoea			
subjects affected / exposed	2 / 35 (5.71%)	2 / 47 (4.26%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 35 (2.86%)	2 / 47 (4.26%)	1 / 12 (8.33%)
occurrences (all)	1	2	1
Cough			
subjects affected / exposed	2 / 35 (5.71%)	3 / 47 (6.38%)	1 / 12 (8.33%)
occurrences (all)	2	3	1
Skin and subcutaneous tissue disorders			
Rash pruritic			
subjects affected / exposed	0 / 35 (0.00%)	1 / 47 (2.13%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Pruritus			
subjects affected / exposed	2 / 35 (5.71%)	2 / 47 (4.26%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	2 / 35 (5.71%)	2 / 47 (4.26%)	0 / 12 (0.00%)
occurrences (all)	2	2	0

Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 35 (5.71%)	2 / 47 (4.26%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Back pain			
subjects affected / exposed	2 / 35 (5.71%)	2 / 47 (4.26%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Arthralgia			
subjects affected / exposed	3 / 35 (8.57%)	3 / 47 (6.38%)	0 / 12 (0.00%)
occurrences (all)	7	7	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 47 (2.13%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Respiratory tract infection			
subjects affected / exposed	2 / 35 (5.71%)	2 / 47 (4.26%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Nasopharyngitis			
subjects affected / exposed	2 / 35 (5.71%)	2 / 47 (4.26%)	0 / 12 (0.00%)
occurrences (all)	3	3	0
Influenza			
subjects affected / exposed	3 / 35 (8.57%)	3 / 47 (6.38%)	0 / 12 (0.00%)
occurrences (all)	3	3	0
COVID-19			
subjects affected / exposed	0 / 35 (0.00%)	1 / 47 (2.13%)	1 / 12 (8.33%)
occurrences (all)	0	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 December 2021	This amendment: required a negative serum pregnancy test within 7 days prior to first dose administration on Day 1 to rule out pregnancy where required by health authority (e. g., the United Kingdom) or local regulations. In countries where this was not required, a negative urine pregnancy test needed to be available prior to dosing on Day 1; excluded participants who took strong CYP3A4/5 inducers or inhibitors; excluded participants who had a long QT syndrome or who took drugs known to prolong the QT interval; added strong CYP3A4/5 inducers, strong CYP3A4/5 inhibitors, and known drugs which cause QT prolongation to the prohibited medications list; specified that 6MWT was only to be conducted on-site to remove testing variability in the assessment; removed the requirement for participants to record investigational medicinal product (IMP) dosing every day in the eDiary; specified that compliance for IMP administration was to be done by medication reconciliation; added coagulation assays (PT, INR, aPTT) and luteinizing hormone and follicle stimulating hormone (FSH) to the safety laboratory panel.
02 March 2022	This amendment: updated clinical safety data; added guidance text for 6MWT and multi-sensor device; updated withdrawal of consent language to improve clarity.
01 November 2022	This amendment: incorporated language regarding the implementation of a data monitoring committee (DMC); updated exclusion criteria with information about sperm donation to reflect the requirements described in the protocol appendix; updated protocol appendix with further guidance details for hepatic and renal alert criteria and event follow-up; updated protocol appendix with considerations about the use of LTP001 in combination with allowed standard therapies.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Notes: