



## Clinical trial results:

### An open-label extension study to investigate efficacy, safety and tolerability of LTP001 in participants with pulmonary arterial hypertension

#### Summary

EudraCT number	2022-002007-38
Trial protocol	ES NL
Global end of trial date	14 May 2024

#### Results information

Result version number	v1 (current)
This version publication date	08 May 2025
First version publication date	08 May 2025

#### Trial information

##### Trial identification

Sponsor protocol code	CLTP001A12201E1
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05764265
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	14 May 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	14 May 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 long-term safety 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	27 March 2023
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	Argentina: 3
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	31
EEA total number of subjects	24

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)	27
From 65 to 84 years	4
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 31 participants who completed the parent study up to the end of treatment were screened for the extension study.

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	LTP001 6 mg (Actual Treatment in CLTP001A12201)

Arm description:

Participants had received LTP001, 6 mg, in Study CLTP001A12201, and continued to receive LTP001, 6 mg, orally once daily in the morning for approximately 52 weeks in this extension study

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:

Participants received LTP001, 6 mg, orally once daily in the morning for approximately 52 weeks

<b>Arm title</b>	LTP001 6 mg (Placebo in CLTP001A12201)
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Arm description:

Participants had received placebo in Study CLTP001A12201, followed by LTP001, 6 mg, orally once daily in the morning for approximately 52 weeks in this extension study

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:

Participants received LTP001, 6 mg, orally once daily in the morning for approximately 52 weeks

<b>Number of subjects in period 1</b>	LTP001 6 mg (Actual Treatment in CLTP001A12201)	LTP001 6 mg (Placebo in CLTP001A12201)
Started	23	8
Completed	0	0
Not completed	23	8
Participant Decision	1	-

Physician decision	1	8
Adverse event, non-fatal	1	-
Study Terminated By Sponsor	20	-

## Baseline characteristics

### Reporting groups

Reporting group title	LTP001 6 mg (Actual Treatment in CLTP001A12201)
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Reporting group description:

Participants had received LTP001, 6 mg, in Study CLTP001A12201, and continued to receive LTP001, 6 mg, orally once daily in the morning for approximately 52 weeks in this extension study

Reporting group title	LTP001 6 mg (Placebo in CLTP001A12201)
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Reporting group description:

Participants had received placebo in Study CLTP001A12201, followed by LTP001, 6 mg, orally once daily in the morning for approximately 52 weeks in this extension study

Reporting group values	LTP001 6 mg (Actual Treatment in CLTP001A12201)	LTP001 6 mg (Placebo in CLTP001A12201)	Total
Number of subjects	23	8	31
Age Categorical Units: Participants			
18 - <65	20	7	27
65 - <85	3	1	4
Age Continuous Units: Years arithmetic mean standard deviation	47.0 ± 11.76	48.4 ± 13.35	-
Sex: Female, Male Units: Participants			
Female	21	6	27
Male	2	2	4
Race/Ethnicity, Customized Units: Subjects			
White	21	7	28
American Indian or Alaskan	2	0	2
Asian	0	1	1

## End points

### End points reporting groups

Reporting group title	LTP001 6 mg (Actual Treatment in CLTP001A12201)
Reporting group description: Participants had received LTP001, 6 mg, in Study CLTP001A12201, and continued to receive LTP001, 6 mg, orally once daily in the morning for approximately 52 weeks in this extension study	
Reporting group title	LTP001 6 mg (Placebo in CLTP001A12201)
Reporting group description: Participants had received placebo in Study CLTP001A12201, followed by LTP001, 6 mg, orally once daily in the morning for approximately 52 weeks in this extension study	

### Primary: Number of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) <sup>[1]</sup>
End point description: Incidence and severity of adverse events (AEs) by treatment group, including changes in the vital signs, electrocardiogram and laboratory results qualifying and reported as AEs.	
End point type	Primary
End point timeframe: 52 weeks	

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 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	8		
Units: Percentage of participants				
number (not applicable)				
AEs	52.2	62.5		
Serious AEs	17.4	0		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Average Cardiac Output (CO) at Week 26

End point title	Change From Baseline in Average Cardiac Output (CO) at Week 26
End point description: Right heart catheterization (RHC) assessment was performed to assess several hemodynamic variables in pulmonary hypertension, including CO.	

End point type	Secondary
End point timeframe:	
Baseline, Week 26	

<b>End point values</b>	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: liters per minute				
arithmetic mean (standard deviation)	-0.111 ( $\pm$ 0.2153)	-0.065 ( $\pm$ 0.5916)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Mean Pulmonary Artery (PA) Pressure at Week 26

End point title	Change From Baseline in Mean Pulmonary Artery (PA) Pressure at Week 26
End point description:	
Right heart catheterization (RHC) assessment was performed to assess several hemodynamic variables in pulmonary hypertension, including PA pressure.	
End point type	Secondary
End point timeframe:	
Baseline, Week 26	

<b>End point values</b>	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: mmHg				
arithmetic mean (standard deviation)	3.8 ( $\pm$ 8.18)	-1.5 ( $\pm$ 7.78)		

### Statistical analyses

No statistical analyses for this end point



**Secondary: Change From Baseline in Pulmonary Capillary Wedge Pressure (PCWP) at Week 26**

End point title	Change From Baseline in Pulmonary Capillary Wedge Pressure (PCWP) at Week 26
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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
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End point timeframe:

Baseline, Week 26

End point values	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: mmHg				
arithmetic mean (standard deviation)	-1.0 ( $\pm$ 1.79)	-0.5 ( $\pm$ 0.71)		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change From Baseline in Right Heart Catheterization Pulmonary Vascular Resistance (PVR) at Week 26**

End point title	Change From Baseline in Right Heart Catheterization Pulmonary Vascular Resistance (PVR) at Week 26
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End point description:

PVR was defined as the resistance against blood flow from the pulmonary artery to the left atrium measured in dynes.sec.cm-5.

End point type	Secondary
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End point timeframe:

Baseline, Week 26

End point values	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: dynes.sec.cm-5				
arithmetic mean (standard deviation)	100.058 ( $\pm$ 95.5879)	-7.445 ( $\pm$ 34.8250)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Right Atrium (RA) Pressures at Week 26

End point title	Change From Baseline in Right Atrium (RA) Pressures at Week 26
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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
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End point timeframe:

Baseline, Week 26

End point values	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: mmHg				
arithmetic mean (standard deviation)	-1.5 ( $\pm$ 6.22)	0.0 ( $\pm$ 2.83)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Systemic Vascular Resistance (SVR) at Week 26

End point title	Change From Baseline in Systemic Vascular Resistance (SVR) at Week 26
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End point description:

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

End point type	Secondary
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End point timeframe:

Baseline, Week 26

End point values	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: dynes.sec.cm-5				
arithmetic mean (standard deviation)	166.748 (± 128.6202)	-49.710 (± 28.5388)		

### 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 participant can walk on a flat, hard surface in a period of 6 minutes.	
End point type	Secondary
End point timeframe: Baseline, Week 26, Week 52	

End point values	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	2		
Units: meters				
arithmetic mean (standard deviation)				
Week 26 n=6,2	-33.7 (± 55.60)	-9.0 (± 25.46)		
End of Treatment n=16,2	-6.3 (± 50.21)	-1.0 (± 1.41)		

### 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, Week 26, Week 52	

<b>End point values</b>	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	2		
Units: centimeters				
arithmetic mean (standard deviation)				
Week 26 n=6,2	0.03 (± 0.175)	0.00 (± 0.283)		
End of Treatment n=7,0	0.01 (± 0.682)	999 (± 999)		

### Statistical analyses

No statistical analyses for this end point

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

End point title	Change From Baseline in Tricuspid Annular Plane 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, Week 26, Week 52	

<b>End point values</b>	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	2		
Units: centimeters per second				
arithmetic mean (standard deviation)				
Week 26 n=6,2	-2.2 (± 3.43)	-0.5 (± 0.71)		
End of Treatment n=7,0	-2.6 (± 1.90)	999 (± 999)		

### 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')
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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 and RV S' data in this results disclosure are the same.

End point type	Secondary
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End point timeframe:

Baseline, Week 26, Week 52

End point values	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	2		
Units: centimeters per second				
arithmetic mean (standard deviation)				
Week 26 n=6,2	-2.2 (± 3.43)	-0.5 (± 0.71)		
End of Treatment n=7,0	-2.6 (± 1.90)	999 (± 999)		

### 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)
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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
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End point timeframe:

Baseline, Week 26, Week 52

End point values	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	1		
Units: percent				
arithmetic mean (standard deviation)				
Week 26 n=6,1	-0.87 (± 6.162)	7.30 (± 999)		
End of Treatment n=6,0	0.97 (± 5.290)	999 (± 999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Quality of Life Measured by the emPHasis-10 Questionnaire

End point title	Change From Baseline in Quality of Life Measured by the emPHasis-10 Questionnaire
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 to Week 52	

End point values	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	1		
Units: score				
arithmetic mean (standard deviation)	1.476 (± 2.3226)	1.000 (± 999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Quality of Life Measured by the PAH-SYMPACT Questionnaire

End point title	Change From Baseline in Quality of Life Measured by the PAH-SYMPACT Questionnaire
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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 to Week 52

End point values	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: score				
arithmetic mean (standard deviation)	2.929 ( $\pm$ 2.3234)	-0.833 ( $\pm$ 999)		

## 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 to Week 52

End point values	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	0 <sup>[2]</sup>		
Units: days				
median (confidence interval 95%)	346.0 (187.0 to 999)	( to )		

Notes:

[2] - There were no participants with available data.

## 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)
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End point description:

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

End point type	Secondary
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End point timeframe:

Baseline to Week 52

End point values	LTP001 6 mg (Actual Treatment in CLTP001A1220 1)	LTP001 6 mg (Placebo in CLTP001A1220 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	6		
Units: picomoles per liter				
arithmetic mean (standard deviation)	3.832 ( $\pm$ 31.2255)	7.250 ( $\pm$ 16.6033)		

## Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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### Reporting groups

Reporting group title	LTP001 6 mg (TRT in LTP001A12201)
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Reporting group description:

LTP001 6 mg (TRT in LTP001A12201)

Reporting group title	Total
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Reporting group description:

Total

Reporting group title	LTP001 6 mg (PBO in LTP001A12201)
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Reporting group description:

LTP001 6 mg (PBO in LTP001A12201)

Serious adverse events	LTP001 6 mg (TRT in LTP001A12201)	Total	LTP001 6 mg (PBO in LTP001A12201)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 23 (17.39%)	4 / 31 (12.90%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Medical device site haemorrhage			
subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	0 / 8 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary arterial hypertension			
subjects affected / exposed	2 / 23 (8.70%)	2 / 31 (6.45%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related infection			

subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	0 / 8 (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
Disseminated gonococcal infection			
subjects affected / exposed	1 / 23 (4.35%)	1 / 31 (3.23%)	0 / 8 (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 (TRT in LTP001A12201)	Total	LTP001 6 mg (PBO in LTP001A12201)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 23 (21.74%)	10 / 31 (32.26%)	5 / 8 (62.50%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	1 / 23 (4.35%)	2 / 31 (6.45%)	1 / 8 (12.50%)
occurrences (all)	1	3	2
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Eye disorders			
Eczema eyelids			
subjects affected / exposed	0 / 23 (0.00%)	1 / 31 (3.23%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Epistaxis			

subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 31 (3.23%) 1	1 / 8 (12.50%) 1
Nasal congestion subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2	2 / 31 (6.45%) 2	0 / 8 (0.00%) 0
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 31 (3.23%) 1	1 / 8 (12.50%) 1
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2	2 / 31 (6.45%) 2	0 / 8 (0.00%) 0
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 31 (3.23%) 1	1 / 8 (12.50%) 1
Musculoskeletal stiffness subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 31 (3.23%) 1	1 / 8 (12.50%) 1
Infections and infestations Tooth abscess subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 31 (3.23%) 1	1 / 8 (12.50%) 1
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2	3 / 31 (9.68%) 3	1 / 8 (12.50%) 1
Bronchitis subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 31 (3.23%) 1	1 / 8 (12.50%) 1
Bartholinitis subjects affected / exposed occurrences (all)	0 / 23 (0.00%) 0	1 / 31 (3.23%) 1	1 / 8 (12.50%) 1

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 January 2023	This amendment: incorporated safety follow-up visits at Weeks 9 and 17; updated the protocol appendix and Safety Assessments table with further guidance for renal alert criteria and follow-up guidelines; removed Inclusion Criterion 4 to avoid the exclusion of participants who may have progressed on placebo; corrected for administrative inconsistencies and added further protocol clarifications to ensure data quality.

Notes:

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### 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: