Clinical trial results:
A Phase 2, Double-Blind, Placebo-Controlled, Randomized Study to Compare the Efficacy and Safety of Sotatercept (ACE-011) Versus Placebo When Added to Standard of Care for the Treatment of Pulmonary Arterial Hypertension (PAH)

Summary

EudraCT number	2017-004738-27
Trial protocol	DE BE ES
Global end of trial date	09 March 2022

Results information

Result version number	v1
This version publication date	22 March 2023
First version publication date	22 March 2023

Trial information

Trial identification

Sponsor protocol code	A011-09

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03496207
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Protocol: MK-7962-001

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.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	09 March 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 March 2022
Global end of trial reached?	Yes
Global end of trial date	09 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Study A011-09 is designed to assesses the efficacy and safety of sotatercept (ACE-011) relative to placebo in adults with pulmonary arterial hypertension (PAH). Eligible participants will receive study treatment for 24 weeks during the placebo-controlled treatment period, and then will be eligible to enroll into a 30-month extension period during which all participants will receive sotatercept. All treated patients will also undergo a follow-up period after last study drug treatment.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 June 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Brazil: 26
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 27
Worldwide total number of subjects	106
EEA total number of subjects	33

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)	87
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study enrolled adults with pulmonary arterial hypertension (PAH). Other inclusion criteria applied.

Period 1

Period 1 title	Base Study
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo plus standard of care (SOC) by SC injection during the 24-week treatment period (Base Study; Cycles 1-8). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Arm type	Placebo
Investigational medicinal product name	Standard of Care (SOC)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection, Tablet, Inhalation solution
Routes of administration	Subcutaneous use, Oral use, Inhalation use, Intravenous use

Dosage and administration details:

SOC therapy refers to approved PAH-specific medications and may consist of monotherapy or combination therapy with endothelin-receptor antagonists, phosphodiesterase 5 (PDE5) inhibitors, soluble guanylate cyclase stimulators, and/or prostacyclin analogues or receptor agonists.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo once every 3 weeks

Arm title	Sotatercept 0.3 mg/kg

Arm description:

Participants received sotatercept 0.3 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) and 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Arm type	Experimental
Investigational medicinal product name	SOC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection, Tablet, Inhalation solution
Routes of administration	Subcutaneous use, Oral use, Inhalation use, Intravenous use

Dosage and administration details:

SOC therapy refers to approved PAH-specific medications and may consist of monotherapy or combination therapy with endothelin-receptor antagonists, phosphodiesterase 5 (PDE5) inhibitors, soluble guanylate cyclase stimulators, and/or prostacyclin analogues or receptor agonists.

Investigational medicinal product name	Sotatercept
Investigational medicinal product code	
Other name	ACE-011, MK-7962
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Sotatercept 0.3 mg/kg once every three weeks

Arm title	Sotatercept 0.7 mg/kg

Arm description:

Participants received sotatercept 0.7 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) and 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Arm type	Experimental
Investigational medicinal product name	SOC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection, Tablet, Inhalation solution
Routes of administration	Subcutaneous use, Oral use, Inhalation use, Intravenous use

Dosage and administration details:

SOC therapy refers to approved PAH-specific medications and may consist of monotherapy or combination therapy with endothelin-receptor antagonists, phosphodiesterase 5 (PDE5) inhibitors, soluble guanylate cyclase stimulators, and/or prostacyclin analogues or receptor agonists.

Investigational medicinal product name	Sotatercept
Investigational medicinal product code	
Other name	ACE-011, MK-7962
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Sotatercept 0.7 mg/kg once every three weeks

Number of subjects in period 1	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg
Started	32	32	42
Completed	30	31	36
Not completed	2	1	6
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	1	-	1
Adverse event, non-fatal	1	1	4

Period 2

Period 2 title	Extension Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Extension Period: PlaceboSotatercept 0.3 mg/kg

Arm description:

This treatment group represents participants from the Placebo arm who received placebo plus standard of care (SOC) by subcutaneous (SC) injection during the 24-week treatment period (Base Study; Cycles 1-8), then transitioned to the 30-month extension period (Cycles 9-51), during which they received sotatercept 0.3 mg/kg plus SOC by SC injection. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Arm type	Placebo-crossed
Investigational medicinal product name	SOC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection, Tablet, Inhalation solution
Routes of administration	Subcutaneous use, Oral use, Inhalation use, Intravenous use

Dosage and administration details:

SOC therapy refers to approved PAH-specific medications and may consist of monotherapy or combination therapy with endothelin-receptor antagonists, phosphodiesterase 5 (PDE5) inhibitors, soluble guanylate cyclase stimulators, and/or prostacyclin analogues or receptor agonists.

Investigational medicinal product name	Sotatercept
Investigational medicinal product code	
Other name	ACE-011, MK-7962
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Sotatercept 0.3 mg/kg once every three weeks

Arm title	Extension Period: PlaceboSotatercept 0.7 mg/kg

Arm description:

This treatment group represents participants from the Placebo arm who received placebo plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8), then transitioned to the 30-month extension period (Cycles 9-51), during which they received sotatercept 0.7 mg/kg plus SOC by SC injection. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Arm type	Placebo-crossed
Investigational medicinal product name	SOC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection, Tablet, Inhalation solution
Routes of administration	Subcutaneous use, Oral use, Inhalation use, Intravenous use

Dosage and administration details:

SOC therapy refers to approved PAH-specific medications and may consist of monotherapy or combination therapy with endothelin-receptor antagonists, phosphodiesterase 5 (PDE5) inhibitors, soluble guanylate cyclase stimulators, and/or prostacyclin analogues or receptor agonists.

Investigational medicinal product name	Sotatercept
Investigational medicinal product code	
Other name	ACE-011, MK-7962
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Sotatercept 0.7 mg/kg once every three weeks

Arm title	Extension Period: Sotatercept 0.3 mg/kg

Arm description:

Participants received sotatercept 0.3 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) and 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Arm type	Experimental
Investigational medicinal product name	SOC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection, Tablet, Inhalation solution
Routes of administration	Subcutaneous use, Oral use, Inhalation use, Intravenous use

Dosage and administration details:

SOC therapy refers to approved PAH-specific medications and may consist of monotherapy or combination therapy with endothelin-receptor antagonists, phosphodiesterase 5 (PDE5) inhibitors, soluble guanylate cyclase stimulators, and/or prostacyclin analogues or receptor agonists.

Investigational medicinal product name	Sotatercept
Investigational medicinal product code	
Other name	ACE-011, MK-7962
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Sotatercept 0.3 mg/kg once every three weeks

Arm title	Extension Period: Sotatercept 0.7 mg/kg

Arm description:

Participants received sotatercept 0.7 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) and 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Arm type	Experimental
Investigational medicinal product name	SOC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection, Tablet, Inhalation solution
Routes of administration	Subcutaneous use, Oral use, Inhalation use, Intravenous use

Dosage and administration details:

SOC therapy refers to approved PAH-specific medications and may consist of monotherapy or combination therapy with endothelin-receptor antagonists, phosphodiesterase 5 (PDE5) inhibitors, soluble guanylate cyclase stimulators, and/or prostacyclin analogues or receptor agonists.

Investigational medicinal product name	Sotatercept
Investigational medicinal product code	
Other name	ACE-011, MK-7962
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Sotatercept 0.7 mg/kg once every three weeks

Number of subjects in period 2	Extension Period: PlaceboSotatercept 0.3 mg/kg	Extension Period: PlaceboSotatercept 0.7 mg/kg	Extension Period: Sotatercept 0.3 mg/kg
Started	15	15	31
Completed	13	15	28
Not completed	2	0	3
Adverse event, serious fatal	1	-	1
Consent withdrawn by subject	1	-	1
Adverse event, non-fatal	-	-	1

Elevated hemoglobin levels	-	-	-

Number of subjects in period 2	Extension Period: Sotatercept 0.7 mg/kg
Started	36
Completed	31
Not completed	5
Adverse event, serious fatal	2
Consent withdrawn by subject	1
Adverse event, non-fatal	1
Elevated hemoglobin levels	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo plus standard of care (SOC) by SC injection during the 24-week treatment period (Base Study; Cycles 1-8). Each cycle was 21 days. Dosing occurred once every 3 weeks.	
Reporting group title	Sotatercept 0.3 mg/kg
Reporting group description:	
Participants received sotatercept 0.3 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) and 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.	
Reporting group title	Sotatercept 0.7 mg/kg
Reporting group description:	
Participants received sotatercept 0.7 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) and 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.	

Reporting group values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg
Number of subjects	32	32	42
Age categorical Units: Subjects			
Age Continuous Units: Years			
arithmetic mean	45.6	49.1	49.8
standard deviation	± 13.38	± 14.34	± 15.05
Sex: Female, Male Units: Participants			
Female	26	29	37
Male	6	3	5
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	1	0	0
Black or African American	0	1	3
White	30	31	37
More than one race	1	0	1
Unknown or Not Reported	0	0	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	10	9	13
Not Hispanic or Latino	21	19	28
Unknown or Not Reported	1	4	1

Reporting group values	Total		
Number of subjects	106		

Age categorical Units: Subjects			

Age Continuous Units: Years arithmetic mean standard deviation	- -		
Sex: Female, Male Units: Participants			
Female	92		
Male	14		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	1		
Black or African American	4		
White	98		
More than one race	2		
Unknown or Not Reported	1		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	32		
Not Hispanic or Latino	68		
Unknown or Not Reported	6		

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo plus standard of care (SOC) by SC injection during the 24-week treatment period (Base Study; Cycles 1-8). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Reporting group title	Sotatercept 0.3 mg/kg

Reporting group description:

Participants received sotatercept 0.3 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) and 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Reporting group title	Sotatercept 0.7 mg/kg

Reporting group description:

Participants received sotatercept 0.7 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) and 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Reporting group title	Extension Period: PlaceboSotatercept 0.3 mg/kg

Reporting group description:

This treatment group represents participants from the Placebo arm who received placebo plus standard of care (SOC) by subcutaneous (SC) injection during the 24-week treatment period (Base Study; Cycles 1-8), then transitioned to the 30-month extension period (Cycles 9-51), during which they received sotatercept 0.3 mg/kg plus SOC by SC injection. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Reporting group title	Extension Period: PlaceboSotatercept 0.7 mg/kg

Reporting group description:

This treatment group represents participants from the Placebo arm who received placebo plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8), then transitioned to the 30-month extension period (Cycles 9-51), during which they received sotatercept 0.7 mg/kg plus SOC by SC injection. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Reporting group title	Extension Period: Sotatercept 0.3 mg/kg

Reporting group description:

Participants received sotatercept 0.3 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) and 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Reporting group title	Extension Period: Sotatercept 0.7 mg/kg

Reporting group description:

Participants received sotatercept 0.7 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) and 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Subject analysis set title	Placebo-Crossed Treatment Group
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received placebo plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) were re-randomized to receive either 0.3 mg/kg or 0.7 mg/kg of sotatercept plus SOC during 30-month extension period (Cycles 9-51). Per protocol, for Delayed-Start Analysis, the Placebo-Crossed Treatment Group included all participants who received 0.3 mg/kg plus SOC or 0.7 mg/kg of sotatercept plus SOC after a full course of placebo, regardless of their dose level. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Subject analysis set title	Continued Sotatercept Treatment Group
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who were randomized to receive either 0.3 mg/kg or 0.7 mg/kg of sotatercept plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) continued to receive sotatercept 0.3 mg/kg or 0.7 mg/kg plus SOC during the 30-month extension period (Cycles 9-51). Per protocol, for Delayed-Start Analysis, the Continued Sotatercept Treatment Group combined participants who received 0.3 mg/kg or 0.7 mg/kg of sotatercept plus SOC. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Subject analysis set title	Placebo-Crossed Treatment Group
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received placebo plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) were re-randomized to receive either 0.3 mg/kg or 0.7 mg/kg of sotatercept plus SOC during 30-month extension period (Cycles 9-51). Per protocol, for Placebo-Crossed Analysis, the Placebo-Crossed Treatment Group included all participants who received 0.3 mg/kg plus SOC or 0.7 mg/kg of sotatercept plus SOC after a full course of placebo, regardless of their dose level. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Subject analysis set title	Placebo-Crossed treatment group
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received placebo plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) were re-randomized to receive either 0.3 mg/kg or 0.7 mg/kg of sotatercept plus SOC during 30-month extension period (Cycles 9-51). Per protocol, for Delayed-Start Analysis, the Placebo-Crossed Treatment Group included all participants who received 0.3 mg/kg plus SOC or 0.7 mg/kg of sotatercept plus SOC after a full course of placebo, regardless of their dose level. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Subject analysis set title	Continued Sotatercept Treatment Group
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who were randomized to receive either 0.3 mg/kg or 0.7 mg/kg of sotatercept plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) continued to receive sotatercept 0.3 mg/kg or 0.7 mg/kg plus SOC during the 30-month extension period (Cycles 9-51). Per protocol, for Delayed-Start Analysis, the Continued Sotatercept Treatment Group combined participants who received 0.3 mg/kg or 0.7 mg/kg of sotatercept plus SOC. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Subject analysis set title	Placebo-Crossed Treatment Group
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received placebo plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) were re-randomized to receive either 0.3 mg/kg or 0.7 mg/kg of sotatercept plus SOC during 30-month extension period (Cycles 9-51). Per protocol, for Placebo-Crossed Analysis, the Placebo-Crossed Treatment Group included all participants who received 0.3 mg/kg plus SOC or 0.7 mg/kg of sotatercept plus SOC after a full course of placebo, regardless of their dose level. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Subject analysis set title	Extension Period: PlaceboSotatercept 0.3 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

This treatment group represents participants from the Placebo arm who received placebo plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8), then transitioned to the 30-month extension period (Cycles 9-51), during which they received sotatercept 0.3 mg/kg plus SOC by SC injection. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Subject analysis set title	Extension Period: PlaceboSotatercept 0.7 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

This treatment group represents participants from the Placebo arm who received placebo plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8), then transitioned to the 30-month extension period (Cycles 9-51), during which they received sotatercept 0.7 mg/kg plus SOC by SC injection. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Subject analysis set title	Extension Period: Sotatercept 0.3 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who received sotatercept 0.3 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) continued to receive sotatercept 0.3 mg/kg plus SOC during the 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Subject analysis set title	Extension Period: Sotatercept 0.7 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who received sotatercept 0.7 mg/kg plus SOC by SC injection during the 24-week treatment

period (Base Study; Cycles 1-8) continued to receive sotatercept 0.7 mg/kg plus SOC during the 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Primary: Base Study: Change from Baseline in Pulmonary Vascular Resistance (PVR) at 24 Weeks

End point title	Base Study: Change from Baseline in Pulmonary Vascular Resistance (PVR) at 24 Weeks

End point description:

Each participant's PVR, at resting supine, was measured by right heart catheterization at baseline and at 24 weeks. The analysis population for this endpoint included all randomized participants administered their assigned treatment who received at least 6 of the same doses during Base Study, had baseline and post-Base Study PVR assessment and End of Treatment (EOT) assessment. Note: Data from participants whose dose was down-titrated were analyzed according to dose received at least 6 times rather than dose originally assigned. Per protocol, only participants who consistently received in 0.3 mg/kg or 0.7 mg/kg of sotatercept were planned to be analyzed.

End point type	Primary

End point timeframe:

Baseline and 24 weeks

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	27	30	
Units: dynes*sec/cm^5				
arithmetic mean (standard deviation)				
Change from Baseline in PVR at 24 Weeks	-27.6 (± 251.08)	-168.4 (± 262.93)	-258.9 (± 169.42)	
Baseline	802.0 (± 331.05)	772.0 (± 285.62)	715.5 (± 267.11)	

Statistical analyses

Statistical analysis title	Difference in Least Squares Means

Statistical analysis description:

Analysis based on calculated LS means.

Comparison groups	Sotatercept 0.3 mg/kg v Placebo
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.003
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-151.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-249.59
upper limit	-52.63
Variability estimate	Standard error of the mean
Dispersion value	49.53

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description: Analysis based on calculated LS means.	
Comparison groups	Placebo v Sotatercept 0.7 mg/kg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-269.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-365.81
upper limit	-173.03
Variability estimate	Standard error of the mean
Dispersion value	48.48

Primary: Extension Period: Change from Baseline in PVR (Delayed-Start Analysis)	
End point title	Extension Period: Change from Baseline in PVR (Delayed-Start Analysis)
End point description: Each participant's PVR, at resting supine, was measured by right heart catheterization at baseline and the timepoint at which the third right heart catheterization was performed, which occurred between Month 18 and Month 24. The analysis population for this endpoint included all randomized participants who received their assigned treatment, transitioned to the extension period, and had data for the respective timepoints.	
End point type	Primary
End point timeframe: Baseline and timepoint at which third right heart catheterization was performed, which occurred between Month 18 and Month 24	

End point values	Placebo-Crossed Treatment Group	Continued Sotatercept Treatment Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	67		
Units: dynes*sec/cm^5				
arithmetic mean (standard deviation)				
Ext: Chg from BL in PVR (Delayed-Start Analysis) Baseline	-246.9 (± 300.01) 802.0 (± 331.05)	-212.6 (± 254.24) 783.7 (± 371.59)		

Statistical analyses

Statistical analysis title	Difference in Least Squares Means
Statistical analysis description: Analysis based on calculated LS means.	
Comparison groups	Placebo-Crossed Treatment Group v Continued Sotatercept Treatment Group
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7851
Method	ANCOVA
Parameter estimate	Difference in Least Squares Means
Point estimate	-13.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-113.85
upper limit	86.06
Variability estimate	Standard error of the mean
Dispersion value	50.95

Primary: Extension Period: Number of Participants Who Experienced One or More Adverse Events (AEs)

End point title	Extension Period: Number of Participants Who Experienced One or More Adverse Events (AEs)[1]

End point description:

An AE is any untoward medical occurrence in a study participant administered a pharmaceutical product that does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product. The analysis population for this endpoint included all randomized participants who transitioned to the extension period and received at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

Up to approximately 32 months

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 was no between-group statistical analysis calculated for this endpoint.

End point values	Extension Period: PlaceboSotatercept 0.3 mg/kg	Extension Period: PlaceboSotatercept 0.7 mg/kg	Extension Period: Sotatercept 0.3 mg/kg	Extension Period: Sotatercept 0.7 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	15	31	36
Units: Participants	14	15	31	36

Statistical analyses

No statistical analyses for this end point

Primary: Extension Period: Change from Baseline in PVR (Placebo-Crossed Analysis)

End point title	Extension Period: Change from Baseline in PVR (Placebo-Crossed Analysis)[2]

End point description:

Each participant's PVR, at resting supine, was measured by right heart catheterization at baseline and the timepoint at which the third right heart catheterization was performed, which occurred between Month 18 and Month 24. The analysis population for this endpoint included all randomized participants who received their assigned treatment, transitioned to the extension period, and had data for the respective timepoints.

End point type	Primary

End point timeframe:

Baseline and the timepoint at which the third right heart catheterization was performed, which occurred between Month 18 and Month 24.

Notes:

[2] - 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 was no between-group statistical analysis calculated for this endpoint.

End point values	Placebo-Crossed Treatment Group			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: dynes*sec/cm^5				
arithmetic mean (standard deviation)				
Ext: Chg from BL in PVR (Placebo-Crossed Analysis)	-246.9 (± 300.01)			
Baseline	802.0 (± 331.05)			

Statistical analyses

No statistical analyses for this end point

Primary: Extension Period: Number of Participants Who Discontinued Study Treatment Due to an AE

End point title	Extension Period: Number of Participants Who Discontinued Study Treatment Due to an AE[3]

End point description:

An AE is any untoward medical occurrence in a study participant administered a pharmaceutical product that does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product. The analysis population for this endpoint included all randomized participants who transitioned to the extension period and received at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

Up to 30 months

Notes:

[3] - 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 was no between-group statistical analysis calculated for this endpoint.

End point values	Extension Period: PlaceboSotatercept 0.3 mg/kg	Extension Period: PlaceboSotatercept 0.7 mg/kg	Extension Period: Sotatercept 0.3 mg/kg	Extension Period: Sotatercept 0.7 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	15	31	36
Units: Participants	1	0	1	3

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Change from Baseline in Concentration of Amino-Terminal Brain Natriuretic Propeptide (NT-proBNP) at 24 Weeks

End point title	Base Study: Change from Baseline in Concentration of Amino-Terminal Brain Natriuretic Propeptide (NT-proBNP) at 24 Weeks

End point description:

Each participant's laboratory biomarkers N-terminal prohormone brain-type natriuretic peptide (NT-proBNP) or brain-type natriuretic peptide (BNP) were measured at baseline and at 24 weeks. The analysis population for this endpoint included all randomized participants administered their assigned treatment who received ≥6 of the same doses during Base Study, had baseline and post-Base Study PVR assessment and EOT assessment, and had data for the outcome measure. Note: Data from participants whose dose was down-titrated were analyzed according to dose received ≥6 times rather than dose originally assigned. Per protocol, only participants who consistently received in 0.3 mg/kg or 0.7 mg/kg of sotatercept were planned to be analyzed.

End point type	Secondary

End point timeframe:

Baseline and 24 Weeks

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	25	28	
Units: pg/mL				
arithmetic mean (standard deviation)	195.9 (± 726.46)	-718.2 (± 965.12)	-359.0 (± 757.58)	

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Change from Baseline in 6-Minute Walk Distance (6MWD) at 24 Weeks

End point title	Base Study: Change from Baseline in 6-Minute Walk Distance (6MWD) at 24 Weeks

End point description:

6MWD is measured by an exercise test known as 6-Minute Walk Test (6MWT) that assesses aerobic capacity and endurance. It measures the distance covered over a time of 6 minutes and is used as an outcome measure by which to compare changes in performance capacity. Each participant's 6MWD was measured at baseline and at 24 weeks. An increase in the distance walked during the 6MWT indicates improvement in basic mobility. The analysis population for this endpoint included all randomized participants administered their assigned treatment who received at least 6 of the same doses during Base Study, had baseline and post-Base Study PVR assessment and EOT assessment. Note: Data from participants whose dose was down-titrated were analyzed according to dose received at least 6 times rather than dose originally assigned. Per protocol, only participants who consistently received in 0.3 mg/kg or 0.7 mg/kg of sotatercept were planned to be analyzed.

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	27	30	
Units: meters				
least squares mean (standard error)	31.4 (± 9.69)	56.0 (± 10.07)	53.6 (± 9.84)	

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Change from Baseline in Tricuspid Annular Plane Systolic Excursion (TAPSE) at 24 Weeks

End point title	Base Study: Change from Baseline in Tricuspid Annular Plane Systolic Excursion (TAPSE) at 24 Weeks

End point description:

Each participant's TAPSE, which is commonly used to evaluate tricuspid valve annulus movement as an indicator of right heart function, was measured by echocardiography at baseline and 24 weeks. The analysis population for this endpoint included all randomized participants administered their assigned treatment who received ≥6 of the same doses during Base Study, had baseline and post-Base Study PVR assessment and EOT assessment, and had data for the outcome measure. Note: Data from participants whose dose was down-titrated were analyzed according to dose received ≥6 times rather

than dose originally assigned. Per protocol, only participants who consistently received in 0.3 mg/kg or 0.7 mg/kg of sotatercept were planned to be analyzed.

End point type	Secondary

End point timeframe:

Baseline and 24 weeks

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	24	28	
Units: cm				
arithmetic mean (standard deviation)	0.0 (± 0.39)	0.1 (± 0.26)	-0.1 (± 0.34)	

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Change from Baseline in Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR) Score at Cycle 9

End point title	Base Study: Change from Baseline in Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR) Score at Cycle 9

End point description:

The CAMPHOR is participant-reported questionnaire that contains 65 items: 25 relating to symptoms, 15 relating to activities, and 25 relating to quality of life (QoL). Symptom and QoL items are both scored from 0-25, with a higher score indicating a worse QoL and greater functional limitation. Activity items are scored from 0-30, with a higher score indicating poorer functioning. Each participant's CAMPHOR score was recorded at baseline and on Day 1 of Cycle 9. Analysis population: all randomized participants administered their assigned treatment who received ≥6 of the same doses during Base Study, had baseline and post-Base Study PVR assessment and EOT assessment, and had data for the outcome measure. Note: Data from participants whose dose was down-titrated were analyzed according to dose received ≥6 times rather than dose originally assigned. Per protocol, only participants who consistently received in 0.3 mg/kg or 0.7 mg/kg of sotatercept were planned to be analyzed.

End point type	Secondary

End point timeframe:

Baseline and Day 1 of Cycle 9, up to 24 weeks (Each cycle was 21 days.)

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	23	21	
Units: Score on a scale				
arithmetic mean (standard deviation)	-10.2 (± 12.91)	-6.9 (± 12.51)	-7.5 (± 7.96)	

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Change from Baseline in 36-Item Short Form Health Survey (SF-36) Score

End point title	Base Study: Change from Baseline in 36-Item Short Form Health Survey (SF-36) Score

End point description:

The SF-36 questionnaire is a participant-reported survey evaluating 8 aspects of physical or mental health. The physical component scores range from 0-100; 100 represents the highest level of physical functioning. The mental component scores also range from 0-100; 100 represents the highest level of mental functioning. Each participant's SF-36 was recorded at baseline and on Day 1 of Cycle 9. Each cycle was 21 days. The analysis population for this endpoint included all randomized participants administered their assigned treatment who received ≥6 of the same doses during Base Study, had baseline and post-Base Study PVR assessment and EOT assessment, and had data for the outcome measure. Note: Data from participants whose dose was down-titrated were analyzed according to dose received ≥6 times rather than dose originally assigned. Per protocol, only participants who consistently received in 0.3 mg/kg or 0.7 mg/kg of sotatercept were planned to be analyzed.

End point type	Secondary

End point timeframe:

Baseline and Day 1 of Cycle 9, up to 24 weeks (Each cycle was 21 days.)

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	27	29	
Units: Score on a scale				
least squares mean (standard error)				
Physical component	3.5 (± 1.07)	4.5 (± 1.12)	3.1 (± 1.11)	
Mental component	3.2 (± 1.33)	3.6 (± 1.39)	0.0 (± 1.40)	

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Number of Participants Who Experienced an Improvement from Baseline in World Health Organization (WHO) Functional Class at 24 Weeks

End point title	Base Study: Number of Participants Who Experienced an Improvement from Baseline in World Health Organization (WHO) Functional Class at 24 Weeks

End point description:

The WHO Functional Class describes the severity of a person's pulmonary hypertension symptoms. There are four different classes: I is the mildest and IV the most severe form of pulmonary hypertension. The analysis population for this endpoint included all randomized participants who received their assigned treatment and at least 6 of the same doses during Base Study, had baseline and post-Base Study PVR assessment and EOT assessment, and had data for Base Study: Number of Participants Who Experienced an Improvement from Baseline in WHO Functional Class at 24 Weeks. Note: Data from participants whose dose was down-titrated were analyzed according to dose received at least 6 times rather than dose to which originally assigned.

End point type	Secondary

End point timeframe:

Baseline and 24 Weeks

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	27	30	
Units: Participants	4	8	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Number of Participants Who Experienced Events Indicative of Clinical Worsening of Pulmonary Arterial Hypertension (PAH)

End point title	Base Study: Number of Participants Who Experienced Events Indicative of Clinical Worsening of Pulmonary Arterial Hypertension (PAH)

End point description:

Events that indicate clinical worsening of PAH include death, need for and/or worsening-related listing for lung and/or heart transplant, need to initiate an approved PAH SOC rescue therapy, PAH-specific hospitalization, or functional deterioration (worsened WHO Functional Class AND 15% decrease in 6MWD). The analysis population for this endpoint included all randomized participants who received their assigned treatment and had data for Base Study: Number of Participants Who Experienced Events Indicative of Clinical Worsening of PAH.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	32	42	
Units: Participants	2	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Number of Participants Who Experienced One or More AEs

End point title	Base Study: Number of Participants Who Experienced One or More AEs

End point description:

An AE is any untoward medical occurrence in a study participant administered a pharmaceutical product that does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product. The analysis population for this

endpoint included all randomized participants who received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Up to 24 months

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	32	42	
Units: Participants	29	29	35	

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Number of Participants Who Discontinued Study Treatment Due to an AE

End point title	Base Study: Number of Participants Who Discontinued Study Treatment Due to an AE

End point description:

An AE is any untoward medical occurrence in a study participant administered a pharmaceutical product that does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product. The analysis population for this endpoint included all randomized participants who received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Up to 24 months

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	32	42	
Units: Participants	1	1	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Change from Baseline in Systolic and Diastolic Blood Pressure at Cycle 9

End point title	Base Study: Change from Baseline in Systolic and Diastolic Blood Pressure at Cycle 9

End point description:

Each participant's systolic and diastolic blood pressure was taken at baseline and on Day 1 of Cycle 9. Each cycle was 21 days. The analysis population for this endpoint included all randomized participants who received their assigned treatment and had data for Base Study: Change from Baseline in Systolic and Diastolic Blood Pressure at Cycle 9.

End point type	Secondary

End point timeframe:

Baseline and Day 1 of Cycle 9, up to 24 weeks (Each cycle was 21 days.)

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	32	36	
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic blood pressure	-0.8 (± 10.06)	3.4 (± 11.75)	2.6 (± 12.28)	
Diastolic blood pressure	2.3 (± 8.06)	4.1 (± 8.64)	1.7 (± 8.69)	

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Change from Baseline in Body Mass Index (BMI) at Cycle 9

End point title	Base Study: Change from Baseline in Body Mass Index (BMI) at Cycle 9

End point description:

Each participant's BMI was measured at baseline and at 24 weeks. The analysis population for this endpoint included all randomized participants who received their assigned treatment and had data for Base Study: Change from Baseline in BMI at Cycle 9.

End point type	Secondary

End point timeframe:

Baseline and Day 1 of Cycle 9, up to 24 weeks (Each cycle was 21 days.)

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	31	36	
Units: kg/m^2				
arithmetic mean (standard deviation)	-0.2 (± 1.25)	0.6 (± 0.89)	0.2 (± 1.07)	

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Change from Baseline in Respiratory Rate at Cycle 9

End point title	Base Study: Change from Baseline in Respiratory Rate at Cycle 9

End point description:

Each participant's blood pressure was measured at baseline and on Day 1 of Cycle 9. Each cycle was 21 days. The analysis population for this endpoint included all randomized participants who received their assigned treatment and had data for Base Study: Change from Baseline in Respiratory Rate at Cycle 9.

End point type	Secondary

End point timeframe:

Baseline and Day 1 of Cycle 9, up to 24 weeks (Each cycle was 21 days.)

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	31	36	
Units: breaths/min				
arithmetic mean (standard deviation)	-0.3 (± 2.10)	-1.3 (± 3.72)	-0.3 (± 3.05)	

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Change from Baseline in QTcF Interval at Cycle 9

End point title	Base Study: Change from Baseline in QTcF Interval at Cycle 9

End point description:

Each participant's QTcF Interval was measured at baseline and on Day 1 of Cycle 9. The analysis population for this endpoint included all randomized participants who received their assigned treatment and had data for Base Study: Change from Baseline in QTcF Interval at Cycle 9.

End point type	Secondary

End point timeframe:

Baseline and Day 1 of Cycle 9, up to 24 weeks (Each cycle was 21 days.)

End point values	Placebo	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	31	35	
Units: milliseconds				
arithmetic mean (standard deviation)	0.7 (± 31.10)	-7.4 (± 20.57)	-9.1 (± 31.55)	

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Maximum Plasma Concentration (Cmax) of Sotatercept

End point title	Base Study: Maximum Plasma Concentration (Cmax) of Sotatercept[4]

End point description:

Cmax is a measure of the maximum amount of drug in the plasma after the dose is given. Based on population pharmacokinetic (PopPK) modeling of previous sotatercept studies, Cmax occurs at Day 8 of Cycle 1 after a sotatercept dose is given. The sotatercept concentration at Day 8 of Cycle 1 (each cycle was 21 days) is presented here as Cmax. The analysis population for this endpoint included all randomized participants who received at least 1 dose of sotatercept and had sufficient pharmacokinetic samples collected and assayed for PK analysis.

End point type	Secondary

End point timeframe:

Day 8 of Cycle 1 (Each cycle was 21 days.)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Placebo arm was not included in the PK analysis.

End point values	Sotatercept 0.3 mg/kg	Sotatercept 0.7 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	42		
Units: ng/mL				
arithmetic mean (standard deviation)	1910.3 (± 715.86)	4598.5 (± 1622.59)		

Statistical analyses

No statistical analyses for this end point

Secondary: Extension Period: Change from Baseline in 6MWD (Delayed-Start Analysis)

End point title	Extension Period: Change from Baseline in 6MWD (Delayed-Start Analysis)

End point description:

6MWD is measured by an exercise test known as 6MWT that assesses aerobic capacity and endurance. It measures the distance covered over a time of 6 minutes and is used as an outcome measure by which to compare changes in performance capacity. Each participant’s 6MWD was measured at baseline and the timepoint at which the third RCH was performed. This occurred between Month 18 and Month 24, at which time each participant's 6MWD was also measured. An increase in the distance walked during the 6MWT indicates improvement in basic mobility. The analysis population for this endpoint included all randomized participants who received their assigned treatment, transitioned to the extension period, and had data for Extension Period: Change from Baseline in 6MWD (Delayed-Start Analysis).

End point type	Secondary

End point timeframe:

Baseline and the timepoint at which third right heart catheterization was performed, which occurred between Month 18 and Month 24

End point values	Placebo-Crossed Treatment Group	Continued Sotatercept Treatment Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	67		
Units: meters				
least squares mean (standard error)	60.1 (± 14.35)	55.7 (± 9.47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Extension Period: Number of Participants Who Experienced an Improvement from Baseline in WHO Functional Class (Delayed-Start Analysis)

End point title	Extension Period: Number of Participants Who Experienced an Improvement from Baseline in WHO Functional Class (Delayed-Start Analysis)

End point description:

The WHO Functional Class describes the severity of a person's pulmonary hypertension symptoms. There are four different classes: I is the mildest and IV the most severe form of pulmonary hypertension. Each participant’s WHO Functional Class was assessed at baseline and the timepoint at which the third right heart catheterization was performed. This occurred between Month 18 and Month 24, at which time each participant's WHO Functional Class was also assessed. The analysis population for this endpoint included all randomized participants who received their assigned treatment, transitioned to the extension period, and had data for Extension Period: Number of Participants Who Experienced an Improvement from Baseline in WHO Functional Class (Delayed-Start Analysis).

End point type	Secondary

End point timeframe:

Baseline and timepoint at which third right heart catheterization was performed, which occurred between Month 18 and Month 24

End point values	Placebo-Crossed treatment group	Continued Sotatercept Treatment Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	66		
Units: Participants	16	27		

Statistical analyses

No statistical analyses for this end point

Secondary: Extension Period: Change from Baseline in 6MWD (Placebo-Crossed Analysis)

End point title	Extension Period: Change from Baseline in 6MWD (Placebo-Crossed Analysis)

End point description:

6MWD is measured by an exercise test known as 6MWT that assesses aerobic capacity and endurance. It measures the distance covered over a time of 6 minutes and is used as an outcome measure by which to compare changes in performance capacity. Each participant's 6MWD was measured at baseline and the timepoint at which the third right heart catheterization was performed. This occurred between Month 18 and Month 24, at which time each participant's 6MWD was also measured. An increase in the distance walked during the 6MWT indicates improvement in basic mobility. The analysis population for this endpoint included all randomized participants who received their assigned treatment, transitioned to the extension period, and had data for Extension Period: Change from Baseline in 6MWD (Placebo-Crossed Analysis).

End point type	Secondary

End point timeframe:

Baseline and timepoint at which third right heart catheterization was performed, which occurred between Month 18 and Month 24

End point values	Placebo-Crossed Treatment Group			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: meters				
arithmetic mean (standard error)	60.5 (± 13.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension Period: Change from Baseline in WHO Functional Class (Placebo-Crossed Analysis)

End point title	Extension Period: Change from Baseline in WHO Functional Class (Placebo-Crossed Analysis)

End point description:

The WHO Functional Class describes the severity of a person's pulmonary hypertension symptoms. There are four different classes: I is the mildest and IV the most severe form of pulmonary hypertension. Each participant's WHO Functional Class was assessed at baseline and the timepoint at which the third right heart catheterization was performed. This occurred between Month 18 and Month 24, at which time each participant's WHO Functional Class was also assessed. The analysis population for this endpoint included all randomized participants who received their assigned treatment, transitioned to the extension period, and had data for Extension Period: Change from Baseline in WHO Functional Class (Placebo-Crossed Analysis).

End point type	Secondary

End point timeframe:

Baseline and timepoint at which third right heart catheterization was performed, which occurred between Month 18 and Month 24

End point values	Placebo-Crossed Treatment Group			
Subject group type	Subject analysis set			
Number of subjects analysed	28			
Units: WHO functional class				
arithmetic mean (standard deviation)	-0.6 (± 0.74)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment period: Up to 24 weeks; Extension period: Up to approximately 32 months.

Adverse event reporting additional description:

The safety analysis population included all participants who received at least 1 dose of study treatment. The analysis population for Deaths (all causes) included all randomized participants.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Base Study: Sotatercept 0.3 mg/kg

Reporting group description:

Participants received sotatercept 0.3 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Reporting group title	Base Study: Placebo

Reporting group description:

Participants received placebo plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Reporting group title	Extension Period: PlaceboSotatercept 0.7 mg/kg

Reporting group description:

This treatment group represents participants from the Placebo arm who received placebo plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8), then transitioned to the 30-month extension period (Cycles 9-51), during which they received sotatercept 0.7 mg/kg plus SOC by SC injection. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Reporting group title	Extension Period: Sotatercept 0.3 mg/kg

Reporting group description:

Participants who received sotatercept 0.3 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) continued to receive sotatercept 0.3 mg/kg plus SOC during the 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Reporting group title	Extension Period: Sotatercept 0.7 mg/kg

Reporting group description:

Participants who received sotatercept 0.7 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8) continued to receive sotatercept 0.7 mg/kg plus SOC during the 30-month extension period (Cycles 9-51). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Reporting group title	Base Study: Sotatercept 0.7 mg/kg

Reporting group description:

Participants received sotatercept 0.7 mg/kg plus SOC by SC injection during the 24-week treatment period (Base Study; Cycles 1-8). Each cycle was 21 days. Dosing occurred once every 3 weeks.

Reporting group title	Extension Period: PlaceboSotatercept 0.3 mg/kg

Reporting group description:

This treatment group represents participants from the Placebo arm who received placebo plus standard of care (SOC) by subcutaneous (SC) injection during the 24-week treatment period (Base Study; Cycles 1-8), then transitioned to the 30-month extension period (Cycles 9-51), during which they received sotatercept 0.3 mg/kg plus SOC by SC injection. Each cycle was 21 days. Dosing occurred once every 3 weeks.

Serious adverse events	Base Study: Sotatercept 0.3 mg/kg	Base Study: Placebo	Extension Period: PlaceboSotatercept 0.7 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 32 (6.25%)	3 / 32 (9.38%)	4 / 15 (26.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon neoplasm			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mass			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device breakage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device dislocation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device malfunction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Red blood cell count increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ankle fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachyarrhythmia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 15 (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
Pericardial effusion			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia paroxysmal			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Chorioretinopathy			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Systemic lupus erythematosus			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Catheter site infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain abscess			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion site infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic embolus			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Extension Period: Sotatercept 0.3 mg/kg	Extension Period: Sotatercept 0.7 mg/kg	Base Study: Sotatercept 0.7 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 31 (32.26%)	12 / 36 (33.33%)	10 / 42 (23.81%)
number of deaths (all causes)	1	2	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon neoplasm			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			

subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mass			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device breakage			

subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device dislocation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device malfunction			
subjects affected / exposed	0 / 31 (0.00%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Red blood cell count increased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tibia fracture			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Tachyarrhythmia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia paroxysmal			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			

subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Chorioretinopathy			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Systemic lupus erythematosus			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (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
Infections and infestations			
Catheter site infection			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			

subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain abscess			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Device related infection			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion site infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			

subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 31 (3.23%)	3 / 36 (8.33%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic embolus			

subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Extension Period: PlaceboSotatercept 0.3 mg/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 15 (40.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon neoplasm			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			

subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vessel puncture site haematoma				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary arterial hypertension				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				

subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary mass				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary hypertension				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Product issues				
Device breakage				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device dislocation				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device malfunction				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Device occlusion				

subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Red blood cell count increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fibula fracture			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial flutter			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Cardiac arrest				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachyarrhythmia				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Right ventricular failure				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachycardia paroxysmal				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Migraine				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neuropathy peripheral				

subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Chorioretinopathy			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Lower gastrointestinal haemorrhage				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Systemic lupus erythematosus				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Catheter site infection				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Brain abscess				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related sepsis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Gastroenteritis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal infection				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infusion site infection				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia viral				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				

subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tuberculosis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic embolus			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Base Study: Sotatercept 0.3 mg/kg	Base Study: Placebo	Extension Period: PlaceboSotatercept 0.7 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 32 (90.63%)	25 / 32 (78.13%)	15 / 15 (100.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	2
Deep vein thrombosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Hypertension			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	2
Hypotension			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	2 / 15 (13.33%)
occurrences (all)	2	2	12
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Asthenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Chest discomfort			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Catheter site haemorrhage			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Chills			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Chest pain			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Cyst			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Discomfort			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	2 / 32 (6.25%)	6 / 32 (18.75%)	4 / 15 (26.67%)
occurrences (all)	2	6	5
Face oedema			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Feeling abnormal			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Injection site erythema			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Infusion site pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Injection site pain			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Injection site pruritus			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Localised oedema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vessel puncture site haematoma			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	3 / 32 (9.38%)	5 / 32 (15.63%)	6 / 15 (40.00%)
occurrences (all)	3	5	6
Pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	5
Pyrexia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Breast hyperplasia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Breast swelling			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Heavy menstrual bleeding			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vaginal ulceration			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal dryness			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 32 (6.25%)	2 / 32 (6.25%)	3 / 15 (20.00%)
occurrences (all)	2	2	4
Dyspnoea			

subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	3 / 15 (20.00%)
occurrences (all)	2	3	6
Nasal congestion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hypoxia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	4 / 32 (12.50%)	1 / 32 (3.13%)	4 / 15 (26.67%)
occurrences (all)	5	1	5
Dyspnoea exertional			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nasal dryness			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	3 / 15 (20.00%)
occurrences (all)	1	0	4
Nasal turbinate hypertrophy			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Respiratory failure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pulmonary mass			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Sinus congestion			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Rhinorrhoea			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Sleep apnoea syndrome			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 32 (6.25%)	2 / 32 (6.25%)	2 / 15 (13.33%)
occurrences (all)	2	2	3
Procedural anxiety			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Product issues			
Device dislocation			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Device occlusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Device leakage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood chloride increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Blood sodium decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Haematocrit increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Haemoglobin decreased			

subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Reticulocyte count increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Intraocular pressure increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Haemoglobin increased			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	5 / 15 (33.33%)
occurrences (all)	1	0	7
Urine albumin/creatinine ratio increased			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Epicondylitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Fall			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	1 / 15 (6.67%)
occurrences (all)	1	1	2
Head injury			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Limb injury			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tendon rupture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Toxicity to various agents			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vaccination complication			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	4
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Atrial fibrillation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Bradycardia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Cardiac failure			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Low cardiac output syndrome			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Palpitations			
subjects affected / exposed	1 / 32 (3.13%)	3 / 32 (9.38%)	3 / 15 (20.00%)
occurrences (all)	1	3	4
Sinus tachycardia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Right ventricular failure			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tachycardia paroxysmal			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 32 (15.63%)	3 / 32 (9.38%)	2 / 15 (13.33%)
occurrences (all)	5	4	2
Facial paralysis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	8 / 32 (25.00%)	6 / 32 (18.75%)	7 / 15 (46.67%)
occurrences (all)	16	10	13
Intention tremor			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Lethargy			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Paraesthesia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Presyncope			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	2 / 15 (13.33%)
occurrences (all)	0	1	6
Sciatica			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	1 / 32 (3.13%)	3 / 32 (9.38%)	0 / 15 (0.00%)
occurrences (all)	1	3	0
Tension headache			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	2 / 15 (13.33%)
occurrences (all)	2	3	2
Blood loss anaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Iron deficiency anaemia			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	4 / 15 (26.67%)
occurrences (all)	1	2	5

Leukocytosis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Leukopenia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Polycythaemia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Thrombocytopenia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	3	0	2
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	2 / 32 (6.25%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences (all)	2	1	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dacryostenosis acquired			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Deposit eye			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Glaucoma			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Keratitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Abdominal pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dental plaque			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Defaecation urgency			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Crohn's disease			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	7 / 32 (21.88%)	5 / 32 (15.63%)	5 / 15 (33.33%)
occurrences (all)	8	6	7
Dyspepsia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	2 / 15 (13.33%)
occurrences (all)	0	1	2
Dry mouth			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Haematochezia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gingival bleeding			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	3 / 32 (9.38%)	5 / 32 (15.63%)	4 / 15 (26.67%)
occurrences (all)	4	9	9
Large intestine polyp			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Peptic ulcer			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Rectal haemorrhage			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Proctalgia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	3 / 32 (9.38%)	4 / 32 (12.50%)	3 / 15 (20.00%)
occurrences (all)	3	10	4
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dermal cyst			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	2 / 32 (6.25%)	2 / 32 (6.25%)	1 / 15 (6.67%)
occurrences (all)	2	2	2
Dermatitis contact			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Ecchymosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hidradenitis			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Pruritus			
subjects affected / exposed	2 / 32 (6.25%)	2 / 32 (6.25%)	0 / 15 (0.00%)
occurrences (all)	2	2	0
Rash			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	2 / 15 (13.33%)
occurrences (all)	1	1	5
Rosacea			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Telangiectasia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	5 / 15 (33.33%)
occurrences (all)	0	0	6
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Microalbuminuria			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	2 / 32 (6.25%)	5 / 32 (15.63%)	5 / 15 (33.33%)
occurrences (all)	2	5	9
Back pain			
subjects affected / exposed	3 / 32 (9.38%)	2 / 32 (6.25%)	2 / 15 (13.33%)
occurrences (all)	3	2	3
Bursitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Exostosis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	1 / 15 (6.67%)
occurrences (all)	0	2	1
Fracture pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Myalgia			
subjects affected / exposed	2 / 32 (6.25%)	1 / 32 (3.13%)	2 / 15 (13.33%)
occurrences (all)	2	1	2
Musculoskeletal chest pain			
subjects affected / exposed	2 / 32 (6.25%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences (all)	2	1	0
Muscle spasms			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Neck pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Pain in extremity			
subjects affected / exposed	3 / 32 (9.38%)	2 / 32 (6.25%)	3 / 15 (20.00%)
occurrences (all)	4	2	3

Pain in jaw			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Tendonitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Cystitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Conjunctivitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Fungal pharyngitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	2 / 32 (6.25%)	2 / 32 (6.25%)	2 / 15 (13.33%)
occurrences (all)	3	2	2
Gingivitis			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Influenza			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Hordeolum			

subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Labyrinthitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 32 (3.13%)	3 / 32 (9.38%)	6 / 15 (40.00%)
occurrences (all)	1	3	7
Onychomycosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Otitis externa			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 32 (0.00%)	3 / 32 (9.38%)	2 / 15 (13.33%)
occurrences (all)	0	3	2
Rhinitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	3 / 15 (20.00%)
occurrences (all)	2	0	5
Tinea pedis			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tonsillitis bacterial			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	4 / 32 (12.50%)	3 / 32 (9.38%)	1 / 15 (6.67%)
occurrences (all)	5	4	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	3 / 32 (9.38%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	3	0	1
Metabolism and nutrition disorders			
Fluid retention			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	1 / 15 (6.67%)
occurrences (all)	0	3	1
Dyslipidaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Decreased appetite			
subjects affected / exposed	2 / 32 (6.25%)	3 / 32 (9.38%)	2 / 15 (13.33%)
occurrences (all)	2	3	2
Folate deficiency			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gout			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	1 / 15 (6.67%)
occurrences (all)	2	1	1
Hypoglycaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Hypervolaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	3 / 32 (9.38%)	4 / 32 (12.50%)	0 / 15 (0.00%)
occurrences (all)	3	4	0
Hypomagnesaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	2 / 15 (13.33%)
occurrences (all)	0	1	2
Vitamin B12 deficiency			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Non-serious adverse events	Extension Period: Sotatercept 0.3 mg/kg	Extension Period: Sotatercept 0.7 mg/kg	Base Study: Sotatercept 0.7 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 31 (96.77%)	36 / 36 (100.00%)	33 / 42 (78.57%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Deep vein thrombosis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	1 / 31 (3.23%)	3 / 36 (8.33%)	1 / 42 (2.38%)
occurrences (all)	1	4	1
Hypertension			
subjects affected / exposed	4 / 31 (12.90%)	3 / 36 (8.33%)	0 / 42 (0.00%)
occurrences (all)	4	3	0
Hypotension			

subjects affected / exposed	2 / 31 (6.45%)	1 / 36 (2.78%)	2 / 42 (4.76%)
occurrences (all)	2	2	2
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	0 / 31 (0.00%)	2 / 36 (5.56%)	1 / 42 (2.38%)
occurrences (all)	0	2	1
Chest discomfort			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Catheter site haemorrhage			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 31 (0.00%)	2 / 36 (5.56%)	1 / 42 (2.38%)
occurrences (all)	0	2	2
Chest pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Cyst			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Discomfort			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	6 / 31 (19.35%)	5 / 36 (13.89%)	4 / 42 (9.52%)
occurrences (all)	9	6	4
Face oedema			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Feeling abnormal			

subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Infusion site pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Injection site pain			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	4 / 42 (9.52%)
occurrences (all)	1	2	4
Injection site pruritus			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Localised oedema			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	2 / 31 (6.45%)	2 / 36 (5.56%)	1 / 42 (2.38%)
occurrences (all)	4	2	1
Vessel puncture site haematoma			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	11 / 31 (35.48%)	7 / 36 (19.44%)	5 / 42 (11.90%)
occurrences (all)	12	8	6
Pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	5 / 31 (16.13%)	3 / 36 (8.33%)	1 / 42 (2.38%)
occurrences (all)	5	3	1
Reproductive system and breast disorders			
Breast mass			

subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Breast hyperplasia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Breast swelling			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Heavy menstrual bleeding			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Vaginal ulceration			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal dryness			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 31 (12.90%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	4	1	0
Dyspnoea			
subjects affected / exposed	5 / 31 (16.13%)	3 / 36 (8.33%)	0 / 42 (0.00%)
occurrences (all)	8	3	0
Nasal congestion			
subjects affected / exposed	1 / 31 (3.23%)	2 / 36 (5.56%)	1 / 42 (2.38%)
occurrences (all)	1	2	1
Hypoxia			
subjects affected / exposed	2 / 31 (6.45%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	5	1	2
Epistaxis			
subjects affected / exposed	7 / 31 (22.58%)	4 / 36 (11.11%)	5 / 42 (11.90%)
occurrences (all)	10	5	6
Dyspnoea exertional			

subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Nasal dryness			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	2 / 31 (6.45%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
Nasal turbinate hypertrophy			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Pulmonary hypertension			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Respiratory failure			
subjects affected / exposed	0 / 31 (0.00%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Pulmonary mass			
subjects affected / exposed	0 / 31 (0.00%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Rhinitis allergic			
subjects affected / exposed	0 / 31 (0.00%)	2 / 36 (5.56%)	1 / 42 (2.38%)
occurrences (all)	0	2	1
Sinus congestion			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Sleep apnoea syndrome			

subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Upper respiratory tract congestion			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 31 (6.45%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	2	1	1
Procedural anxiety			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 31 (0.00%)	3 / 36 (8.33%)	0 / 42 (0.00%)
occurrences (all)	0	3	0
Depression			
subjects affected / exposed	5 / 31 (16.13%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	5	1	0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Device occlusion			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Device leakage			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 31 (6.45%)	3 / 36 (8.33%)	2 / 42 (4.76%)
occurrences (all)	2	3	2
Aspartate aminotransferase increased			

subjects affected / exposed	2 / 31 (6.45%)	3 / 36 (8.33%)	1 / 42 (2.38%)
occurrences (all)	2	3	1
Blood chloride increased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Haematocrit increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Reticulocyte count increased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	1	1	1
Intraocular pressure increased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Haemoglobin increased			
subjects affected / exposed	0 / 31 (0.00%)	5 / 36 (13.89%)	7 / 42 (16.67%)
occurrences (all)	0	5	7
Urine albumin/creatinine ratio increased			
subjects affected / exposed	1 / 31 (3.23%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences (all)	2	2	0

Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Epicondylitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Fall			
subjects affected / exposed	5 / 31 (16.13%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	5	0	0
Head injury			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	2 / 31 (6.45%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
Limb injury			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Tendon rupture			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			

subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Toxicity to various agents			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Vaccination complication			
subjects affected / exposed	2 / 31 (6.45%)	3 / 36 (8.33%)	0 / 42 (0.00%)
occurrences (all)	2	5	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Bradycardia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	3	0	0
Low cardiac output syndrome			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	2 / 31 (6.45%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	4	1	1
Sinus tachycardia			
subjects affected / exposed	2 / 31 (6.45%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
Right ventricular failure			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0

Tachycardia			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	1	1	1
Tachycardia paroxysmal			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 31 (12.90%)	5 / 36 (13.89%)	4 / 42 (9.52%)
occurrences (all)	6	6	5
Facial paralysis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	9 / 31 (29.03%)	6 / 36 (16.67%)	6 / 42 (14.29%)
occurrences (all)	16	10	8
Intention tremor			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	1 / 31 (3.23%)	4 / 36 (11.11%)	1 / 42 (2.38%)
occurrences (all)	1	5	1
Presyncope			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Sciatica			

subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	1	0	1
Syncope			
subjects affected / exposed	0 / 31 (0.00%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Tension headache			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 31 (25.81%)	1 / 36 (2.78%)	2 / 42 (4.76%)
occurrences (all)	13	2	2
Blood loss anaemia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	1 / 31 (3.23%)	3 / 36 (8.33%)	0 / 42 (0.00%)
occurrences (all)	1	3	0
Leukocytosis			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Leukopenia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	5	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Polycythaemia			
subjects affected / exposed	0 / 31 (0.00%)	3 / 36 (8.33%)	0 / 42 (0.00%)
occurrences (all)	0	3	0

Thrombocytopenia			
subjects affected / exposed	3 / 31 (9.68%)	3 / 36 (8.33%)	5 / 42 (11.90%)
occurrences (all)	3	8	8
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	3 / 31 (9.68%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	3	0	0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 31 (3.23%)	3 / 36 (8.33%)	0 / 42 (0.00%)
occurrences (all)	2	5	0
Dacryostenosis acquired			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Deposit eye			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	2 / 31 (6.45%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences (all)	2	2	0
Glaucoma			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Keratitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	1	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	3 / 31 (9.68%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	4	0	1
Constipation			
subjects affected / exposed	3 / 31 (9.68%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	4	1	0
Dental plaque			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Defaecation urgency			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Crohn's disease			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	9 / 31 (29.03%)	5 / 36 (13.89%)	6 / 42 (14.29%)
occurrences (all)	14	5	6
Dyspepsia			
subjects affected / exposed	0 / 31 (0.00%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Dry mouth			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	2 / 42 (4.76%)
occurrences (all)	1	1	2
Gastritis			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	3	1	1

Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 31 (3.23%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences (all)	1	2	0
Haematochezia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Haemorrhoids			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	9 / 31 (29.03%)	5 / 36 (13.89%)	5 / 42 (11.90%)
occurrences (all)	11	7	5
Large intestine polyp			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Peptic ulcer			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	5	0	0
Proctalgia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	6 / 31 (19.35%)	4 / 36 (11.11%)	3 / 42 (7.14%)
occurrences (all)	9	5	3
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Dermal cyst			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	1 / 31 (3.23%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences (all)	1	2	0
Dry skin			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Hidradenitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Rash			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Rosacea			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Skin lesion			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	2	1	0

Telangiectasia			
subjects affected / exposed	5 / 31 (16.13%)	7 / 36 (19.44%)	0 / 42 (0.00%)
occurrences (all)	5	8	0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 31 (0.00%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Proteinuria			
subjects affected / exposed	3 / 31 (9.68%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	3	1	0
Microalbuminuria			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	3	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 31 (25.81%)	5 / 36 (13.89%)	1 / 42 (2.38%)
occurrences (all)	12	5	1
Back pain			
subjects affected / exposed	7 / 31 (22.58%)	2 / 36 (5.56%)	1 / 42 (2.38%)
occurrences (all)	10	3	1
Bursitis			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Exostosis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Fracture pain			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1

Joint swelling			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	4 / 31 (12.90%)	4 / 36 (11.11%)	3 / 42 (7.14%)
occurrences (all)	4	4	3
Musculoskeletal chest pain			
subjects affected / exposed	2 / 31 (6.45%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
Muscle spasms			
subjects affected / exposed	4 / 31 (12.90%)	1 / 36 (2.78%)	4 / 42 (9.52%)
occurrences (all)	4	1	4
Neck pain			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	8 / 31 (25.81%)	3 / 36 (8.33%)	5 / 42 (11.90%)
occurrences (all)	11	4	6
Pain in jaw			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Tendonitis			
subjects affected / exposed	2 / 31 (6.45%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
Infections and infestations			
COVID-19			
subjects affected / exposed	3 / 31 (9.68%)	5 / 36 (13.89%)	0 / 42 (0.00%)
occurrences (all)	3	6	0
Bronchitis			
subjects affected / exposed	3 / 31 (9.68%)	3 / 36 (8.33%)	0 / 42 (0.00%)
occurrences (all)	3	4	0
Cystitis			

subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	2 / 31 (6.45%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	4	1	0
Ear infection			
subjects affected / exposed	2 / 31 (6.45%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	2	3	0
Fungal pharyngitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	5 / 31 (16.13%)	2 / 36 (5.56%)	4 / 42 (9.52%)
occurrences (all)	5	2	4
Gingivitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 31 (0.00%)	5 / 36 (13.89%)	0 / 42 (0.00%)
occurrences (all)	0	5	0
Hordeolum			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Labyrinthitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	10 / 31 (32.26%)	1 / 36 (2.78%)	4 / 42 (9.52%)
occurrences (all)	14	1	4
Onychomycosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Oral herpes			

subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Otitis externa			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	2	0	1
Respiratory tract infection			
subjects affected / exposed	2 / 31 (6.45%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	3	1	1
Rhinitis			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Sinusitis			
subjects affected / exposed	2 / 31 (6.45%)	3 / 36 (8.33%)	0 / 42 (0.00%)
occurrences (all)	3	4	0
Tinea pedis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Tonsillitis bacterial			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	6 / 31 (19.35%)	6 / 36 (16.67%)	2 / 42 (4.76%)
occurrences (all)	9	8	2
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Urinary tract infection			

subjects affected / exposed	5 / 31 (16.13%)	5 / 36 (13.89%)	0 / 42 (0.00%)
occurrences (all)	7	5	0
Metabolism and nutrition disorders			
Fluid retention			
subjects affected / exposed	2 / 31 (6.45%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	3	1	0
Dyslipidaemia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Decreased appetite			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	4	0	1
Folate deficiency			
subjects affected / exposed	0 / 31 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Gout			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Hypoglycaemia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	3	0	0
Hypervolaemia			
subjects affected / exposed	1 / 31 (3.23%)	1 / 36 (2.78%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Hyperkalaemia			
subjects affected / exposed	1 / 31 (3.23%)	3 / 36 (8.33%)	1 / 42 (2.38%)
occurrences (all)	1	4	1
Hypokalaemia			
subjects affected / exposed	4 / 31 (12.90%)	1 / 36 (2.78%)	5 / 42 (11.90%)
occurrences (all)	8	1	5
Hypomagnesaemia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	3	0	1
Iron deficiency			
subjects affected / exposed	3 / 31 (9.68%)	6 / 36 (16.67%)	1 / 42 (2.38%)
occurrences (all)	3	8	1

Vitamin B12 deficiency			
subjects affected / exposed	0 / 31 (0.00%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	Extension Period: PlaceboSotatercept 0.3 mg/kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 15 (93.33%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Deep vein thrombosis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	4		
Chest discomfort			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Catheter site haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		

Chills				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Chest pain				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Cyst				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Discomfort				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Fatigue				
subjects affected / exposed	6 / 15 (40.00%)			
occurrences (all)	7			
Face oedema				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Feeling abnormal				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Injection site erythema				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Infusion site pain				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Injection site pain				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Injection site pruritus				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Localised oedema				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			

Non-cardiac chest pain subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2		
Vessel puncture site haematoma subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Oedema peripheral subjects affected / exposed occurrences (all)	4 / 15 (26.67%) 4		
Pain subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Pyrexia subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2		
Reproductive system and breast disorders			
Breast mass subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Breast hyperplasia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Breast swelling subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Heavy menstrual bleeding subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2		
Vaginal ulceration subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Vulvovaginal dryness subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Respiratory, thoracic and mediastinal disorders			

Cough				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences (all)	4			
Dyspnoea				
subjects affected / exposed	3 / 15 (20.00%)			
occurrences (all)	4			
Nasal congestion				
subjects affected / exposed	3 / 15 (20.00%)			
occurrences (all)	3			
Hypoxia				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Epistaxis				
subjects affected / exposed	3 / 15 (20.00%)			
occurrences (all)	7			
Dyspnoea exertional				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Nasal dryness				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Oropharyngeal pain				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences (all)	4			
Nasal turbinate hypertrophy				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Productive cough				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Pulmonary arterial hypertension				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	2			
Pulmonary hypertension				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			

Respiratory failure			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Pulmonary mass			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Rhinitis allergic			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Sinus congestion			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Sleep apnoea syndrome			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Upper respiratory tract congestion			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	3		
Procedural anxiety			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Depression			

subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Product issues			
Device dislocation			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Device occlusion			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Device leakage			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Blood chloride increased			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Blood bicarbonate decreased			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Blood pressure increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Blood sodium decreased			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Haematocrit increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Glomerular filtration rate decreased			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Haemoglobin decreased			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Reticulocyte count increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Intraocular pressure increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Haemoglobin increased			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Urine albumin/creatinine ratio increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Epicondylitis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Head injury			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Ligament sprain			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Limb injury			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Tendon rupture			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Tooth fracture			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Road traffic accident			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Toxicity to various agents			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Vaccination complication			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	4		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Atrial fibrillation			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Bradycardia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		

Cardiac failure			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Low cardiac output syndrome			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Pericardial effusion			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Sinus tachycardia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Right ventricular failure			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Tachycardia paroxysmal			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 15 (26.67%)		
occurrences (all)	5		
Facial paralysis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hypoaesthesia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Headache			

subjects affected / exposed	4 / 15 (26.67%)		
occurrences (all)	21		
Intention tremor			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Lethargy			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Tension headache			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Blood loss anaemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		

Iron deficiency anaemia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Leukocytosis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Leukopenia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Neutropenia subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2		
Polycythaemia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2		
Thrombocytopenia subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 3		
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Ear pain subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2		
Vertigo subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Eye disorders Cataract subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Dacryostenosis acquired			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Deposit eye			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Dry eye			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Glaucoma			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Keratitis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Periorbital oedema			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Dental plaque			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		

Defaecation urgency				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Crohn's disease				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Diarrhoea				
subjects affected / exposed	3 / 15 (20.00%)			
occurrences (all)	3			
Dyspepsia				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	4			
Dry mouth				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Gastritis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Gastrooesophageal reflux disease				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences (all)	2			
Haematochezia				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Gingival bleeding				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences (all)	2			
Haemorrhoids				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	3 / 15 (20.00%)			
occurrences (all)	3			
Large intestine polyp				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			

Peptic ulcer subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Rectal haemorrhage subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Proctalgia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Vomiting subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 3		
Hepatobiliary disorders Gallbladder polyp subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Dermal cyst subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Erythema subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Dermatitis contact subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Dry skin subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Ecchymosis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Eczema			

subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hidradenitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Rosacea			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Skin lesion			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Telangiectasia			
subjects affected / exposed	4 / 15 (26.67%)		
occurrences (all)	5		
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Proteinuria			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Microalbuminuria			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Endocrine disorders			
Hypothyroidism			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Bursitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Exostosis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Fracture pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Neck pain			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	6		
Pain in jaw			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Tendonitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Bronchitis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Ear infection			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Fungal pharyngitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Gingivitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		

Influenza				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Hordeolum				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Herpes zoster				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Labyrinthitis				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	5 / 15 (33.33%)			
occurrences (all)	9			
Onychomycosis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Oral herpes				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Oral candidiasis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Otitis externa				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Pharyngitis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Respiratory tract infection				
subjects affected / exposed	3 / 15 (20.00%)			
occurrences (all)	4			
Rhinitis				
subjects affected / exposed	2 / 15 (13.33%)			
occurrences (all)	4			

Sinusitis			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Tinea pedis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Tonsillitis bacterial			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Fluid retention			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Dyslipidaemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Folate deficiency			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Gout			

subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	6		
Hypoglycaemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Hypervolaemia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hyperkalaemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	5		
Hypomagnesaemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Iron deficiency			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	6		
Vitamin B12 deficiency			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 February 2018	Amendment 01A: Revisions to the following sections: Synopsis, Overall Design, Study Design, Schedule of Events, Objectives and Endpoints, Pharmacodynamics, Exclusion Criteria, Six-Minute-Walk Distance, Clinical Worsening.
05 May 2018	Amendment 02A: Revisions to the following sections: Schedule of Events, Inclusion Criteria, Treatment Administration and Schedule, Interim Analysis, Appendix 7: Genetics.
27 December 2018	Amendment 05A: Revisions to the following items or sections: Table 1, Schedule of Events, Study Design, Figure 1, Study Rationale, Overall Design, Dose Modification, Randomization and Blinding, Efficacy Assessments, Populations for Analyses, Sample Size Determination, Inclusion Criteria, Exclusions Criteria, Standard of Care Therapy, Interim Analysis, Benefit/Risk Assessment, Screen Failures, Discontinuation of Study Treatment, Adverse Events, Safety Assessments, Electrocardiograms, Clinical Safety Laboratory Assessments, Appendix 6: Contraceptive Guidance and Collection of Pregnancy Information, Appendix 8: National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0.
11 March 2020	Amendment 06A: Extended treatment by adding additional cycles 35 to 51 (a 1-year extension), additional evaluations and safety monitoring, dose modification adjustments; also updated the blinding process.
21 August 2020	Amendment 07A: Revisions to the following sections: Synopsis, Overall Design, Schedule of Events, Dose Modification, Pulmonary Vascular Resistance by Right Heart Catheterization, and Statistical Analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported