Clinical trial results:
A Phase 2 Open Label Extension Study to Assess the Long-term Safety, Tolerability, Pharmacokinetics and Efficacy of Recifercept in Children with Achondroplasia

Summary

EudraCT number	2021-003149-39
Trial protocol	ES IT PT BE DK
Global end of trial date	30 March 2023

Results information

Result version number	v1 (current)
This version publication date	15 October 2023
First version publication date	15 October 2023

Trial information

Trial identification

Sponsor protocol code	C4181008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05116046
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquires@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquires@pfizer.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 April 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 March 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Evaluate the long-term safety and tolerability of recifercept doses and dosing regimens in subjects aged greater than or equal to (>=) 15 months to less than (<) 12 years with achondroplasia. To assess long-term efficacy of recifercept to increase height growth in children with achondroplasia.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 December 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Denmark: 6
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	35
EEA total number of subjects	26

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)	33
Adolescents (12-17 years)	2
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eligible subjects aged more than or equal to (>=)15 months to less than (<) 12 years (inclusive) diagnosed with achondroplasia from study C4181005 (NCT04638153) were enrolled.

Pre-assignment

Screening details:

A total of 35 subjects were enrolled and assigned to study treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Recifercept 1 milligram per kilogram (mg/kg) once weekly

Arm description:

Subjects with achondroplasia who completed study C4181005 (NCT04638153) continued to receive recifercept 1 mg/kg once weekly via the subcutaneous route for up to 24 months.

Arm type	Experimental
Investigational medicinal product name	Recifercept
Investigational medicinal product code	PF-07256472
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 mg/kg once weekly

Arm title	Recifercept 2 mg/kg twice weekly

Arm description:

Subjects with achondroplasia who completed study C4181005 (NCT04638153) continued to receive recifercept 2 mg/kg twice weekly via the subcutaneous route for up to 24 months.

Arm type	Experimental
Investigational medicinal product name	Recifercept
Investigational medicinal product code	PF-07256472
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

2 mg/kg once weekly

Arm title	Recifercept 1.5 mg/kg once daily

Arm description:

Subjects with achondroplasia who completed study C4181005 (NCT04638153) continued to receive recifercept 1.5 mg/kg once daily via the subcutaneous route for up to 24 months.

Arm type	Experimental

Investigational medicinal product name	Recifercept
Investigational medicinal product code	PF-07256472
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1.5 mg/kg once weekly

Number of subjects in period 1	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily
Started	16	17	2
Completed	0	0	0
Not completed	16	17	2
Study terminated by sponsor	14	16	1
Withdrawal by parent/guardian	2	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Recifercept 1 milligram per kilogram (mg/kg) once weekly
Reporting group description:	
Subjects with achondroplasia who completed study C4181005 (NCT04638153) continued to receive recifercept 1 mg/kg once weekly via the subcutaneous route for up to 24 months.	
Reporting group title	Recifercept 2 mg/kg twice weekly
Reporting group description:	
Subjects with achondroplasia who completed study C4181005 (NCT04638153) continued to receive recifercept 2 mg/kg twice weekly via the subcutaneous route for up to 24 months.	
Reporting group title	Recifercept 1.5 mg/kg once daily
Reporting group description:	
Subjects with achondroplasia who completed study C4181005 (NCT04638153) continued to receive recifercept 1.5 mg/kg once daily via the subcutaneous route for up to 24 months.	

Reporting group values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily
Number of subjects	16	17	2
Age Categorical Units: Subjects			
Children (2-11 years)	15	16	2
Adolescents (12-17 years)	1	1	0
Age Continuous Units: years			
arithmetic mean	7.5	6.6	9.5
standard deviation	± 2.66	± 2.50	± 0.71
Gender Categorical Units: Subjects			
Female	9	9	2
Male	7	8	0
Race Units: Subjects			
White	14	17	2
Black or African American	0	0	0
Asian	1	0	0
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Other	0	0	0
Unknown	0	0	0
Multiracial	1	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	2	0	1
Not Hispanic or Latino	14	17	1

Reporting group values	Total		
Number of subjects	35		

Age Categorical Units: Subjects			
Children (2-11 years)	33		
Adolescents (12-17 years)	2		
Age Continuous Units: years arithmetic mean standard deviation	 -		
Gender Categorical Units: Subjects			
Female	20		
Male	15		
Race Units: Subjects			
White	33		
Black or African American	0		
Asian	1		
American Indian or Alaska Native	0		
Native Hawaiian or Other Pacific Islander	0		
Other	0		
Unknown	0		
Multiracial	1		
Ethnicity Units: Subjects			
Hispanic or Latino	3		
Not Hispanic or Latino	32		

End points

End points reporting groups

Reporting group title	Recifercept 1 milligram per kilogram (mg/kg) once weekly
Reporting group description:	
Subjects with achondroplasia who completed study C4181005 (NCT04638153) continued to receive recifercept 1 mg/kg once weekly via the subcutaneous route for up to 24 months.	
Reporting group title	Recifercept 2 mg/kg twice weekly
Reporting group description:	
Subjects with achondroplasia who completed study C4181005 (NCT04638153) continued to receive recifercept 2 mg/kg twice weekly via the subcutaneous route for up to 24 months.	
Reporting group title	Recifercept 1.5 mg/kg once daily
Reporting group description:	
Subjects with achondroplasia who completed study C4181005 (NCT04638153) continued to receive recifercept 1.5 mg/kg once daily via the subcutaneous route for up to 24 months.	

Primary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and Severe AEs

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and Severe AEs[1]

End point description:

An AE is any untoward medical occurrence in a subject or clinical study subject, temporally associated with the use of study intervention, whether or not considered related to the study intervention. SAE was an AE resulting in any of the following outcomes or considered medically significant: death; initial or prolonged inpatient hospitalisation; life-threatening experience; persistent or significant disability/incapacity; congenital anomaly or birth defect; suspected transmission via a Pfizer product of an infectious agent, pathogenic or non-pathogenic. Severe AEs were AEs that were medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling, limiting self-care activities of daily living. Full Analysis Set consisted of all subjects who received at least one dose of recifercept. Subjects were analysed according to the dose they actually received.

End point type	Primary

End point timeframe:

From first dose of recifercept until 28 days after last dose of study treatment (maximum up to 24 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: Only descriptive analysis was planned for this endpoint.

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	17	2	
Units: Subjects				
AEs	9	11	0	
SAEs	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Height at Month 24

End point title	Change From Baseline in Height at Month 24[2]

End point description:

Height was measured using anthropometric measurements. FAS included all subjects who received at least one dose of recifercept. Subjects were planned to be analysed according to the dose they actually received.

End point type	Primary

End point timeframe:

Baseline 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: Only descriptive analysis was planned for this endpoint.

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[3]	0[4]	0[5]	
Units: Centimeter (cm)				
least squares mean (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[3] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[4] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[5] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in arm Span to Height/Length Difference at Months 3, 6, 9

End point title	Change From Baseline in arm Span to Height/Length Difference at Months 3, 6, 9

End point description:

Height was calculated with anthropometric measurements. FAS included all subjects who received at least one dose of recifercept. Subjects were planned to be analysed according to the dose they actually received.

End point type	Secondary

End point timeframe:

Baseline and months 3, 6, 9

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[6]	0[7]	0[8]	
Units: Centimeters				
least squares mean (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[6] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[7] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[8] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Sitting Height to Standing Height Ratio at Months 3, 6, 9

End point title	Change From Baseline in Sitting Height to Standing Height Ratio at Months 3, 6, 9

End point description:

Height was calculated based upon the anthropometric measurements. FAS included all subjects who received at least one dose of recifercept. Subjects were planned to be analysed according to the dose they actually received.

End point type	Secondary

End point timeframe:

Baseline and Months 3, 6, 9

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[9]	0[10]	0[11]	
Units: Ratio				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[9] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[10] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[11] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL/F) of Recifercept

End point title	Clearance (CL/F) of Recifercept

End point description:

Clearance of a drug was a measure of the rate at which a drug is metabolised or eliminated by normal biological processes. Pharmacokinetic (PK) concentration set included all subjects who received at least 1 dose of recifercept and had at least 1 evaluable concentration result.

End point type	Secondary

End point timeframe:

Day 91, 181, 271, 361 and 451.

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[12]	0[13]	0[14]	
Units: milliliters per minute (mL/min)				
geometric mean (geometric coefficient of variation)	()	()	()	

Notes:

[12] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[13] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[14] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Knee Height to Lower Segment Ratio at Months 3, 6, 9

End point title	Change From Baseline in Knee Height to Lower Segment Ratio at Months 3, 6, 9

End point description:

Knee height was defined as the distance from the sole of the foot to the most anterior surface of the femoral condyles of the thigh (medial being more anterior), with the ankle and knee each flexed to a 90-degree angle. Lower segment of the leg included tibia and foot height. FAS included all subjects who received at least one dose of recifercept. Subjects were planned to be analysed according to the dose they actually received.

End point type	Secondary

End point timeframe:

Baseline and months 3, 6, 9

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[15]	0[16]	0[17]	

Units: Ratio				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[15] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[16] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[17] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Occipito-Frontal Circumference at Months 3, 6, 9

End point title	Change From Baseline in Occipito-Frontal Circumference at Months 3, 6, 9

End point description:

Occipito-frontal circumference was measured by anthropometric measurements. It was measured over the most prominent part on the back of the head (occiput) and just above the eyebrows (supraorbital ridges). FAS included all subjects who received at least one dose of recifercept. Subjects were planned to be analysed according to the dose they actually received.

End point type	Secondary

End point timeframe:

Baseline and months 3, 6, 9

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[18]	0[19]	0[20]	
Units: Centimeters				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[18] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[19] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[20] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Occipito-Frontal Distance to Occipito-mid-Face Measurements Ratio at Months 3, 6, 9

End point title	Change From Baseline in Occipito-Frontal Distance to Occipito-mid-Face Measurements Ratio at Months 3, 6, 9

End point description:

Occipito-frontal circumference was measured by anthropometric measurements. FAS included all subjects who were planned to receive at least one dose of recifercept.

End point type	Secondary
End point timeframe: Baseline, months 3, 6, 9	

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[21]	0[22]	0[23]	
Units: Ratio				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[21] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[22] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[23] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Mass Index (BMI) at Months 3, 6, 9

End point title	Change From Baseline in Body Mass Index (BMI) at Months 3, 6, 9
End point description: FAS included all subjects who were planned to receive at least one dose of recifercept.	
End point type	Secondary
End point timeframe: At Months 3, 6, 9	

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[24]	0[25]	0[26]	
Units: Kilograms per meter square				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[24] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[25] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[26] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Z-Score for Occipito-frontal Circumference, Arm Span, Sitting Height and Skull Morphology at Months 3, 6, 9

End point title	Change From Baseline in Z-Score for Occipito-frontal Circumference, Arm Span, Sitting Height and Skull Morphology at Months 3, 6, 9

End point description:

The Z-score described how many standard deviations a given measurement lies above or below a size or age-specific population mean. A Z-score above the population mean will have a positive value, whereas a Z-score below the population mean will have a negative value. The greater the deviation of the Z-score from zero (in a positive or negative direction), the greater the magnitude of deviation from the mean.

End point type	Secondary

End point timeframe:

Baseline, months 3, 6, 9

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[27]	0[28]	0[29]	
Units: Units on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[27] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[28] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[29] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fixed Flexion Angles at Elbow at Months 3, 6, 9

End point title	Change From Baseline in Fixed Flexion Angles at Elbow at Months 3, 6, 9

End point description:

Fixed Flexion Angles was measured by anthropometric measurements. FAS included all subjects who were planned to receive at least one dose of recifercept.

End point type	Secondary

End point timeframe:

Baseline, months 3, 6, 9

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[30]	0[31]	0[32]	
Units: Degrees				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[30] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[31] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[32] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Meaningful Findings in Laboratory Test Parameters Through The Study

End point title	Number of Subjects With Clinically Meaningful Findings in Laboratory Test Parameters Through The Study

End point description:

Laboratory parameters such as lymphocytes, neutrophils, eosinophils, monocytes and potassium were assessed. Clinically significant abnormal laboratory findings were determined by the investigator's decision. FAS included all subjects who were planned to receive at least one dose of recifercept.

End point type	Secondary

End point timeframe:

From baseline up to follow-up

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	16	2	
Units: Subjects				
Hematology: Lymphocytes	0	1	0	
Hematology:Neutrophils	0	1	0	
Hematology: Eosinophils	1	3	0	
Hematology: Monocytes	2	0	0	
Chemistry: Potassium	2	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Waist to Chest Circumference Ratio at Months 3, 6, 9

End point title	Change From Baseline in Waist to Chest Circumference Ratio at Months 3, 6, 9

End point description:

FAS included all subjects who were planned to receive at least one dose of recifercept.

End point type	Secondary

End point timeframe:

Baseline, Months 3, 6, 9

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[33]	0[34]	0[35]	
Units: Ratio				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[33] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[34] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).
[35] - Data was not collected as study was terminated based on sponsor discretion (not related to safety).

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Positive Anti-Drug Antibodies (ADA)

End point title	Number of Subjects With Positive Anti-Drug Antibodies (ADA)

End point description:

End point type	Secondary

End point timeframe:

From Day 91 up to Month 24

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	17	2	
Units: Subjects	12	15	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Findings in Vital Signs Through The Study

End point title	Number of Subjects With Clinically Significant Findings in Vital Signs Through The Study

End point description:

Absolute values and changes from baseline in supine systolic and diastolic blood pressure, oral temperature, and pulse rate were planned to be summarised by treatment in accordance with the sponsor reporting standards.

End point type	Secondary

End point timeframe:

From baseline up to follow-up

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	17	2	
Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Findings in Physical Examination Through The Study

End point title	Number of Subjects With Clinically Significant Findings in Physical Examination Through The Study

End point description:

A complete physical examination included cardiovascular, respiratory, gastrointestinal systems, and skin. Height and weight will also be measured and recorded as part of the anthropometric measurements collected.

End point type	Secondary

End point timeframe:

From baseline up to follow-up

End point values	Recifercept 1 milligram per kilogram (mg/kg) once weekly	Recifercept 2 mg/kg twice weekly	Recifercept 1.5 mg/kg once daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	17	2	
Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of the study treatment up to follow-up (approximately 24 months)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	Recifercept 1 mg/kg once weekly
Reporting group description:	
Subjects with achondroplasia who completed study C4181005 (NCT04638153) continued to receive recifercept 1 mg/kg once weekly via the subcutaneous route for up to 24 months.	
Reporting group title	Recifercept 1.5 mg/kg once daily
Reporting group description:	
Subjects with achondroplasia who completed study C4181005 (NCT04638153) continued to receive recifercept 1.5 mg/kg once daily via the subcutaneous route for up to 24 months.	
Reporting group title	Recifercept 2 mg/kg twice weekly
Reporting group description:	
Subjects with achondroplasia who completed study C4181005 (NCT04638153) continued to receive recifercept 2 mg/kg twice weekly via the subcutaneous route for up to 24 months.	

Serious adverse events	Recifercept 1 mg/kg once weekly	Recifercept 1.5 mg/kg once daily	Recifercept 2 mg/kg twice weekly
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	0 / 17 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

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

Non-serious adverse events	Recifercept 1 mg/kg once weekly	Recifercept 1.5 mg/kg once daily	Recifercept 2 mg/kg twice weekly
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 16 (56.25%)	0 / 2 (0.00%)	11 / 17 (64.71%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
General disorders and administration site conditions			

Injection site rash			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Fatigue			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Injection site haematoma			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 16 (18.75%)	0 / 2 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Catarrh			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Investigations			
Blood phosphorous increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Blood urea increase			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Platelet count increased			

subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	2
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Vaccination complication			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Nervous system disorders			
Nystagmus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Tympanic membrane perforation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Eustachian tube dysfunction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Odynophagia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 16 (12.50%)	0 / 2 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Otitis externa			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Oral herpes			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Nasopharyngiti			
subjects affected / exposed	3 / 16 (18.75%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	2
Influenza			
subjects affected / exposed	2 / 16 (12.50%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
Gastroenteritis viral			

subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Ear infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Conjunctivitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Otitis media			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Viral infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 2 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Skin candida			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	4 / 17 (23.53%)
occurrences (all)	1	0	4
Otitis media acute			
subjects affected / exposed	1 / 16 (6.25%)	0 / 2 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported