Clinical trial results:
A Three-Part, Single-Arm, Open-Label Study To Evaluate The Efficacy, Safety, And Pharmacokinetics Of Evinacumab In Pediatric Patients With Homozygous Familial Hypercholesterolemia

Summary

EudraCT number	2019-001931-30
Trial protocol	AT NL
Global end of trial date	30 May 2023

Results information

Result version number	v1 (current)
This version publication date	13 December 2023
First version publication date	13 December 2023

Trial information

Trial identification

Sponsor protocol code	R1500-CL-17100

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04233918
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, NY, United States, 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002298-PIP01-17
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	30 May 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective for Part A of the study is to assess the pharmacokinetics (PK) of evinacumab in pediatric participants with homozygous familial hypercholesterolemia (HoFH).

The primary objective for Part B of the study is to demonstrate a reduction of low-density lipoprotein cholesterol (LDL-C) by evinacumab in pediatric (5 to 11 years of age) participants with HoFH.

Protection of trial subjects:

It is the responsibility of both the sponsor and the investigator(s) to ensure that this clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the ICH guidelines for GCP and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 June 2020
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	Austria: 5
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	20
EEA total number of subjects	9

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)	20
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 23 participants were screened to Part A and Part B. 6 participants were enrolled in Part A, 14 participants in Part B. 3 participants were considered screen failures. 2 withdrew consent, 1 due to Other. Participants who enrolled in Part A of study were not eligible to participate in Part B. All 20 participants completed part C.

Period 1

Period 1 title	Period 1: Part A and B
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Evinacumab 15mg/Kg IV

Arm description:

In Part A, Participants received single IV infusion of evinacumab at a dose of 15 mg/kg on Day 1.

Arm type	Experimental
Investigational medicinal product name	evinacumab
Investigational medicinal product code	R1500
Other name	Evkeeza
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received a single dose of evinacumab 15 milligrams per kilogram (mg/kg) administered by intravenous (IV) infusion

Arm title	Part B: Evinacumab 15mg/Kg IV Q4W

Arm description:

In Part B, Participants received IV infusion of evinacumab at a dose of 15 mg/kg Q4W from Day 1 up to Week 24.

Arm type	Experimental
Investigational medicinal product name	evinacumab
Investigational medicinal product code	R1500
Other name	Evkeeza
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received evinacumab 15 milligrams per kilogram (mg/kg) administered by intravenous (IV) infusion every four weeks (Q4W) from Week 0 to Week 24

Number of subjects in period 1	Part A: Evinacumab 15mg/Kg IV	Part B: Evinacumab 15mg/Kg IV Q4W
Started	6	14
Completed	6	14

Period 2	
Period 2 title	Part C (Extension Period)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Part A to C

Arm description:

All participants who completed Part A received IV infusion of evinacumab at a dose of 15 mg/kg Q4W from Day 1 up to Week 48 in Part C.

Arm type	Experimental
Investigational medicinal product name	evinacumab
Investigational medicinal product code	R1500
Other name	Evkeeza
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All participants from Part A who entered Part C initially received open-label evinacumab 15 mg/kg IV Q4W. The final dose in Part C was the same as the dose in Part B, 15 mg/kg IV Q4W, during the 48 week treatment period.

Arm title	Part B to C

Arm description:

All participants who completed Part B received IV infusion of evinacumab at a dose of 15 mg/kg Q4W from Day 1 up to Week 48 in Part C.

Arm type	Experimental
Investigational medicinal product name	evinacumab
Investigational medicinal product code	R1500
Other name	Evkeeza
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All participants from Part B who entered Part C initially received open-label evinacumab 15 mg/kg IV Q4W. The final dose in Part C was the same as the dose in Part B, 15 mg/kg IV Q4W, during the 48 week treatment period.

Number of subjects in period 2	Part A to C	Part B to C
Started	6	14
Completed	6	14

Baseline characteristics

Reporting groups	
Reporting group title	Part A: Evinacumab 15mg/Kg IV
Reporting group description:	
In Part A, Participants received single IV infusion of evinacumab at a dose of 15 mg/kg on Day 1.	
Reporting group title	Part B: Evinacumab 15mg/Kg IV Q4W
Reporting group description:	
In Part B, Participants received IV infusion of evinacumab at a dose of 15 mg/kg Q4W from Day 1 up to Week 24.	

Reporting group values	Part A: Evinacumab 15mg/Kg IV	Part B: Evinacumab 15mg/Kg IV Q4W	Total
Number of subjects	6	14	20
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	6	14	20
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	8.8	9.1	
standard deviation	± 1.72	± 1.94	-
Sex: Female, Male Units: participants			
Female	4	8	12
Male	2	6	8
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	0	2	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	6	8	14
More than one race	0	0	0
Unknown or Not Reported	0	2	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	5	13	18
Unknown or Not Reported	0	1	1

End points

End points reporting groups

Reporting group title	Part A: Evinacumab 15mg/Kg IV
Reporting group description:	
In Part A, Participants received single IV infusion of evinacumab at a dose of 15 mg/kg on Day 1.	
Reporting group title	Part B: Evinacumab 15mg/Kg IV Q4W
Reporting group description:	
In Part B, Participants received IV infusion of evinacumab at a dose of 15 mg/kg Q4W from Day 1 up to Week 24.	
Reporting group title	Part A to C
Reporting group description:	
All participants who completed Part A received IV infusion of evinacumab at a dose of 15 mg/kg Q4W from Day 1 up to Week 48 in Part C.	
Reporting group title	Part B to C
Reporting group description:	
All participants who completed Part B received IV infusion of evinacumab at a dose of 15 mg/kg Q4W from Day 1 up to Week 48 in Part C.	

Primary: Part A: Maximum Observed Serum Concentration (Cmax) of Evinacumab

End point title	Part A: Maximum Observed Serum Concentration (Cmax) of Evinacumab[1][2]
End point description:	
Cmax was obtained directly from the plasma concentration versus time curve.	
End point type	Primary
End point timeframe:	
At day 12	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analysis was used for this endpoint.

[2] - 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: This endpoint was pre-specified for Part A only

End point values	Part A: Evinacumab 15mg/Kg IV			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Milligrams per Liter (mg/L)				
arithmetic mean (standard deviation)	238 (± 90.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Area Under the Serum Concentration-Time Curve from Time Zero to the Time of the Last Measurable Concentration (AUClast) of Evinacumab

End point title	Part A: Area Under the Serum Concentration-Time Curve from Time Zero to the Time of the Last Measurable Concentration (AUClast) of Evinacumab[3][4]

End point description:

AUClast was defined as area under the serum concentration time-curve from zero to the last measured concentration.

End point type	Primary

End point timeframe:

Pre-dose at Week 0; End of infusion at Week 0.006, 1, 2, 4, 8 and 12

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: Descriptive analysis was used for this endpoint.

[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: This endpoint was pre-specified for Part A only

End point values	Part A: Evinacumab 15mg/Kg IV			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Days*Milligrams per Liter (day*mg/L)				
arithmetic mean (standard deviation)	4576 (± 1568)			

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Terminal Half-Life (t1/2) of Evinacumab

End point title	Part A: Terminal Half-Life (t1/2) of Evinacumab[5][6]

End point description:

T1/2 was defined as the time required for the plasma concentration of drug to decrease 50 percent in the final stage of its elimination.

End point type	Primary

End point timeframe:

Pre-dose at Week 0; End of infusion at Week 0.006, 1, 2, 4, 8 and 12

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analysis was used for this endpoint.

[6] - 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: This endpoint was pre-specified for Part A only

End point values	Part A: Evinacumab 15mg/Kg IV			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Days				
median (full range (min-max))	7.69 (6.18 to 12.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Percent Change in Calculated Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Week 24

End point title	Part B: Percent Change in Calculated Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Week 24[7][8]

End point description:

Percent change was calculated as 100 multiplied by (calculated LDL-C value at Week 24 minus calculated LDL-C value at baseline) divided by calculated LDL-C value at baseline.

End point type	Primary

End point timeframe:

Baseline to Week 24

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analysis was used for this endpoint.

[8] - 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: This endpoint was pre-specified for Part B only

End point values	Part B: Evinacumab 15mg/Kg IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Percent Change				
arithmetic mean (confidence interval 95%)	-48.3 (-68.8 to -27.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A and Part B: Number of Participants with Treatment-Emergent Adverse Events (TEAEs)

End point title	Part A and Part B: Number of Participants with Treatment-Emergent Adverse Events (TEAEs)

End point description:

Any untoward medical occurrence in a participant who received investigational medicinal product (IMP) was considered an AE without regard to possibility of causal relationship with this treatment. A serious adverse event (SAE) was defined as any untoward medical occurrence that resulted in any of the following outcomes: death, life-threatening, required initial or prolonged in-patient hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect, or considered as medically important event. TEAE was defined as AE starting/worsening after first intake of study drug. TEAE included participants with both serious and non-serious AEs.

End point type	Secondary

End point timeframe:

Part A: up to Week 24; Part B: up to Week 48

End point values	Part A: Evinacumab 15mg/Kg IV	Part B: Evinacumab 15mg/Kg IV Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	14		
Units: Participants	5	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percent Change in Apolipoprotein B (Apo B) From Baseline to Week 24

End point title	Part B: Percent Change in Apolipoprotein B (Apo B) From Baseline to Week 24[9]

End point description:

Percent change in Apo B from baseline to Week 24 was reported.

End point type	Secondary

End point timeframe:

Baseline to Week 24

Notes:

[9] - 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: This endpoint was pre-specified for Part B only

End point values	Part B: Evinacumab 15mg/Kg IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Percent Change				
arithmetic mean (confidence interval 95%)	-41.3 (-58.9 to -23.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percent Change in Total Cholesterol (TC) From Baseline to Week 24

End point title	Part B: Percent Change in Total Cholesterol (TC) From Baseline

	to Week 24[10]

End point description:

Percent change in TC from baseline to Week 24 was reported.

End point type	Secondary

End point timeframe:

Baseline to Week 24

Notes:

[10] - 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: This endpoint was pre-specified for Part B only

End point values	Part B: Evinacumab 15mg/Kg IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Percent Change				
arithmetic mean (confidence interval 95%)	-49.1 (-64.9 to -33.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percent Change in Non-High-Density Lipoprotein Cholesterol (Non-HDL-C) From Baseline to Week 24

End point title	Part B: Percent Change in Non-High-Density Lipoprotein Cholesterol (Non-HDL-C) From Baseline to Week 24[11]

End point description:

Percent change in Non-HDL-C from baseline to Week 24 was reported.

End point type	Secondary

End point timeframe:

Baseline to Week 24

Notes:

[11] - 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: This endpoint was pre-specified for Part B only

End point values	Part B: Evinacumab 15mg/Kg IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Percent Change				
arithmetic mean (confidence interval 95%)	-48.9 (-68.1 to -29.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants With ≥50 Percent (%) Reduction in Calculated Low-Density Lipoprotein Cholesterol (LDL-C) at Week 24

End point title	Part B: Percentage of Participants With ≥50 Percent (%) Reduction in Calculated Low-Density Lipoprotein Cholesterol (LDL-C) at Week 24[12]

End point description:

Percentage of participants who achieved reduction in calculated LDL-C ≥ 50% at Week 24 was reported.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[12] - 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: This endpoint was pre-specified for Part B only

End point values	Part B: Evinacumab 15mg/Kg IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Percentage of Participants				
number (not applicable)	78.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Absolute Change in Low-density Lipoprotein Cholesterol (LDL-C) From Baseline at Week 24

End point title	Part B: Absolute Change in Low-density Lipoprotein Cholesterol (LDL-C) From Baseline at Week 24[13]

End point description:

Absolute change in LDL-C from baseline at Week 24 was reported

End point type	Secondary

End point timeframe:

Baseline, Week 24

Notes:

[13] - 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: This endpoint was pre-specified for Part B only

End point values	Part B: Evinacumab 15mg/Kg IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Milligrams per Deciliter (mg/dL)				
arithmetic mean (standard error)	-131.9 (± 30.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percent Change in Lipoprotein A (Lp[a]) From Baseline to Week 24

End point title	Part B: Percent Change in Lipoprotein A (Lp[a]) From Baseline to Week 24[14]

End point description:

Percent change in Lp(a) from baseline to Week 24 was reported.

End point type	Secondary

End point timeframe:

Baseline to Week 24

Notes:

[14] - 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: This endpoint was pre-specified for Part B only

End point values	Part B: Evinacumab 15mg/Kg IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Percent Change				
arithmetic mean (confidence interval 95%)	-37.3 (-42.2 to -32.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percent Change in Calculated Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Week 24 in Participants who have Negative/Negative and Null/Null Mutations

End point title	Part B: Percent Change in Calculated Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Week 24 in Participants who have Negative/Negative and Null/Null Mutations[15]

End point description:

Participants with HoFH was classified based on the phenotype of the Low-density lipoprotein receptor

(LDLR) mutation(s), ranging from defective mutations (where the LDLR retains some LDL-binding functionality) to null or negative mutations where no functioning LDLR was expressed. Participants who have LDLR activity <15% are considered null and participants whose LDLR activity was impaired but >15% are LDLR defective. Percent change in calculated LDL-C from baseline to Week 24 in participants who have negative/negative and null/null mutations was reported.

End point type	Secondary

End point timeframe:

Baseline to Week 24

Notes:

[15] - 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: This endpoint was pre-specified for Part B only

End point values	Part B: Evinacumab 15mg/Kg IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percent Change				
arithmetic mean (standard error)				
Negative/negative mutations (n=3)	-67.7 (± 6.5)			
Null/Null mutations (n=1)	-57.2 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Serum Concentration of Total Evinacumab

End point title	Part B: Serum Concentration of Total Evinacumab[16]

End point description:

Serum concentration of total evinacumab was reported. Pre-dose samples at week 0 were assayed and the reported value is based on actual measurement.

End point type	Secondary

End point timeframe:

Pre-dose at Weeks 0, 4, 8, 12; End of infusion at Weeks 0.006, 4.006, 8.006, 12.006 and 24

Notes:

[16] - 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: This endpoint was pre-specified for Part B only

End point values	Part B: Evinacumab 15mg/Kg IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Milligrams per Liter (mg/L)				
arithmetic mean (standard deviation)				
Week 0	0 (± 0)			
Week 0.006	256 (± 58.0)			

Week 4	62.6 (± 22.6)			
Week 4.006	293 (± 92.3)			
Week 8	98.8 (± 37.7)			
Week 8.006	356 (± 76)			
Week 12	120 (± 46.5)			
Week 12.006	363 (± 82.1)			
Week 24	140 (± 92.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Maximum Serum Concentration at Steady State (Cmax,ss) of Evinacumab

End point title	Part B: Maximum Serum Concentration at Steady State (Cmax,ss) of Evinacumab[17]

End point description:

Maximum serum concentration (Cmax,ss) steady state following drug administration.

End point type	Secondary

End point timeframe:

Post-dose on Days 1, 29, 57, 85 and 169

Notes:

[17] - 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: This endpoint was pre-specified for Part B only

End point values	Part B: Evinacumab 15mg/Kg IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Milligrams per Liter (mg/L)				
arithmetic mean (standard deviation)	428.9 (± 113.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Minimum Serum Concentration at Steady State (Ctrough.ss) of Evinacumab

End point title	Part B: Minimum Serum Concentration at Steady State (Ctrough.ss) of Evinacumab[18]

End point description:

Ctrough.ss was defined as minimum serum concentration at steady state of evinacumab

End point type	Secondary

End point timeframe:

Post-dose on Days 1, 29, 57, 85 and 169

Notes:

[18] - 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: This endpoint was pre-specified for Part B only

End point values	Part B: Evinacumab 15mg/Kg IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Milligrams per Liter (mg/L)				
arithmetic mean (standard deviation)	171.8 (± 79.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Area Under the Serum Concentration-time Curve at Steady State (AUCtau.ss) of Evinacumab

End point title	Part B: Area Under the Serum Concentration-time Curve at Steady State (AUCtau.ss) of Evinacumab[19]

End point description:

AUCtau.ss was defined as area under the serum concentration-time curve at steady state of evinacumab

End point type	Secondary

End point timeframe:

Post-dose on Days 1, 29, 57, 85 and 169

Notes:

[19] - 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: This endpoint was pre-specified for Part B only

End point values	Part B: Evinacumab 15mg/Kg IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Day*Milligrams per Liter (Day*mg/L)				
arithmetic mean (standard deviation)	7019 (± 2561)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percent Change in Calculated Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Week 24 in Participants who have by null/null vs. non-null/null and negative/negative vs.non-negative/negative Mutations

End point title	Part B: Percent Change in Calculated Low-Density Lipoprotein Cholesterol (LDL-C) From Baseline to Week 24 in Participants who have by null/null vs. non-null/null and negative/negative vs.non-negative/negative Mutations[20]

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 24

Notes:

[20] - 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: This endpoint was pre-specified for Part B only

End point values	Part B: Evinacumab 15mg/Kg IV Q4W			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Percent Change				
arithmetic mean (standard error)				
Negative/Negative	-67.7 (± 6.5)			
Non-Negative/Negative	-43.0 (± 12.8)			
Null/Null	-57.2 (± 99999)			
Non-Null/Null	-47.6 (± 11.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From first dose up to week 96 (24 weeks in Part A/B + 48 weeks of treatment in Part C + 24 weeks of follow-up)	
Adverse event reporting additional description: Part A - up to week 24 Part B - up to Week 48 or up to the day before the first dose in Part C for participants entering Part C Part C - up to a 48-week treatment period and 24-week follow-up	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	Part A Evinacumab 15mg
Reporting group description: Participants received single intravenous (IV) infusion of evinacumab at a dose of 15 milligrams per kilogram (mg/kg) on Day 1 in Part A.	
Reporting group title	Part B-C Evinacumab 15mg
Reporting group description: All participants who completed Part B received IV infusion of evinacumab at a dose of 15 mg/kg Q4W from Day 1 up to Week 48 in Part C.	
Reporting group title	Part A-C Evinacumab 15mg
Reporting group description: All participants who completed Part A received IV infusion of evinacumab at a dose of 15 mg/kg Q4W from Day 1 up to Week 48 in Part C.	
Reporting group title	Part B Evinacumab 15mg
Reporting group description: Participants received IV infusion of evinacumab at a dose of 15 mg/kg every four weeks (Q4W) from Day 1 up to Week 24 in Part B.	

Serious adverse events	Part A Evinacumab 15mg	Part B-C Evinacumab 15mg	Part A-C Evinacumab 15mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
Aortic valve stenosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (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
Infections and infestations			

Tonsillitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	0 / 6 (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	Part B Evinacumab 15mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 14 (7.14%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Cardiac disorders			
Aortic valve stenosis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Tonsillitis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part A Evinacumab 15mg	Part B-C Evinacumab 15mg	Part A-C Evinacumab 15mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	11 / 14 (78.57%)	6 / 6 (100.00%)
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	1 / 6 (16.67%)
occurrences (all)	0	1	2
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	4 / 14 (28.57%)	2 / 6 (33.33%)
occurrences (all)	0	5	2
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Infusion site extravasation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infusion site swelling			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 6 (33.33%)	4 / 14 (28.57%)	1 / 6 (16.67%)
occurrences (all)	2	6	2
Cough			
subjects affected / exposed	2 / 6 (33.33%)	2 / 14 (14.29%)	2 / 6 (33.33%)
occurrences (all)	2	3	2
Rhinitis allergic			
subjects affected / exposed	2 / 6 (33.33%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Product issues			
Device malfunction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	2
Investigations			

Body temperature increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vitamin D decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Lipoprotein (a) increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Apheresis related complication			
subjects affected / exposed	1 / 6 (16.67%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Burn oral cavity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sunburn			

subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Thermal burn			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 6 (16.67%)	4 / 14 (28.57%)	1 / 6 (16.67%)
occurrences (all)	1	7	1
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Poikilocytosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Retinal thickening			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Papilloedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	1 / 6 (16.67%)
occurrences (all)	0	1	2
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	3 / 14 (21.43%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Abdominal discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	3 / 14 (21.43%)	1 / 6 (16.67%)
occurrences (all)	1	3	2
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 14 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	2 / 14 (14.29%)	0 / 6 (0.00%)
occurrences (all)	1	4	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash			

subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Miliaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	2 / 14 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal and connective tissue disorders			
Osteochondrosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Gastrointestinal viral infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Otitis media			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Rhinitis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 14 (7.14%)	2 / 6 (33.33%)
occurrences (all)	1	1	2
Tonsillitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis viral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
COVID-19			

subjects affected / exposed	1 / 6 (16.67%)	10 / 14 (71.43%)	4 / 6 (66.67%)
occurrences (all)	1	10	4
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	2 / 14 (14.29%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	1 / 6 (16.67%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vitamin D deficiency			
subjects affected / exposed	2 / 6 (33.33%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Part B Evinacumab 15mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 14 (78.57%)		
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Infusion site extravasation			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Infusion site swelling			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Cough			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	3		
Rhinitis allergic			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Product issues			
Device malfunction			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Investigations			

Body temperature increased			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Vitamin D decreased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Lipoprotein (a) increased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Apheresis related complication			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Skin abrasion			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Burn oral cavity			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Limb injury			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Sunburn			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Thermal burn			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	3		
Neuropathy peripheral			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Poikilocytosis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Ear pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Retinal thickening			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Papilloedema			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		

Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Abdominal discomfort			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Gastritis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Rash			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Miliaria			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Osteochondrosis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Gastrointestinal viral infection			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Otitis media			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Tonsillitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
COVID-19			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Ear infection			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Vitamin D deficiency			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 May 2020	Study designed revised to reduce treatment periods of Parts B and C; Updated exclusion criteria; Added endpoint; Added information for Events that Require Expedited reporting to Sponsor; Other clarifications and editorial updates
25 May 2022	Amendment to allow participants who entered the compassionate use program or early access program to forgo the follow-up period of the study since the follow-up period was intended to be an off-drug follow-up period; Overall target and Part B populations reduced.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported