Clinical trial results:
An Open-Label Study to Evaluate the Long-Term Safety and Efficacy of Evinacumab in Patients With Homozygous Familial Hypercholesterolemia

Summary

EudraCT number	2017-003170-13
Trial protocol	NL NO CZ FR GR GB AT IT
Global end of trial date	13 April 2023

Results information

Result version number	v1 (current)
This version publication date	27 October 2023
First version publication date	27 October 2023

Trial information

Trial identification

Sponsor protocol code	R1500-CL-1719

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03409744
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	13 April 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

An open-label study of long-term treatment with evinacumab (15 mg/kg IV every 4 weeks), in participants with homozygous familial hypercholesterolemia.

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	13 March 2018
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	Austria: 5
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Czechia: 3
Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Greece: 6
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Japan: 11
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	South Africa: 14
Country: Number of subjects enrolled	Ukraine: 7
Country: Number of subjects enrolled	United States: 19
Worldwide total number of subjects	116
EEA total number of subjects	50

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)	14
Adults (18-64 years)	93
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 118 participants were planned to be enrolled. 116 participants were enrolled & treated. Reasons for screen fail were: 1 participant was unwilling to use protocol defined contraception, and 1 participant had a Low-density lipoprotein cholesterol (LDL-C) level less than the lower limit required for inclusion.

Period 1

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

Arms

Arm title	Total evinacumab

Arm description:

Includes all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.

Arm type	Experimental
Investigational medicinal product name	evinacumab
Investigational medicinal product code	REGN1500
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

15 milligrams per kilogram (mg/kg) administered intravenously (IV) every 4 weeks (Q4W)

Number of subjects in period 1	Total evinacumab
Started	116
Completed	106
Not completed	10
Adverse event, serious fatal	2
Physician decision	5
Pregnancy	1
Lost to follow-up	1
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	116	116	
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	38.8		
standard deviation	± 15.92	-	
Gender Categorical Units: Subjects			
Female	57	57	
Male	59	59	
Race (NIH/OMB) Units: Subjects			
White	80	80	
Black or African American	4	4	
Asian	12	12	
American Indian or Alaska Native	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Not Reported	11	11	
Other	9	9	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	6	6	
Not Hispanic or Latino	100	100	
Not Reported	10	10	

End points

End points reporting groups

Reporting group title	Total evinacumab
Reporting group description:	
Includes all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.	
Subject analysis set title	Total evinacumab
Subject analysis set type	Safety analysis
Subject analysis set description:	
Includes all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.	

Primary: Number of Participants with Treatment-Emergent Adverse Events (TEAEs) Up to Week 216

End point title	Number of Participants with Treatment-Emergent Adverse Events (TEAEs) Up to Week 216[1]
End point description:	
The safety analysis set (SAF) included all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.	
End point type	Primary
End point timeframe:	
Up to 216 weeks	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Descriptive statistics were used for this endpoint.	

End point values	Total evinacumab			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: Number of participants				
Participants with any TEAE	93			
Participants with at least one serious TEAE	27			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Low-Density Lipoprotein Cholesterol (LDL-C) over time

End point title	Percent change in Low-Density Lipoprotein Cholesterol (LDL-C) over time
End point description:	
The safety analysis set (SAF) included all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.	
End point type	Secondary
End point timeframe:	
Up to 120 weeks	

End point values	Total evinacumab			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: milligrams per deciliter (mg/dL)				
arithmetic mean (standard deviation)				
Week 8 (n=109)	-46.45 (± 35.504)			
Week 24 (n=86)	-43.64 (± 37.606)			
Week 48 (n=95)	-43.88 (± 36.037)			
Week 72 (n=92)	-45.17 (± 31.571)			
Week 96 (n=66)	-38.00 (± 52.859)			
Week 120 (n=39)	-33.10 (± 65.888)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in LDL-C over time

End point title	Absolute change in LDL-C over time

End point description:

The safety analysis set (SAF) included all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.

End point type	Secondary

End point timeframe:

Up to 120 weeks

End point values	Total evinacumab			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 8 (n=109)	-142.1 (± 114.61)			
Week 24 (n=86)	-132.0 (± 124.37)			
Week 48 (n=95)	-132.8 (± 133.29)			
Week 72 (n=92)	-135.1 (± 121.91)			

Week 96 (n=66)	-131.4 (± 129.29)			
Week 120 (n=39)	-132.5 (± 132.03)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Apolipoprotein B (Apo B) over time

End point title	Percent change in Apolipoprotein B (Apo B) over time

End point description:

The safety analysis set (SAF) included all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.

End point type	Secondary

End point timeframe:

Up to 120 weeks

End point values	Total evinacumab			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 8 (n=109)	-39.74 (± 25.338)			
Week 24 (n=86)	-36.98 (± 27.574)			
Week 48 (n=96)	-35.85 (± 29.998)			
Week 72 (n=93)	-37.60 (± 27.292)			
Week 96 (n=66)	-32.54 (± 39.969)			
Week 120 (n=39)	-27.73 (± 51.722)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in Apo B over time

End point title	Absolute change in Apo B over time

End point description:

The safety analysis set (SAF) included all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.

End point type	Secondary

End point timeframe:

Up to 120 weeks

End point values	Total evinacumab			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 8 (n=109)	-78.0 (± 59.78)			
Week 24 (n=86)	-70.5 (± 61.96)			
Week 48 (n=96)	-69.4 (± 69.95)			
Week 72 (n=93)	-73.9 (± 61.51)			
Week 96 (n=66)	-71.5 (± 66.66)			
Week 120 (n=39)	-70.7 (± 76.05)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in non-High-Density Lipoprotein Cholesterol (HDL-C) over time

End point title	Percent change in non-High-Density Lipoprotein Cholesterol (HDL-C) over time

End point description:

The safety analysis set (SAF) included all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.

End point type	Secondary

End point timeframe:

Up to 120 weeks

End point values	Total evinacumab			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 8 (n=109)	-48.47 (± 28.369)			
Week 24 (n=86)	-46.14 (± 29.117)			

Week 48 (n=95)	-45.15 (± 33.566)			
Week 72 (n=92)	-46.69 (± 28.534)			
Week 96 (n=66)	-40.88 (± 46.588)			
Week 120 (n=39)	-35.85 (± 58.374)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in non-HDL-C over time

End point title	Absolute change in non-HDL-C over time

End point description:

The safety analysis set (SAF) included all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.

End point type	Secondary

End point timeframe:

Up to 120 weeks

End point values	Total evinacumab			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 8 (n=109)	-153.7 (± 115.66)			
Week 24 (n=86)	-143.9 (± 125.03)			
Week 48 (n=95)	-144.1 (± 136.95)			
Week 72 (n=92)	-147.3 (± 122.76)			
Week 96 (n=66)	-144.5 (± 131.15)			
Week 120 (n=39)	-142.9 (± 136.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Total Cholesterol (TC) over time

End point title	Percent change in Total Cholesterol (TC) over time

End point description:

The safety analysis set (SAF) included all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.

End point type	Secondary

End point timeframe:

Up to 120 weeks

End point values	Total evinacumab			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 8 (n=109)	-47.04 (± 20.722)			
Week 24 (n=86)	-44.17 (± 24.224)			
Week 48 (n=95)	-43.78 (± 27.838)			
Week 72 (n=93)	-44.58 (± 25.700)			
Week 96 (n=66)	-40.33 (± 38.163)			
Week 120 (n=39)	-36.92 (± 47.469)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in TC over time

End point title	Absolute change in TC over time

End point description:

The safety analysis set (SAF) included all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.

End point type	Secondary

End point timeframe:

Up to 120 weeks

End point values	Total evinacumab			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 8 (n=109)	-167.3 (± 115.76)			

Week 24 (n=86)	-157.4 (± 125.93)			
Week 48 (n=95)	-158.2 (± 136.51)			
Week 72 (n=93)	-160.7 (± 123.09)			
Week 96 (n=66)	-157.2 (± 132.40)			
Week 120 (n=39)	-153.8 (± 138.26)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Triglycerides (TGs) over time

End point title	Percent change in Triglycerides (TGs) over time

End point description:

The safety analysis set (SAF) included all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.

End point type	Secondary

End point timeframe:

Up to 120 weeks

End point values	Total evinacumab			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 8 (n=107)	-45.97 (± 26.024)			
Week 24 (n=84)	-46.93 (± 24.582)			
Week 48 (n=94)	-43.25 (± 37.443)			
Week 72 (n=92)	-46.50 (± 25.826)			
Week 96 (n=66)	-48.28 (± 24.136)			
Week 120 (n=36)	-42.06 (± 36.945)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in TGs over time

End point title	Absolute change in TGs over time

End point description:

The safety analysis set (SAF) included all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.

End point type	Secondary

End point timeframe:

Up to 120 weeks

End point values	Total evinacumab			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 8 (n=107)	-64.4 (± 89.77)			
Week 24 (n=84)	-68.1 (± 97.29)			
Week 48 (n=94)	-66.7 (± 97.02)			
Week 72 (n=92)	-68.8 (± 91.52)			
Week 96 (n=66)	-75.2 (± 107.49)			
Week 120 (n=36)	-66.7 (± 110.95)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From signing of Informed Consent to week 216	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	Overall
Reporting group description:	
Includes all participants who were enrolled and received at least 1 dose or part of a dose of open-label study treatment.	

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 116 (23.28%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Peripheral artery stenosis			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arteriosclerosis			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aortic stenosis			

subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 116 (1.72%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Food allergy			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst ruptured			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Scapula fracture			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular pseudoaneurysm			

subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cervical vertebral fracture				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arteriovenous fistula site complication				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Coronary artery occlusion				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac valve disease				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure chronic				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				

subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Atrial fibrillation				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 116 (0.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	2 / 116 (1.72%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Aortic valve disease				
subjects affected / exposed	2 / 116 (1.72%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	2 / 116 (1.72%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	2 / 116 (1.72%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Supravalvular aortic stenosis				

subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery stenosis			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal epidural haematoma			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Glaucoma			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cataract			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Intestinal ischaemia			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatitis acute			

subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal infarct			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Oesophageal candidiasis			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 116 (0.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 116 (0.86%)		
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	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 116 (68.10%)		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	6 / 116 (5.17%)		
occurrences (all)	6		
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 116 (16.38%)		
occurrences (all)	29		

Dizziness			
subjects affected / exposed	7 / 116 (6.03%)		
occurrences (all)	9		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	10 / 116 (8.62%)		
occurrences (all)	16		
Influenza like illness			
subjects affected / exposed	17 / 116 (14.66%)		
occurrences (all)	23		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 116 (8.62%)		
occurrences (all)	21		
Abdominal pain			
subjects affected / exposed	7 / 116 (6.03%)		
occurrences (all)	10		
Toothache			
subjects affected / exposed	7 / 116 (6.03%)		
occurrences (all)	10		
Vomiting			
subjects affected / exposed	7 / 116 (6.03%)		
occurrences (all)	11		
Nausea			
subjects affected / exposed	14 / 116 (12.07%)		
occurrences (all)	17		
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 116 (5.17%)		
occurrences (all)	6		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	6 / 116 (5.17%)		
occurrences (all)	7		
Cough			
subjects affected / exposed	12 / 116 (10.34%)		
occurrences (all)	16		

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	15 / 116 (12.93%)		
occurrences (all)	22		
Pain in extremity			
subjects affected / exposed	8 / 116 (6.90%)		
occurrences (all)	10		
Back pain			
subjects affected / exposed	14 / 116 (12.07%)		
occurrences (all)	20		
Myalgia			
subjects affected / exposed	7 / 116 (6.03%)		
occurrences (all)	10		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	10 / 116 (8.62%)		
occurrences (all)	16		
Upper respiratory tract infection			
subjects affected / exposed	9 / 116 (7.76%)		
occurrences (all)	14		
Nasopharyngitis			
subjects affected / exposed	23 / 116 (19.83%)		
occurrences (all)	42		
COVID-19			
subjects affected / exposed	19 / 116 (16.38%)		
occurrences (all)	20		
Gastroenteritis			
subjects affected / exposed	10 / 116 (8.62%)		
occurrences (all)	11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 July 2018	The primary purpose of this amendment was to revise the participant population to allow participants with HoFH who had not participated in a previous evinacumab study to enter this study; minor editorial revisions; clarification of wording; added assessments to schedule of events; clarification of inclusion/exclusion criteria and study population
11 October 2019	After completion of the 2A and 2B versions of the protocol, a country-specific version was required, which became R1500-CL-1719 2B FR. Subsequently, the R1500-CL-1719 2B FR was amended to become R1500-CL-1719 3B FR. To avoid confusion and maintain the sequence, the numbering of present amendment became R1500-CL-1719 4B.
01 November 2019	The primary purpose for this amendment was to increase the number of participants from 100 to 120 and to add objectives to assess efficacy and safety in adolescent participants with HoFH. This also resulted in changes to the statistical analyses.
29 May 2020	Editorial revisions; clarified exclusion criteria; updated schedule of events and study design

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported