Clinical trial results:
A Randomized, Actively Controlled, Open-label, Multicenter Study of Efficacy and Safety of Evolocumab Compared With Low Density Lipoprotein Cholesterol (LDL-C) Apheresis, Followed by Single-Arm Evolocumab Administration in Subjects Receiving LDL-C Apheresis Prior to Study Enrollment

Summary

EudraCT number	2015-001343-37
Trial protocol	DE ES CZ IT
Global end of trial date	20 January 2017

Results information

Result version number	v1 (current)
This version publication date	19 January 2018
First version publication date	19 January 2018

Trial information

Trial identification

Sponsor protocol code	20140316

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02585895
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 January 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the efficacy of subcutaneous evolocumab, compared with regularly scheduled low-density lipoprotein cholesterol (LDL-C) apheresis, on reducing the need for future apheresis.

Protection of trial subjects:

This study was conducted in accordance with International Council on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines.
The study was reviewed by an independent ethics committee (IEC) or institutional review board (IRB). All subjects provided written informed consent before undergoing any study-related procedures, including screening procedures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Czech Republic: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	39
EEA total number of subjects	30

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	21
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 15 centers in the following 8 countries: Australia, Czech Republic, France, Germany, Italy, Spain, the United Kingdom, and the United States. Participants were enrolled from 21 December 2015 to 21 July 2016.

Pre-assignment

Screening details:

Participants were randomized in a 1:1 ratio to continue apheresis on the same schedule as before study entry, or to stop apheresis and receive evolocumab. Randomization was stratified by screening low-density lipoprotein cholesterol (LDL-C) (< 160 mg/dL [4.1 mmol/L] vs ≥ 160 mg/dL).

Period 1

Period 1 title	Primary Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Apheresis

Arm description:

Participants continued apheresis at the same schedule, every week (QW) or every two weeks (Q2W), as prior to study entry, for 6 weeks during the primary period of the study.

Arm type	Comparator procedure

No investigational medicinal product assigned in this arm

Arm title	Evolocumab

Arm description:

Participants received 140 mg evolocumab every 2 weeks (Q2W) administered by subcutaneous injection for 6 weeks during the primary period of the study.

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	AMG 145
Other name	Repatha
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection once every 2 weeks

Number of subjects in period 1	Apheresis	Evolocumab
Started	20	19
Completed	20	19

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Apheresis/Evolocumab

Arm description:

Participants who received apheresis for 6 weeks during the primary period of the study then received 140 mg evolocumab Q2W from week 6 to week 24 in the post-primary period.

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	AMG 145
Other name	Repatha
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection once every 2 weeks

Arm title	Evolocumab/Evolocumab

Arm description:

Participants who received 140 mg evolocumab Q2W for 6 weeks during the primary period of the study continued receiving 140 mg evolocumab Q2W from week 6 to week 24 in the post-primary period.

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	AMG 145
Other name	Repatha
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection once every 2 weeks

Number of subjects in period 2	Apheresis/Evolocumab	Evolocumab/Evolocumab
Started	20	19
Completed	20	19

Baseline characteristics

Reporting groups	
Reporting group title	Apheresis
Reporting group description:	
Participants continued apheresis at the same schedule, every week (QW) or every two weeks (Q2W), as prior to study entry, for 6 weeks during the primary period of the study.	
Reporting group title	Evolocumab
Reporting group description:	
Participants received 140 mg evolocumab every 2 weeks (Q2W) administered by subcutaneous injection for 6 weeks during the primary period of the study.	

Reporting group values	Apheresis	Evolocumab	Total
Number of subjects	20	19	39
Age, Customized Units: Subjects			
< 65 years	14	7	21
≥ 65 years	6	12	18
Age Continuous Units: years			
arithmetic mean	59.6	65.4	
standard deviation	± 10.0	± 8.1	-
Gender, Male/Female Units: Subjects			
Female	7	9	16
Male	13	10	23
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black or African American	0	1	1
Native Hawaiian or Other Pacific Islander|	0	0	0
White	20	18	38
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	2	2
Not Hispanic or Latino	20	17	37
Unknown or Not Reported	0	0	0
Stratification Factor: Screening LDL-C Level Units: Subjects			
< 160 mg/dL	11	11	22
≥ 160 mg/dL	9	8	17
LDL-C Concentration Units: mg/dL			
arithmetic mean	150.6	152.4	
standard deviation	± 25.6	± 21.2	-

End points

End points reporting groups

Reporting group title	Apheresis
Reporting group description:	
Participants continued apheresis at the same schedule, every week (QW) or every two weeks (Q2W), as prior to study entry, for 6 weeks during the primary period of the study.	
Reporting group title	Evolocumab
Reporting group description:	
Participants received 140 mg evolocumab every 2 weeks (Q2W) administered by subcutaneous injection for 6 weeks during the primary period of the study.	
Reporting group title	Apheresis/Evolocumab
Reporting group description:	
Participants who received apheresis for 6 weeks during the primary period of the study then received 140 mg evolocumab Q2W from week 6 to week 24 in the post-primary period.	
Reporting group title	Evolocumab/Evolocumab
Reporting group description:	
Participants who received 140 mg evolocumab Q2W for 6 weeks during the primary period of the study continued receiving 140 mg evolocumab Q2W from week 6 to week 24 in the post-primary period.	

Primary: Percentage of participants with Apheresis Avoidance at the End of Randomized Therapy

End point title	Percentage of participants with Apheresis Avoidance at the End of Randomized Therapy
End point description:	
Avoidance of apheresis at end of randomized therapy was defined as no apheresis at week 5 and week 6. Aperesis at weeks 5 or 6 was based on LDL-C level at week 4: participants with LDL-C ≥ 100 mg/dL at week 4 received apheresis at week 5 (participants who received apheresis QW before study entry) or week 6 (participants who received apheresis Q2W prior to study entry). If LDL-C was < 100 mg/dL at week 4, no apheresis was performed at week 5 or week 6, irrespective of assigned treatment group. Participants who ended the study prior to week 6 were considered as not achieving apheresis avoidance.	
End point type	Primary
End point timeframe:	
Week 5 and week 6	

End point values	Apheresis	Evolocumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	19		
Units: percentage of participants				
number (confidence interval 95%)	10.0 (2.8 to 30.1)	84.2 (62.4 to 94.5)		

Statistical analyses

Statistical analysis title	Primary Analysis of Apheresis Avoidance
Comparison groups	Apheresis v Evolocumab

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	74.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	44.6
upper limit	86.8

Notes:

[1] - Based on Cochran-Mantel-Haenszel (CMH) test stratified by screening LDL-C level

Secondary: Percent Change from Baseline in Low-density Lipoprotein Cholesterol

End point title	Percent Change from Baseline in Low-density Lipoprotein Cholesterol

End point description:

End point type	Secondary

End point timeframe:

Baseline and week 4

End point values	Apheresis	Evolocumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: percent change				
least squares mean (standard error)	2.61 (± 3.97)	-50.13 (± 4.03)		

Statistical analyses

Statistical analysis title	Analysis of Percent Change From Baseline in LDL-C
Comparison groups	Apheresis v Evolocumab
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	Repeated measures linear effects model
Parameter estimate	Treatment Difference
Point estimate	-52.74

Confidence interval	
level	95 %
sides	2-sided
lower limit	-64.18
upper limit	-41.3
Variability estimate	Standard error of the mean
Dispersion value	5.64

Notes:

[2] - Model included treatment group, screening LDL-C level, scheduled visit, and the interaction of treatment group with scheduled visit as covariates.

Secondary: Percent Change from Baseline in Non-high-density Lipoprotein-Cholesterol

End point title	Percent Change from Baseline in Non-high-density Lipoprotein-Cholesterol

End point description:

End point type	Secondary

End point timeframe:

Baseline and Week 4

End point values	Apheresis	Evolocumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: percent change				
least squares mean (standard error)	1.80 (± 3.29)	-44.58 (± 3.34)		

Statistical analyses

Statistical analysis title	Analysis of Change from Baseline in Non-HDL-C
Comparison groups	Apheresis v Evolocumab
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [3]
Method	Repeated measures linear effects model
Parameter estimate	Treatment Difference
Point estimate	-46.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.85
upper limit	-36.9
Variability estimate	Standard error of the mean
Dispersion value	4.67

Notes:

[3] - Model included treatment group, screening LDL-C level, scheduled visit, and the interaction of treatment group with scheduled visit as covariates.

Secondary: Percent Change from Baseline in Total cholesterol/High-density Lipoprotein Cholesterol Ratio

End point title	Percent Change from Baseline in Total cholesterol/High-density Lipoprotein Cholesterol Ratio

End point description:

End point type	Secondary

End point timeframe:

Baseline and Week 4

End point values	Apheresis	Evolocumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: percent change				
least squares mean (standard error)	0.15 (± 2.65)	-35.65 (± 2.67)		

Statistical analyses

Statistical analysis title	Analysis of Change from Baseline in TC/HDL-C Ratio
Comparison groups	Apheresis v Evolocumab
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [4]
Method	Repeated measures linear effects model
Parameter estimate	Treatment Difference
Point estimate	-35.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-43.39
upper limit	-28.21
Variability estimate	Standard error of the mean
Dispersion value	3.74

Notes:

[4] - Model included treatment group, screening LDL-C level, scheduled visit, and the interaction of treatment group with scheduled visit as covariates.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
6 Weeks for the primary period, and 20 Weeks for post-primary period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	Primary Period: Apheresis QW
Reporting group description:	
Participants received apheresis every week (QW) for 6 weeks during the primary period of the study.	
Reporting group title	Primary Period: Apheresis Q2W
Reporting group description:	
Participants received apheresis every 2 weeks (Q2W) for 6 weeks during the primary period of the study.	
Reporting group title	Primary Period: Evolocumab
Reporting group description:	
Participants received 140 mg evolocumab every 2 weeks (Q2W) administered by subcutaneous injection for 6 weeks during the primary period of the study.	
Reporting group title	Post-primary Period: Apheresis/Evolocumab
Reporting group description:	
Starting at week 6 participants received 140 mg evolocumab Q2W up to week 24.	
Reporting group title	Post-primary Period: Evolocumab/Evolocumab
Reporting group description:	
Participants received 140 mg evolocumab Q2W from week 6 to week 24.	

Serious adverse events	Primary Period: Apheresis QW	Primary Period: Apheresis Q2W	Primary Period: Evolocumab
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	2 / 16 (12.50%)	0 / 19 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 19 (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
Eye disorders			
Retinal vein occlusion			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (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
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 19 (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

Serious adverse events	Post-primary Period: Apheresis/Evolocumab	Post-primary Period: Evolocumab/Evolocumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal vein occlusion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Primary Period: Apheresis QW	Primary Period: Apheresis Q2W	Primary Period: Evolocumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	5 / 16 (31.25%)	10 / 19 (52.63%)
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Social circumstances			

Menopause			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Psychiatric disorders			
Mood swings			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arteriovenous fistula site complication			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Cervicobrachial syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dizziness			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	4
Restless legs syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Eye disorders			
Visual acuity reduced			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastric disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Skin lesion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Gouty arthritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	2 / 19 (10.53%)
occurrences (all)	0	1	2
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rheumatoid arthritis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Mastitis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 4 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Tooth abscess			
subjects affected / exposed	1 / 4 (25.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

Non-serious adverse events	Post-primary Period: Apheresis/Evolocumab	Post-primary Period: Evolocumab/Evolocumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 20 (30.00%)	8 / 19 (42.11%)	
Vascular disorders			
Phlebitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Chest pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	

Fatigue			
subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Influenza like illness			
subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Injection site erythema			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Injection site pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Social circumstances			
Menopause			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Mood swings			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Arteriovenous fistula site complication			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Ligament sprain			

subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Palpitations			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Cervicobrachial syndrome			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	2 / 20 (10.00%)	1 / 19 (5.26%)	
occurrences (all)	2	6	
Restless legs syndrome			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	2	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Visual acuity reduced			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	6	0	
Diarrhoea			
subjects affected / exposed	2 / 20 (10.00%)	1 / 19 (5.26%)	
occurrences (all)	6	1	
Gastric disorder			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Vomiting			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	3	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Skin lesion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Gouty arthritis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			

subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Mastitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Otitis externa			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Tooth abscess			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Hyperkalaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	
occurrences (all)	0	0	
Hyperuricaemia			

subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 19 (0.00%) 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