Clinical trial results:
A Multicenter, Open-label Extension (OLE) Study to Assess the Long-term Safety and Efficacy of Evolocumab

Summary

EudraCT number	2014-001524-30
Trial protocol	HU IT BE DE IS GB ES CZ IE NL SE GR
Global end of trial date	09 March 2018

Results information

Result version number	v1 (current)
This version publication date	16 March 2019
First version publication date	16 March 2019

Trial information

Trial identification

Sponsor protocol code	20140128

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02304484
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	09 March 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to characterize the safety and tolerability of long-term administration of evolocumab in subjects with known coronary artery disease and hypercholesterolemia.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines.
The protocol, proposed informed consent form, and other written subject information, was submitted to the Independent Ethics Committee/Institutional Review Board (IEC/IRB) for written approval before recruitment of subjects into the study.
Before a subject's participation in the clinical study, the investigator was responsible for obtaining written informed consent from the subject after adequate explanation of the aims, methods, anticipated benefits, and potential hazards of the study and before any protocol-specific screening procedures or any investigational products were administered.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 November 2014
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	Canada: 50
Country: Number of subjects enrolled	United States: 72
Country: Number of subjects enrolled	Belgium: 22
Country: Number of subjects enrolled	Czech Republic: 30
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Greece: 9
Country: Number of subjects enrolled	Hungary: 128
Country: Number of subjects enrolled	Iceland: 7
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Italy: 22
Country: Number of subjects enrolled	Netherlands: 120
Country: Number of subjects enrolled	Norway: 14
Country: Number of subjects enrolled	Poland: 80
Country: Number of subjects enrolled	Russian Federation: 63

Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Sweden: 10
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Argentina: 8
Country: Number of subjects enrolled	Brazil: 1
Country: Number of subjects enrolled	Chile: 8
Country: Number of subjects enrolled	Mexico: 6
Country: Number of subjects enrolled	Australia: 18
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Malaysia: 7
Country: Number of subjects enrolled	South Africa: 38
Country: Number of subjects enrolled	Taiwan: 2
Worldwide total number of subjects	770
EEA total number of subjects	486

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)	536
From 65 to 84 years	234
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 126 centers in 29 countries in the regions of Europe (71.8%), North America (15.8%), Asia Pacific (9.4%) and Latin America (3.0%). Participants were enrolled from 24 November 2014 to 31 August 2016.

Pre-assignment

Screening details:

Participants who successfully completed week 80 of the parent Study 20120153 (2012-004208-37) and did not discontinue study drug in the parent study for any reason were eligible for this study. All participants received open-label evolocumab.

Period 1

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

Arms

Arm title	Evolocumab

Arm description:

Participants received 420 mg evolocumab once a month for up to 2 years.

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 pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Evolocumab 420 mg administered by subcutaneous injection once a month

Number of subjects in period 1	Evolocumab
Started	770
Completed	745
Not completed	25
Adverse event, serious fatal	9
Consent withdrawn by subject	14
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Evolocumab
Reporting group description:	
Participants received 420 mg evolocumab once a month for up to 2 years.	

Reporting group values	Evolocumab	Total	
Number of subjects	770	770	
Age, Customized Units: Subjects			
18 - 64 years	536	536	
≥ 65 years	234	234	
Age Continuous Units: years			
arithmetic mean	59.5		
standard deviation	± 8.8	-	
Sex: Female, Male Units: Subjects			
Female	202	202	
Male	568	568	
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	19	19	
Black or African American	5	5	
Native Hawaiian or Other Pacific Islander	1	1	
White	729	729	
Multiple	11	11	
Other	4	4	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	38	38	
Not Hispanic or Latino	732	732	
Unknown or Not Reported	0	0	
Low-density Lipoprotein Cholesterol (LDL-C) Concentration			
Baseline is defined as parent study 20120153 baseline.			
Units: mg/dL			
arithmetic mean	92.2		
standard deviation	± 27.3	-	

End points

End points reporting groups

Reporting group title	Evolocumab

Reporting group description:

Participants received 420 mg evolocumab once a month for up to 2 years.

Primary: Number of Participants with Adverse Events

End point title	Number of Participants with Adverse Events[1]

End point description:

The severity of each adverse event (AE) was graded using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 criteria, where Grade 1 = Mild AE, Grade 2 = Moderate AE, Grade 3 = Severe or medically significant AE, Grade 4 = Life-threatening consequences, and Grade 5 = death related to AE. An adverse device effect was defined as any adverse event related to the use of a medical device (autoinjector/pen or automated mini doser [AMD]), including but not limited to, AEs resulting from insufficient or inadequate Instructions for Use, AEs resulting from any malfunction of the device, or AEs resulting from use error or from intentional misuse of the device.

End point type	Primary

End point timeframe:

From first dose of evolocumab up to 30 days after the last dose, or end of study, whichever was earlier, up to 108 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: Statistical analyses in this open-label extension study were descriptive in nature. No statistical inference was planned.

End point values	Evolocumab			
Subject group type	Reporting group			
Number of subjects analysed	770			
Units: participants				
Any adverse event	526			
Adverse events ≥ Grade 2	415			
Adverse events ≥ Grade 3	206			
Adverse events ≥ Grade 4	38			
Serious adverse events	153			
AEs leading to discontinuation of evolocumab	14			
Fatal adverse events	6			
Device-related adverse events	12			
Device-related adverse events ≥ Grade 2	2			
Device-related adverse events ≥ Grade 3	1			
Device-related adverse events ≥ Grade 4	0			
Serious device-related adverse events	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Low-density Lipoprotein Cholesterol (LDL-C)

End point title	Percent Change from Baseline in Low-density Lipoprotein Cholesterol (LDL-C)

End point description:

End point type	Secondary

End point timeframe:

Baseline (of study 20120153) and weeks 0, 4, 12, 24, 36, 48, 52, 76, and 104 of study 20140128

End point values	Evolocumab			
Subject group type	Reporting group			
Number of subjects analysed	770			
Units: percent change				
arithmetic mean (standard deviation)				
Percent change from baseline to week 0 (n = 751)	-21.52 (± 40.49)			
Percent change from baseline to week 4 (n = 752)	-57.23 (± 22.19)			
Percent change from baseline to week 12 (n = 746)	-58.54 (± 25.60)			
Percent change from baseline to week 24 (n = 747)	-55.26 (± 28.51)			
Percent change from baseline to week 36 (n = 738)	-51.72 (± 30.34)			
Percent change from baseline to week 48 (n = 709)	-53.65 (± 28.72)			
Percent change from baseline to week 52 (n = 725)	-51.30 (± 28.48)			
Percent change from baseline to week 76 (n = 722)	-51.73 (± 32.49)			
Percent change from baseline to week 104 (n = 607)	-47.94 (± 36.49)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Total deaths are reported from the 1st dose of evolocumab up to the end of study; AEs are reported from the 1st dose of evolocumab up to 30 days after the last dose or end of study, whichever is earlier. The maximum duration of treatment was 24.6 months.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Evolocumab

Reporting group description:

Participants received 420 mg evolocumab once a month for up to 2 years.

Serious adverse events	Evolocumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	153 / 770 (19.87%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign salivary gland neoplasm			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder transitional cell carcinoma metastatic			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colon adenoma			
subjects affected / exposed	2 / 770 (0.26%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastric cancer			

subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Lung cancer metastatic				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung neoplasm malignant				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Metastases to stomach				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastatic gastric cancer				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Metastases to urinary tract				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal carcinoma				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Metastatic malignant melanoma				

subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Venous thrombosis			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	4 / 770 (0.52%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Non-cardiac chest pain				
subjects affected / exposed	6 / 770 (0.78%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Vascular stent occlusion				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Contrast media reaction				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Benign prostatic hyperplasia				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	4 / 770 (0.52%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				

subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Idiopathic pulmonary fibrosis			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device loosening			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Anticoagulation drug level above therapeutic			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Injury, poisoning and procedural complications			
Anastomotic leak			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Contusion			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Concussion			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	3 / 770 (0.39%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Epicondylitis			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Intentional overdose				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meniscus injury				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Muscle strain				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic fracture				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural haemorrhage				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haematoma				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thoracic vertebral fracture				

subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	4 / 770 (0.52%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 1			
Angina pectoris				
subjects affected / exposed	13 / 770 (1.69%)			
occurrences causally related to treatment / all	0 / 14			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	5 / 770 (0.65%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Arteriospasm coronary				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	5 / 770 (0.65%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				

subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block complete				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Cardiac failure				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure chronic				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	3 / 770 (0.39%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cardiac ventricular thrombosis				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Congestive cardiomyopathy				

subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	4 / 770 (0.52%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Left ventricular failure				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Palpitations				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial ischaemia				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sinus bradycardia				

subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sinus tachycardia				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ventricular tachycardia				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Carotid artery stenosis				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Carpal tunnel syndrome				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cervical radiculopathy				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Generalised tonic-clonic seizure				

subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Parkinsonism				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sciatica				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	3 / 770 (0.39%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Haemorrhagic anaemia				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Tinnitus				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vertigo				

subjects affected / exposed	2 / 770 (0.26%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	2 / 770 (0.26%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Diplopia			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Duodenal perforation			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspepsia			

subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis erosive				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Incarcerated umbilical hernia				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal haemorrhage				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestine polyp				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis chronic				

subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peptic ulcer				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Bile duct stone				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholangitis				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	3 / 770 (0.39%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cholecystitis chronic				

subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Portal vein thrombosis				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Skin haemorrhage				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetic foot				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angioedema				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin ulcer				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematuria				

subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal cyst				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Arthritis				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lumbar spinal stenosis				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	5 / 770 (0.65%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Periarthritis				

subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Synovial cyst				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Appendicitis				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacterial colitis				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic sinusitis				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dengue fever				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetic foot infection				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				

subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung abscess				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lymph gland infection				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pertussis				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	4 / 770 (0.52%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	2 / 770 (0.26%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 770 (0.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Staphylococcal osteomyelitis				

subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 770 (0.26%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gout			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertriglyceridaemia			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 770 (0.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 770 (0.13%)		
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	Evolocumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 770 (6.36%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	49 / 770 (6.36%)		
occurrences (all)	54		

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