Clinical trial results:
An 8-Week Open-Label, Sequential, Repeated Dose-Finding Study to Evaluate the Efficacy and Safety of Alirocumab in Children and Adolescents with Heterozygous Familial Hypercholesterolemia Followed by an Extension Phase

Summary

EudraCT number	2015-003766-85
Trial protocol	SE ES CZ FR Outside EU/EEA
Global end of trial date	22 February 2019

Results information

Result version number	v1 (current)
This version publication date	01 September 2019
First version publication date	01 September 2019

Trial information

Trial identification

Sponsor protocol code	DFI14223

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02890992
WHO universal trial number (UTN)	U1111-1178-4764
Other trial identifiers	STUDY NAME: ODYSSEY KIDS

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001169-PIP01-11
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	03 May 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of alirocumab administered every 2 weeks (Q2W) or every 4 weeks (Q4W) on low-density lipoprotein cholesterol (LDL-C) levels after 8 weeks of treatment in heterozygous familial hypercholesterolemia (heFH) subjects aged of 8 to 17 years, with LDL-C greater than or equals (>=) 130 milligram/deciLitre (mg/dL) (3.37 millimoles/Litre [mmol/L]) on optimal stable daily dose of statin therapy ± other lipid modifying therapies (LMTs) or a stable dose of non-statin LMTs in case of intolerance to statins, for at least 4 weeks prior to the screening period.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric subjects. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Background therapy:

Statins, Cholesterol absorption inhibitors (ezetimibe), Bile acid-binding sequestrants (such as cholestyramine, colestipol, colesevelam), Nicotinic acid, Fenofibrate, Omega-3 fatty acids (>=1000 mg daily) were used as background therapy.

Evidence for comparator: -

Actual start date of recruitment	30 June 2016
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	Norway: 1
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Czech Republic: 11
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	South Africa: 1
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	42
EEA total number of subjects	28

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)	13
Adolescents (12-17 years)	29
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 16 sites in 10 countries. Overall 63 subjects were screened between 15 September 2016 and 13 June 2018, of whom 21 subjects were screen failures. Screen failures were mainly due to exclusion criteria met.

Pre-assignment

Screening details:

A total of 42 subjects were included in this study.

Period 1

Period 1 title	12 Weeks Open-Label Dose Finding Period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg

Arm description:

Subjects with body weight less than (<) 50 kilograms (kg) received subcutaneous (SC) injection of alirocumab 30 milligram(mg) administered every 2 weeks (Q2W) up to 8 weeks added to lipid modifying therapy (LMT).

Arm type	Experimental
Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 0.5 millilitre (mL) in the abdomen, thigh, or outer area of the upper arm.

Arm title	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg

Arm description:

Subjects with body weight greater than or equal to (>=) 50 kg received SC injection of alirocumab 50 mg administered Q2W up to 8 weeks added to LMT.

Arm type	Experimental
Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 0.5 mL in the abdomen, thigh, or outer area of the upper arm.

Arm title	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg

Arm description:

Subjects with body weight < 50 kg received SC injection of alirocumab 40 mg administered Q2W up to 8 weeks added to LMT.

Arm type	Experimental

Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 0.5 mL in the abdomen, thigh, or outer area of the upper arm.

Arm title	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg

Arm description:

Subjects with body weight >= 50 kg received SC injection of alirocumab 75 mg administered Q2W up to 8 weeks added to LMT.

Arm type	Experimental
Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 0.5 mL in the abdomen, thigh, or outer area of the arm.

Arm title	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg

Arm description:

Subjects with body weight < 50 kg received SC injection of alirocumab 75 mg administered every 4 weeks (Q4W) up to 8 weeks added to LMT.

Arm type	Experimental
Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 1 mL in the abdomen, thigh, or outer area of the upper arm.

Arm title	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg

Arm description:

Subjects with body weight >= 50 kg received SC injection of alirocumab 150 mg administered Q4W up to Week 8 added to LMT.

Arm type	Experimental
Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 1 mL in the abdomen, thigh, or outer area of the upper arm, Q4W.

Arm title	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg

Arm description:

Subjects with body weight < 50 kg received SC injection of alirocumab 150 mg administered Q4W up to 12 weeks added to LMT.

Arm type	Experimental

Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 1 mL in the abdomen, thigh, or outer area of the upper arm.

Arm title	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg

Arm description:

Subjects with body weight >=50 kg received SC injection of Alirocumab 300 mg administered Q4W up to 12 weeks added to LMT.

Arm type	Experimental
Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 1 mL in the abdomen, thigh, or outer area of the upper arm.

Number of subjects in period 1	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg
Started	4	6	4
Treated	4	6	4
Completed	4	6	4

Number of subjects in period 1	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg
Started	6	6	5
Treated	6	6	5
Completed	6	6	5

Number of subjects in period 1	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Started	6	5
Treated	6	5
Completed	6	5

Period 2

Period 2 title	130 Weeks Open-Label Extension Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg

Arm description:

Period 1: Subjects with body weight < 50 kg received SC injection of alirocumab 30 mg administered Q2W up to 8 weeks added to LMT.
Period 2: Subjects with body weight < 50 kg received SC injection of alirocumab 30 mg administered Q2W from Week 16 until switch to Cohort 2 dosage including dose adjustment to body weight as required, then Cohort 2 dosage: if body weight was still < 50 kg, subjects received SC injection of alirocumab 40 mg administered Q2W until Week 130; if body weight was > = 50 kg subjects received SC injection of alirocumab 75 mg administered Q2W until Week 130.

Arm type	Experimental
Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 0.5 millilitre (mL) in the abdomen, thigh, or outer area of the upper arm.

Arm title	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg

Arm description:

Period 1: Subjects with body weight >= 50 kg received SC injection of alirocumab 50 mg administered Q2W up to 8 weeks added to LMT.
Period 2: Subjects with body weight >= 50 kg received SC injection of alirocumab 50 mg administered Q2W from Week 16 until switch to Cohort 2 dosage then SC injection of alirocumab 75 mg administered Q2W until Week 130.

Arm type	Experimental
Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 0.5 mL in the abdomen, thigh, or outer area of the upper arm.

Arm title	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg

Arm description:

Period 1: Subjects with body weight < 50 kg received SC injection of alirocumab 40 mg administered Q2W up to 8 weeks added to LMT.
Period 2: Subjects with body weight < 50 kg received SC injection of alirocumab 40 mg administered Q2W from Week 16 until switch of dosage in Cohorts 1 and 3. If body weight was still < 50 kg, subjects continued to receive SC injection of alirocumab 40 mg administered Q2W until Week 130; if body weight was > = 50 kg subjects received SC injection of alirocumab 75 mg administered Q2W until Week 130.

Arm type	Experimental

Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 0.5 mL in the abdomen, thigh, or outer area of the upper arm.

Arm title	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg

Arm description:

Period 1: Subjects with body weight >= 50 kg received SC injection of alirocumab 75 mg administered Q2W up to 8 weeks added to LMT.
Period 2: Subjects with body weight >= 50 kg received SC injection of alirocumab 75 mg administered Q2W from Week 16 until Week 130.

Arm type	Experimental
Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 0.5 mL in the abdomen, thigh, or outer area of the arm.

Arm title	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg

Arm description:

Period 1: Subjects with body weight < 50 kg received SC injection of alirocumab 75 mg administered Q4W up to 8 weeks added to LMT.
Period 2: Subjects with body weight < 50 kg received SC injection of alirocumab 75 mg administered Q4W from Week 14 until switch to Cohort 2 dosage including dose adjustment to body weight as required, then Cohort 2 dosage: if body weight was still < 50 kg, subjects received SC injection of alirocumab 40 mg administered Q2W until Week 130; if body weight was > = 50 kg subjects received SC injection of alirocumab 75 mg administered Q2W until Week 130.

Arm type	Experimental
Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 1 mL in the abdomen, thigh, or outer area of the upper arm.

Arm title	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg

Arm description:

Period 1: Subjects with body weight >= 50 kg received SC injection of alirocumab 150 mg administered Q4W up to Week 8 added to LMT.
Period 2: Subjects with body weight >= 50 kg received SC injection of alirocumab 150 mg administered Q4W from Week 14 until switch to Cohort 2 dosage then SC injection of alirocumab 75 mg administered Q2W until Week 130.

Arm type	Experimental

Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 1 mL in the abdomen, thigh, or outer area of the upper arm.

Arm title	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg

Arm description:

Period 1: Subjects with body weight < 50 kg received SC injection of alirocumab 150 mg administered Q4W up to 12 weeks added to LMT.
Period 2: Subjects with body weight < 50 kg received SC injection of alirocumab 150 mg administered Q4W from Week 12 until Week 48.

Arm type	Experimental
Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 1 mL in the abdomen, thigh, or outer area of the upper arm

Arm title	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg

Arm description:

Period 1: Subjects with body weight >= 50 kg received SC injection of alirocumab 300 mg administered Q4W up to 12 weeks added to LMT.
Period 2: Subjects with body weight >= 50 kg received SC injection of alirocumab 300 mg administered Q4W from Week 12 until Week 48.

Arm type	Experimental
Investigational medicinal product name	Alirocumab
Investigational medicinal product code	SAR236553, REGN727
Other name	Praluent®
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Alirocumab administered as SC injection of 1 mL in the abdomen, thigh, or outer area of the upper arm.

Number of subjects in period 2[1]	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg
Started	3	6	4
Treated	3	6	4
Completed	3	3	4
Not completed	0	3	0
Adverse Event	-	1	-
Other than specified	-	2	-
Included but not treated	-	-	-

Number of subjects in period 2[1]	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg
Started	6	6	5
Treated	6	6	5
Completed	6	6	5
Not completed	0	0	0
Adverse Event	-	-	-
Other than specified	-	-	-
Included but not treated	-	-	-

Number of subjects in period 2[1]	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Started	6	5
Treated	5	4
Completed	5	4
Not completed	1	1
Adverse Event	-	-
Other than specified	-	-
Included but not treated	1	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Out of 4 subjects from Period 1 of arm 'Cohort 1 - Alirocumab 30 mg Q2W: <50 kg', 3 subjects entered into the open-label extension (OLE) period.

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg
Reporting group description:	
Subjects with body weight less than (<) 50 kilograms (kg) received subcutaneous (SC) injection of alirocumab 30 milligram(mg) administered every 2 weeks (Q2W) up to 8 weeks added to lipid modifying therapy (LMT).	
Reporting group title	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg
Reporting group description:	
Subjects with body weight greater than or equal to (>=) 50 kg received SC injection of alirocumab 50 mg administered Q2W up to 8 weeks added to LMT.	
Reporting group title	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg
Reporting group description:	
Subjects with body weight < 50 kg received SC injection of alirocumab 40 mg administered Q2W up to 8 weeks added to LMT.	
Reporting group title	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Reporting group description:	
Subjects with body weight >= 50 kg received SC injection of alirocumab 75 mg administered Q2W up to 8 weeks added to LMT.	
Reporting group title	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg
Reporting group description:	
Subjects with body weight < 50 kg received SC injection of alirocumab 75 mg administered every 4 weeks (Q4W) up to 8 weeks added to LMT.	
Reporting group title	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg
Reporting group description:	
Subjects with body weight >= 50 kg received SC injection of alirocumab 150 mg administered Q4W up to Week 8 added to LMT.	
Reporting group title	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg
Reporting group description:	
Subjects with body weight < 50 kg received SC injection of alirocumab 150 mg administered Q4W up to 12 weeks added to LMT.	
Reporting group title	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Reporting group description:	
Subjects with body weight >=50 kg received SC injection of Alirocumab 300 mg administered Q4W up to 12 weeks added to LMT.	

Reporting group values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg
Number of subjects	4	6	4
Age categorical			
Units: subjects			
Age continuous			
Units: years			
arithmetic mean	11.0	13.8	11.3
standard deviation	± 2.0	± 2.7	± 2.2
Gender categorical			
Units: subjects			
Female	2	4	2
Male	2	2	2

Race Units: Subjects			
Black or African American	0	0	0
White	0	0	0
Black or African American/White	4	6	4
Low Density Lipoprotrein Cholesterol (LDL-C) Units: mmol/L			
arithmetic mean	5.169	4.339	3.596
standard deviation	± 0.736	± 1.200	± 0.630

Reporting group values	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg
Number of subjects	6	6	5
Age categorical Units: subjects			
Age continuous Units: years			
arithmetic mean	14.3	9.8	13.8
standard deviation	± 2.3	± 1.9	± 1.6
Gender categorical Units: subjects			
Female	2	3	3
Male	4	3	2
Race Units: Subjects			
Black or African American	0	0	0
White	0	1	0
Black or African American/White	6	5	5
Low Density Lipoprotrein Cholesterol (LDL-C) Units: mmol/L			
arithmetic mean	4.510	4.337	4.642
standard deviation	± 1.052	± 1.147	± 1.272

Reporting group values	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg	Total
Number of subjects	6	5	42
Age categorical Units: subjects			
Age continuous Units: years			
arithmetic mean	11.3	13.6	
standard deviation	± 2.2	± 2.1	-
Gender categorical Units: subjects			
Female	1	2	19
Male	5	3	23

Race Units: Subjects			
Black or African American	0	2	2
White	0	0	1
Black or African American/White	6	3	39
Low Density Lipoprotrein Cholesterol (LDL-C) Units: mmol/L			
arithmetic mean	5.100	4.641	
standard deviation	± 1.136	± 0.926	-

End points

End points reporting groups

Reporting group title	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg

Reporting group description:

Subjects with body weight less than (<) 50 kilograms (kg) received subcutaneous (SC) injection of alirocumab 30 milligram(mg) administered every 2 weeks (Q2W) up to 8 weeks added to lipid modifying therapy (LMT).

Reporting group title	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg

Reporting group description:

Subjects with body weight greater than or equal to (>=) 50 kg received SC injection of alirocumab 50 mg administered Q2W up to 8 weeks added to LMT.

Reporting group title	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg

Reporting group description:

Subjects with body weight < 50 kg received SC injection of alirocumab 40 mg administered Q2W up to 8 weeks added to LMT.

Reporting group title	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg

Reporting group description:

Subjects with body weight >= 50 kg received SC injection of alirocumab 75 mg administered Q2W up to 8 weeks added to LMT.

Reporting group title	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg

Reporting group description:

Subjects with body weight < 50 kg received SC injection of alirocumab 75 mg administered every 4 weeks (Q4W) up to 8 weeks added to LMT.

Reporting group title	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg

Reporting group description:

Subjects with body weight >= 50 kg received SC injection of alirocumab 150 mg administered Q4W up to Week 8 added to LMT.

Reporting group title	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg

Reporting group description:

Subjects with body weight < 50 kg received SC injection of alirocumab 150 mg administered Q4W up to 12 weeks added to LMT.

Reporting group title	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg

Reporting group description:

Subjects with body weight >=50 kg received SC injection of Alirocumab 300 mg administered Q4W up to 12 weeks added to LMT.

Reporting group title	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg

Reporting group description:

Period 1: Subjects with body weight < 50 kg received SC injection of alirocumab 30 mg administered Q2W up to 8 weeks added to LMT.
Period 2: Subjects with body weight < 50 kg received SC injection of alirocumab 30 mg administered Q2W from Week 16 until switch to Cohort 2 dosage including dose adjustment to body weight as required, then Cohort 2 dosage: if body weight was still < 50 kg, subjects received SC injection of alirocumab 40 mg administered Q2W until Week 130; if body weight was > = 50 kg subjects received SC injection of alirocumab 75 mg administered Q2W until Week 130.

Reporting group title	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg

Reporting group description:

Period 1: Subjects with body weight >= 50 kg received SC injection of alirocumab 50 mg administered Q2W up to 8 weeks added to LMT.
Period 2: Subjects with body weight >= 50 kg received SC injection of alirocumab 50 mg administered Q2W from Week 16 until switch to Cohort 2 dosage then SC injection of alirocumab 75 mg administered Q2W until Week 130.

Reporting group title	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg

Reporting group description:

Period 1: Subjects with body weight < 50 kg received SC injection of alirocumab 40 mg administered Q2W up to 8 weeks added to LMT.
Period 2: Subjects with body weight < 50 kg received SC injection of alirocumab 40 mg administered Q2W from Week 16 until switch of dosage in Cohorts 1 and 3. If body weight was still < 50 kg, subjects continued to receive SC injection of alirocumab 40 mg administered Q2W until Week 130; if body weight was > = 50 kg subjects received SC injection of alirocumab 75 mg administered Q2W until Week 130.

Reporting group title	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg

Reporting group description:

Period 1: Subjects with body weight >= 50 kg received SC injection of alirocumab 75 mg administered Q2W up to 8 weeks added to LMT.
Period 2: Subjects with body weight >= 50 kg received SC injection of alirocumab 75 mg administered Q2W from Week 16 until Week 130.

Reporting group title	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg

Reporting group description:

Period 1: Subjects with body weight < 50 kg received SC injection of alirocumab 75 mg administered Q4W up to 8 weeks added to LMT.
Period 2: Subjects with body weight < 50 kg received SC injection of alirocumab 75 mg administered Q4W from Week 14 until switch to Cohort 2 dosage including dose adjustment to body weight as required, then Cohort 2 dosage: if body weight was still < 50 kg, subjects received SC injection of alirocumab 40 mg administered Q2W until Week 130; if body weight was > = 50 kg subjects received SC injection of alirocumab 75 mg administered Q2W until Week 130.

Reporting group title	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg

Reporting group description:

Period 1: Subjects with body weight >= 50 kg received SC injection of alirocumab 150 mg administered Q4W up to Week 8 added to LMT.
Period 2: Subjects with body weight >= 50 kg received SC injection of alirocumab 150 mg administered Q4W from Week 14 until switch to Cohort 2 dosage then SC injection of alirocumab 75 mg administered Q2W until Week 130.

Reporting group title	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg

Reporting group description:

Period 1: Subjects with body weight < 50 kg received SC injection of alirocumab 150 mg administered Q4W up to 12 weeks added to LMT.
Period 2: Subjects with body weight < 50 kg received SC injection of alirocumab 150 mg administered Q4W from Week 12 until Week 48.

Reporting group title	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg

Reporting group description:

Period 1: Subjects with body weight >= 50 kg received SC injection of alirocumab 300 mg administered Q4W up to 12 weeks added to LMT.
Period 2: Subjects with body weight >= 50 kg received SC injection of alirocumab 300 mg administered Q4W from Week 12 until Week 48.

Primary: Percent Change From Baseline in Calculated Low Density Lipoprotein Cholesterol (LDL-C) at Week 8

End point title	Percent Change From Baseline in Calculated Low Density Lipoprotein Cholesterol (LDL-C) at Week 8[1]

End point description:

Percent change in calculated LDL-C was defined as 100*(calculated LDL-C value at Week 8 - calculated

LDL-C value at baseline)/calculated LDL-C value at baseline. All available baseline & post-baseline calculated LDL-C value during OLDFI efficacy treatment period & within 1 of the analysis windows upto Week 8 were used in model. OLDFI efficacy treatment period: period from first investigational medicinal product (IMP) injection to last OLDFI IMP injection + 21 days(for Cohorts 1 & 2) or +35 days (for Cohorts 3 & 4). Adjusted Least-squares (LS) mean & standard error (SE) at Week 8 were obtained from mixed-effect model with repeated measures (MMRM) analysis, with fixed categorical effects of alirocumab dose/dose regimen, time point & dose/dose regimen-by-time point interaction. Modified intent-to-treat (mITT)population included all subjects who received at least 1 dose or partial dose of IMP injection & had an evaluable endpoint during open-label dose finding efficacy treatment period.

End point type	Primary

End point timeframe:

Baseline, Week 8

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: percent change				
least squares mean (standard error)	-41.1 (± 12.6)	-7.9 (± 10.3)	-40.6 (± 13.2)	-49.8 (± 10.6)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: percent change				
least squares mean (standard error)	-17.5 (± 10.3)	4.0 (± 11.2)	-31.9 (± 10.3)	-59.8 (± 11.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Calculated Low Density Lipoprotein Cholesterol at Week 8

End point title	Absolute Change From Baseline in Calculated Low Density Lipoprotein Cholesterol at Week 8

End point description:

Absolute change in LDL-C was calculated by subtracting baseline value from Week 8 value. Adjusted LS means and SE were obtained using MMRM analysis, with fixed categorical effects of alirocumab dose/dose regimen, time point and dose/dose regimen-by-time point interaction. Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: milligram per deciliter (mg/dL)				
least squares mean (standard error)	-83.7 (± 19.5)	-27.6 (± 15.9)	-55.5 (± 20.8)	-88.3 (± 16.5)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: milligram per deciliter (mg/dL)				
least squares mean (standard error)	-32.4 (± 15.9)	0.1 (± 17.4)	-55.9 (± 15.9)	-104.3 (± 17.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Calculated Low Density Lipoprotein Cholesterol <130 mg/dL (3.37 mmol/L) at Week 8

End point title	Percentage of Subjects Achieving Calculated Low Density Lipoprotein Cholesterol <130 mg/dL (3.37 mmol/L) at Week 8

End point description:

Combined estimate for percentage of subjects was obtained by averaging out all the imputed percentage of subjects reaching the level of interest. A two-step multiple imputation procedure was used to address missing values in the mITT population in the two steps respectively; with number of imputations = 1000. In the first step, the monotone missing pattern was induced in the multiply-imputed data. In the second step, the missing data at subsequent visits were imputed using the regression method for continuous variables. Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

At Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: percentage of subjects				
number (not applicable)	100.0	33.3	97.6	83.0

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: percentage of subjects				
number (not applicable)	33.3	20.0	66.7	80.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Calculated Low Density Lipoprotein Cholesterol <110 mg/dL (2.84 mmol/L) at Week 8

End point title	Percentage of Subjects Achieving Calculated Low Density Lipoprotein Cholesterol <110 mg/dL (2.84 mmol/L) at Week 8

End point description:

Combined estimate for percentage of subjects was obtained by averaging out all the imputed percentage of subjects reaching the level of interest. A two-step multiple imputation procedure was used to address missing values in the mITT population in the two steps respectively; with number of imputations = 1000. In the first step, the monotone missing pattern was induced in the multiply-imputed data. In the second step, the missing data at subsequent visits were imputed using the regression method for continuous variables. Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

At Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: percentage of subjects				
number (not applicable)	0.0	0.0	93.4	65.7

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: percentage of subjects				
number (not applicable)	16.7	20.0	66.7	80.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Calculated Low Density Lipoprotein Cholesterol at Week 12: Cohort 4

End point title	Percent Change From Baseline in Calculated Low Density Lipoprotein Cholesterol at Week 12: Cohort 4[2]

End point description:

Adjusted LS means and SE at Week 12 were obtained from MMRM analysis, with fixed categorical effects of Alirocumab dose/dose regimen, time point and dose/dose regimen-by-time point interaction. Analysis was performed on mITT population. Data for this endpoint was planned to be collected for Cohort 4 only.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was planned to be collected for Cohort 4 only.

End point values	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: percent change				
least squares mean (standard error)	-29.7 (± 6.9)	-49.2 (± 7.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Apolipoprotein (Apo) B at Week 8

End point title	Percent Change From Baseline in Apolipoprotein (Apo) B at Week 8

End point description:

Adjusted LS means and SE at Week 8 were obtained from MMRM analysis, with fixed categorical effects of alirocumab dose/dose regimen, time point and dose/dose regimen-by-time point interaction. All available baseline values and post-baseline values in at least one of the analysis windows up to Week 8 were used in the model. Analysis was performed on mITT population. Here, number of subjects analysed=subjects with available data for this endpoint.

End point type	Secondary
End point timeframe: Baseline, Week 8	

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	3	6
Units: percent change				
least squares mean (standard error)	-38.4 (± 12.8)	-9.7 (± 9.1)	-36.4 (± 12.8)	-40.1 (± 9.9)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: percent change				
least squares mean (standard error)	-12.6 (± 9.1)	-0.9 (± 9.9)	-27.2 (± 9.1)	-51.4 (± 9.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Non-High-Density Lipoprotein Cholesterol (Non-HDL-C) at Week 8

End point title	Percent Change From Baseline in Non-High-Density Lipoprotein Cholesterol (Non-HDL-C) at Week 8

End point description:

Adjusted LS means and SE at Week 8 were obtained from MMRM analysis, with fixed categorical effects of alirocumab dose group, time point and dose-by-time point interaction. All available baselines value and post-baseline values in at least one of the analysis windows up to Week 8 were used in the model. Analysis was performed on mITT population.

End point type	Secondary
End point timeframe: Baseline, Week 8	

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: percent change				
least squares mean (standard error)	-39.6 (± 11.9)	-7.1 (± 9.7)	-39.7 (± 12.5)	-43.9 (± 10.0)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: percent change				
least squares mean (standard error)	-14.4 (± 9.7)	3.2 (± 10.7)	-31.5 (± 9.7)	-54.6 (± 10.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Total Cholesterol (Total-C) at Week 8

End point title	Percent Change From Baseline in Total Cholesterol (Total-C) at Week 8

End point description:

Adjusted LS means and SE at Week 8 were obtained from MMRM analysis, with fixed categorical effects of alirocumab dose group, time point and dose-by-time point interaction. All available baseline values and post-baseline values in at least one of the analysis windows up to Week 8 were used in the model. Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: percent change				
least squares mean (standard error)	-29.0 (± 9.7)	-4.1 (± 7.9)	-28.6 (± 10.1)	-34.2 (± 8.1)

End point values	Cohort 3 - Alirocumab 75	Cohort 3 - Alirocumab 150	Cohort 4 - Alirocumab 150	Cohort 4 - Alirocumab 300

	mg Q4W: <50 kg	mg Q4W: >=50 kg	mg Q4W: <50 kg	mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: percent change				
least squares mean (standard error)	-10.7 (± 7.9)	5.2 (± 8.6)	-24.0 (± 7.9)	-41.8 (± 8.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Lipoprotein (a) at Week 8

End point title	Percent Change From Baseline in Lipoprotein (a) at Week 8

End point description:

Combined estimates and SE were obtained by combining adjusted means and SE from robust regression model analyses of the different imputed data sets. The robust regression models included the fixed categorical effect of alirocumab dose group. A two-step multiple imputation procedure was used to address missing values in the mITT population in the two steps respectively (with number of imputations = 1000). In the first step, the monotone missing pattern was induced in the multiply-imputed data. In the second step, the missing data at subsequent visits were imputed using the regression method for continuous variables. Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: percent change				
least squares mean (standard error)	4.5 (± 21.1)	-26.9 (± 11.6)	1.5 (± 15.1)	-25.2 (± 14.4)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: percent change				
least squares mean (standard error)	2.2 (± 10.5)	-7.7 (± 11.4)	0.1 (± 10.2)	-7.7 (± 11.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Fasting Triglyceride (TG) at Week 8

End point title	Percent Change From Baseline in Fasting Triglyceride (TG) at Week 8

End point description:

Combined estimates and SE were obtained by combining adjusted means and SE from robust regression model analyses of the different imputed data sets. The robust regression models included the fixed categorical effect of alirocumab dose group. A two-step multiple imputation procedure was used to address missing values in the mITT population (in the two steps respectively; with number of imputations = 1000). In the first step, the monotone missing pattern was induced in the multiply-imputed data. In the second step, the missing data at subsequent visits were imputed using the regression method for continuous variables. Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: percent change				
least squares mean (standard error)	-0.4 (± 19.6)	-4.0 (± 16.0)	-7.4 (± 28.4)	-14.5 (± 19.0)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: percent change				
least squares mean (standard error)	19.3 (± 16.0)	-3.1 (± 17.5)	-32.1 (± 16.0)	-7.1 (± 17.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in High Density Lipoprotein Cholesterol (HDL-C) at Week 8

End point title	Percent Change From Baseline in High Density Lipoprotein Cholesterol (HDL-C) at Week 8

End point description:

Adjusted LS means and SE at Week 8 were obtained from MMRM analysis, with fixed categorical effects of alirocumab dose/dose regimen group, time point and dose/dose regimen-by-time point interaction. All available baseline values and post-baseline values in at least one of the analysis windows up to Week 8 were used in the model. Analysis was performed on mITT population.

End point type	Secondary
End point timeframe: Baseline, Week 8	

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: percent change				
least squares mean (standard error)	9.7 (± 7.1)	16.5 (± 5.8)	14.7 (± 7.7)	10.6 (± 6.1)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: percent change				
least squares mean (standard error)	5.2 (± 5.8)	13.8 (± 6.4)	4.5 (± 5.8)	2.8 (± 6.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Apolipoprotein A-1 (Apo A-1) at Week 8

End point title	Percent Change From Baseline in Apolipoprotein A-1 (Apo A-1) at Week 8

End point description:

Adjusted LS means and SE at Week 8 were obtained from MMRM analysis, with fixed categorical effects of alirocumab dose/dose regimen group, time point and dose/dose regimen-by-time point interaction. All available baseline values and post-baseline values in at least one of the analysis windows up to Week 8 were used in the model. Analysis was performed on mITT population. Here, number of subjects analysed=subjects with available data for this endpoint.

End point type	Secondary
End point timeframe: Baseline, Week 8	

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	3	5
Units: percent change				
least squares mean (standard error)	4.4 (± 7.2)	14.8 (± 5.1)	10.7 (± 7.2)	1.8 (± 5.6)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: percent change				
least squares mean (standard error)	8.9 (± 5.1)	7.4 (± 5.6)	5.8 (± 5.1)	7.2 (± 5.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Apolipoprotein B at Week 8

End point title	Absolute Change From Baseline in Apolipoprotein B at Week 8

End point description:

Adjusted LS means and SE at Week 8 were obtained from MMRM analysis, with fixed categorical effects of alirocumab dose group, time point and dose-by-time point interaction. All available baseline value and a post-baseline value in at least one of the analysis windows up to Week 8 were used in the model. Analysis was performed on mITT population. Here, number of subjects analysed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	3	5
Units: mg/dL				
least squares mean (standard error)	-51.7 (± 15.8)	-18.5 (± 11.1)	-35.3 (± 15.8)	-53.4 (± 12.2)

End point values	Cohort 3 - Alirocumab 75	Cohort 3 - Alirocumab 150	Cohort 4 - Alirocumab 150	Cohort 4 - Alirocumab 300

	mg Q4W: <50 kg	mg Q4W: >=50 kg	mg Q4W: <50 kg	mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: mg/dL				
least squares mean (standard error)	-15.3 (± 11.1)	-5.4 (± 12.2)	-34.2 (± 11.1)	-63.5 (± 12.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Non-High-Density Lipoprotein (Non-HDL-C) at Week 8

End point title	Absolute Change From Baseline in Non-High-Density Lipoprotein (Non-HDL-C) at Week 8

End point description:

Adjusted LS means and standard error at Week 8 were obtained from MMRM analysis, with fixed categorical effects of alirocumab dose/dose regimen, time point and dose/dose regimen-by-time point interaction. All available baseline values and post-baseline values in at least one of the analysis windows up to Week 8 were used in the model. Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: mg/dL				
least squares mean (standard error)	-86.1 (± 20.8)	-28.7 (± 17.0)	-62.7 (± 22.1)	-88.5 (± 17.6)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: mg/dL				
least squares mean (standard error)	-29.5 (± 17.0)	-0.6 (± 18.6)	-63.1 (± 17.0)	-106.4 (± 18.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Total Cholesterol (Total-C) at Week 8

End point title	Absolute Change From Baseline in Total Cholesterol (Total-C) at Week 8

End point description:

Adjusted LS means and standard error at Week 8 were obtained from MMRM analysis, with fixed categorical effects of alirocumab dose/dose regimen, time point and dose/dose regimen-by-time point interaction. All available baseline values and post-baseline values in at least one of the analysis windows up to Week 8 were used in the model. Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: mg/dL				
least squares mean (standard error)	-80.1 (± 21.4)	-20.8 (± 17.5)	-57.1 (± 22.8)	-84.4 (± 18.1)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: mg/dL				
least squares mean (standard error)	27.2 (± 17.5)	5.3 (± 19.1)	-60.7 (± 17.5)	-105.1 (± 19.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Lipoprotein (a) at Week 8

End point title	Absolute Change From Baseline in Lipoprotein (a) at Week 8

End point description:

Combined estimates and standard errors (SE) were obtained by combining adjusted means and SE from robust regression model analyses of the different imputed data sets. The robust regression models included the fixed categorical effect of alirocumab dose/dose regimen group. A two-step multiple imputation procedure was used to address missing values in the mITT population in the two steps respectively (with number of imputations= 1000). In the first step, the monotone missing pattern was induced in the multiply-imputed data. In the second step, the missing data at subsequent visits were imputed using the regression method for continuous variables. Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: gram/Litre (g/L)				
least squares mean (standard error)	0.003 (± 0.022)	-0.021 (± 0.017)	0.007 (± 0.073)	-0.025 (± 0.020)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: gram/Litre (g/L)				
least squares mean (standard error)	0.023 (± 0.018)	-0.031 (± 0.019)	-0.002 (± 0.017)	-0.120 (± 0.020)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in High Density Lipoprotein Cholesterol at Week 8

End point title	Absolute Change From Baseline in High Density Lipoprotein Cholesterol at Week 8

End point description:

Adjusted LS means and SE at Week 8 were obtained from MMRM analysis, with fixed categorical effects of alirocumab dose/dose regimen, time point and dose/dose regimen-by-time point interaction. All available baseline values and post-baseline values in at least one of the analysis windows up to Week 8 were used in the model. Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: mg/dL				
least squares mean (standard error)	5.9 (± 3.4)	7.7 (± 2.8)	5.5 (± 3.7)	4.9 (± 2.9)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: mg/dL				
least squares mean (standard error)	2.4 (± 2.8)	5.9 (± 3.1)	2.2 (± 2.8)	1.2 (± 3.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Fasting Triglyceride at Week 8

End point title	Absolute Change From Baseline in Fasting Triglyceride at Week 8

End point description:

Combined estimates and SE were obtained by combining adjusted means and SE from robust regression model analyses of the different imputed data sets. The robust regression models included the fixed categorical effect of alirocumab dose group. A two-step multiple imputation procedure was used to address missing values in the mITT population (in the two steps respectively; with number of imputations = 1000). In the first step, the monotone missing pattern was induced in the multiply-imputed data. In the second step, the missing data at subsequent visits were imputed using the regression method for continuous variables. Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	4	6
Units: mmol/L				
least squares mean (standard error)	-0.121 (± 0.193)	-0.076 (± 0.157)	0.168 (± 0.226)	0.111 (± 0.188)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: mmol/L				
least squares mean (standard error)	0.117 (± 0.157)	-0.045 (± 0.172)	-0.402 (± 0.157)	-0.107 (± 0.172)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Apolipoprotein A-1 at Week 8

End point title	Absolute Change From Baseline in Apolipoprotein A-1 at Week 8

End point description:

Adjusted LS means and SE at Week 8 were obtained from MMRM analysis, with fixed categorical effects of alirocumab dose/dose regimen, time point and dose/dose regimen-by-time point interaction. All available baseline values and post-baseline values in at least one of the analysis windows up to Week 8 were used in the model. Analysis was performed on mITT population. Here, number of subjects analysed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	3	5
Units: mg/dL				
least squares mean (standard error)	4.0 (± 9.3)	17.7 (± 6.5)	11.3 (± 9.3)	-0.4 (± 7.2)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: mg/dL				
least squares mean (standard error)	10.5 (± 6.5)	8.0 (± 7.2)	7.5 (± 6.5)	11.0 (± 7.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Ratio Apolipoprotein B/Apolipoprotein A-1 at Week 8

End point title	Absolute Change From Baseline in Ratio Apolipoprotein B/Apolipoprotein A-1 at Week 8

End point description:

Adjusted LS means and SE at Week 8 were obtained from MMRM analysis, with fixed categorical effects of alirocumab dose/dose regimen, time point and dose/dose regimen-by-time point interaction. All available baseline values and post-baseline values in at least one of the analysis windows up to Week 8 were used in the model. Analysis was performed on mITT population. Here, number of subjects analysed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	3	5
Units: ratio (Apo B/Apo A-1)				
least squares mean (standard error)	-0.363 (± 0.123)	-0.262 (± 0.087)	-0.370 (± 0.123)	-0.402 (± 0.096)

End point values	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	6	5
Units: ratio (Apo B/Apo A-1)				
least squares mean (standard error)	-0.190 (± 0.087)	-0.086 (± 0.096)	-0.282 (± 0.087)	-0.473 (± 0.096)

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AEs) were collected from the time of first dose of investigational medicinal product (IMP) up to the end of study (Week 152) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Subjects from Cohorts 1, 2 and 3 had an option to switch to cohort 2 dosage according to their weight category. 7 subjects from Cohort 1 and 11 subjects from Cohort 2 and 3 switched the dosage. Safety population included population who actually received at least one dose or part of a dose of the open-label IMP.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg

Reporting group description:

Subjects with body weight < 50 kg received SC injection of alirocumab 30 mg administered Q2W up to the switch of dosage added to LMT.

Reporting group title	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg

Reporting group description:

Subjects with body weight >= 50 kg received SC injection of alirocumab 50 mg administered Q2W up to the switch of dosage added to LMT.

Reporting group title	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg

Reporting group description:

Subjects with body weight < 50 kg received SC injection of alirocumab 40 mg administered Q2W up to the switch of dosage added to LMT.

Reporting group title	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg

Reporting group description:

Subjects with body weight >= 50 kg received SC injection of alirocumab 75 mg administered Q2W up to the switch of dosage added to LMT.

Reporting group title	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg

Reporting group description:

Subjects with body weight < 50 kg received SC injection of alirocumab 75 mg administered Q4W up to the switch of dosage added to LMT.

Reporting group title	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg

Reporting group description:

Subjects with body weight >= 50 kg received SC injection of alirocumab 150 mg administered Q4W up to the switch of dosage added to LMT.

Reporting group title	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg

Reporting group description:

Subjects with body weight < 50 kg received SC injection of alirocumab 150 mg administered Q4W up to the end of the OLE period (up to 130 weeks) added to LMT.

Reporting group title	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg

Reporting group description:

Subjects with body weight >= 50 kg received SC injection of alirocumab 300 mg administered Q4W up to the end of the OLE period (up to 130 weeks) added to LMT.

Reporting group title	Alirocumab 40 Q2W Post-switch

Reporting group description:

Subjects with body weight < 50 kg from cohort 1, 2 and 3 switched to dosage and received SC injection of alirocumab 40 mg administered Q2W from the switch up to the end of the OLE period (up to 130 weeks) added to LMT.

Reporting group title	Alirocumab 75 Q2W Post-switch

Reporting group description:

Subjects from Cohort 1 (7 subjects), Cohort 2 and Cohort 3 (11 subjects) switched to dosage and received SC injection of alirocumab 75 mg administered Q2W up to the end of the OLE period (up to 130 weeks) added to LMT.

Serious adverse events	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Cohort 4 - Alirocumab 150 mg Q4W: <50 kg	Cohort 4 - Alirocumab 300 mg Q4W: >=50 kg	Alirocumab 40 Q2W Post-switch
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Alirocumab 75 Q2W Post-switch		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Cohort 1 - Alirocumab 30 mg Q2W: <50 kg	Cohort 1 - Alirocumab 50 mg Q2W: >=50 kg	Cohort 2 - Alirocumab 40 mg Q2W: <50 kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	5 / 6 (83.33%)	1 / 4 (25.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pyogenic Granuloma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Pallor			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Influenza Like Illness			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	4	0
Injection Site Reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Food Allergy			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Premenstrual Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Epistaxis			

subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sinus Congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Alcohol Abuse			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Anxiety Disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Depressed Mood			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood Follicle Stimulating Hormone Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood Luteinising Hormone Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Low Density Lipoprotein Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Animal Scratch			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Arthropod Bite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Concussion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hand Fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ligament Sprain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Post-Traumatic Pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Radius Fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Road Traffic Accident			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Traumatic Haematoma			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Syncope			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Thoracic Outlet Syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Excessive Eye Blinking			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vomiting			

subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Flank Pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Muscle Spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Tendon Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abscess Limb			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cystitis Bacterial			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cytomegalovirus Hepatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ear Infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis Viral			

subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Infectious Mononucleosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 4 (25.00%)	2 / 6 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	5	0
Otitis Externa			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Otitis Media			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Pharyngitis Streptococcal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Post Procedural Infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pyelonephritis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urinary Tract Infection			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Varicella			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal Mycotic Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Type 1 Diabetes Mellitus			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Vitamin D Deficiency			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Cohort 2 - Alirocumab 75 mg Q2W: >=50 kg	Cohort 3 - Alirocumab 75 mg Q4W: <50 kg	Cohort 3 - Alirocumab 150 mg Q4W: >=50 kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	5 / 6 (83.33%)	3 / 5 (60.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pyogenic Granuloma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Vascular disorders			
Pallor			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Influenza Like Illness			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injection Site Reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Food Allergy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Premenstrual Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sinus Congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Alcohol Abuse			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Anxiety Disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Depressed Mood			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Investigations			
Blood Follicle Stimulating Hormone Decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood Luteinising Hormone Decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Low Density Lipoprotein Decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Animal Scratch			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Arthropod Bite			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Concussion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hand Fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ligament Sprain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Post-Traumatic Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Radius Fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Road Traffic Accident			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Traumatic Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Thoracic Outlet Syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Excessive Eye Blinking			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Abdominal Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Flank Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle Spasms			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tendon Pain			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abscess Limb			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cystitis Bacterial			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cytomegalovirus Hepatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ear Infection			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Gastroenteritis Viral			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Infectious Mononucleosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Otitis Externa			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Otitis Media			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pharyngitis Streptococcal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Post Procedural Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pyelonephritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	2	1	2
Urinary Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Varicella			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal Mycotic Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Type 1 Diabetes Mellitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vitamin D Deficiency			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Cohort 4 - Alirocumab 150 mg	Cohort 4 - Alirocumab 300 mg	Alirocumab 40 Q2W Post-switch

	Q4W: <50 kg	Q4W: >=50 kg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	4 / 5 (80.00%)	7 / 10 (70.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pyogenic Granuloma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Pallor			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Influenza Like Illness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	2
Injection Site Reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Immune system disorders			
Food Allergy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Premenstrual Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Oropharyngeal Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Sinus Congestion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Alcohol Abuse			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Anxiety Disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Depressed Mood			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood Follicle Stimulating Hormone Decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood Luteinising Hormone Decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Low Density Lipoprotein Decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Animal Scratch			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Arthropod Bite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Concussion			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hand Fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ligament Sprain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Post-Traumatic Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Radius Fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Road Traffic Accident			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Traumatic Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Thoracic Outlet Syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Excessive Eye Blinking			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Abdominal Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flank Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle Spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tendon Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abscess Limb			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cystitis Bacterial			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cytomegalovirus Hepatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gastroenteritis Viral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	3 / 10 (30.00%)
occurrences (all)	0	0	3
Infectious Mononucleosis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Otitis Externa			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Otitis Media			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pharyngitis Streptococcal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Post Procedural Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pyelonephritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Urinary Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Varicella			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal Mycotic Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Type 1 Diabetes Mellitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vitamin D Deficiency			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1

Non-serious adverse events	Alirocumab 75 Q2W Post-switch		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 18 (50.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pyogenic Granuloma			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Pallor			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Influenza Like Illness			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Injection Site Reaction			

subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Immune system disorders Food Allergy subjects affected / exposed occurrences (all)	 0 / 18 (0.00%) 0		
Reproductive system and breast disorders Premenstrual Pain subjects affected / exposed occurrences (all)	 0 / 18 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Oropharyngeal Pain subjects affected / exposed occurrences (all) Sinus Congestion subjects affected / exposed occurrences (all)	 0 / 18 (0.00%) 0 1 / 18 (5.56%) 1 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0		
Psychiatric disorders Alcohol Abuse subjects affected / exposed occurrences (all) Anxiety Disorder subjects affected / exposed occurrences (all) Depressed Mood subjects affected / exposed occurrences (all)	 0 / 18 (0.00%) 0 1 / 18 (5.56%) 1 0 / 18 (0.00%) 0		
Investigations Blood Follicle Stimulating Hormone Decreased			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Blood Luteinising Hormone Decreased			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Low Density Lipoprotein Decreased			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Animal Scratch			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Arthropod Bite			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Concussion			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Hand Fracture			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Ligament Sprain			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Post-Traumatic Pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Radius Fracture			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Road Traffic Accident			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Traumatic Haematoma			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Presyncope			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Thoracic Outlet Syndrome			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Eye disorders			
Excessive Eye Blinking			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Abdominal Pain			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Toothache			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Flank Pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Muscle Spasms			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Tendon Pain			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Infections and infestations			
Abscess Limb			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Cystitis Bacterial			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Cytomegalovirus Hepatitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Ear Infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Gastroenteritis Viral			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Infectious Mononucleosis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Otitis Externa			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Otitis Media			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Pharyngitis Streptococcal			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		

Post Procedural Infection			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Pyelonephritis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Tonsillitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Urinary Tract Infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Varicella			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Vulvovaginal Mycotic Infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Type 1 Diabetes Mellitus			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Vitamin D Deficiency			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 August 2016	Following amendments were made: - Clarifications regarding statin dosing requirements. - Replacement of a 2-option screening period, each of different lengths, with a single, up to 6-week (+1 week), screening period for all subjects, to allow inclusion as soon as eligibility was confirmed. - Clarification related to genotyping performed to confirm a diagnosis of heFH only. - Referral to an eye specialist in case of visual problems concomitant with very low LDL-C levels. Modifications related to approval of protocol amendments to include approval by Health Agencies. - Addition of a recommendation for providing sexual counseling. - Modifications of the levels of certain laboratory values used to define an abnormality requiring additional actions for this pediatric population (neutropenia, thrombocytopenia, acute renal failure, and suspicion of rhabdomyolysis). - Addition of use of clinical judgment in performing follow-up testing, in light of the constraints on amount of blood that could be drawn in the pediatric population.
11 December 2017	- Addition of a cohort (Cohort 4) using Q4W dosing regimen, evaluating doses of 150 mg for body weight <50 kg and 300 mg for body weight >=50 kg. - Clarification regarding the last alirocumab injection planned during the OLE period.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported