

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 \pm 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
Aim title	Condit 2 - Amocumab 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 arm.	of 0.5 mL in the abdomen, thigh, or outer area of the upper
Arm title	Cohort 2 - Alirocumab 75 mg Q2W: > = 50 kg
Arm description:	
Subjects with body weight > = 50 kg rec 8 weeks added to LMT.	eived SC injection of alirocumab 75 mg administered Q2W up to
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:	
•	ved SC injection of alirocumab 75 mg administered every 4
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:	
9	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:	
	eived SC injection of alirocumab 150 mg administered Q4W up
to Week 8 added to LMT.	erved 30 injection of amocumab 130 mg administered 24W up
to Week 8 added to LMT.	Experimental
to Week 8 added to LMT. Arm type	
to Week 8 added to LMT. Arm type Investigational medicinal product name	Experimental
to Week 8 added to LMT. Arm type Investigational medicinal product name Investigational medicinal product code	Experimental Alirocumab
to Week 8 added to LMT. Arm type Investigational medicinal product name Investigational medicinal product code Other name	Experimental Alirocumab SAR236553, REGN727 Praluent®
to Week 8 added to LMT. Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms	Experimental Alirocumab SAR236553, REGN727 Praluent® Solution for injection
to Week 8 added to LMT. Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration	Experimental Alirocumab SAR236553, REGN727 Praluent®
to Week 8 added to LMT. Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Alirocumab administered as SC injection	Experimental Alirocumab SAR236553, REGN727 Praluent® Solution for injection Subcutaneous use
to Week 8 added to LMT. Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details:	Experimental Alirocumab SAR236553, REGN727 Praluent® Solution for injection
to Week 8 added to LMT. Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Alirocumab administered as SC injection Q4W. Arm title	Experimental Alirocumab SAR236553, REGN727 Praluent® Solution for injection Subcutaneous use of 1 mL in the abdomen, thigh, or outer area of the upper arm
to Week 8 added to LMT. Arm type Investigational medicinal product name Investigational medicinal product code Other name Pharmaceutical forms Routes of administration Dosage and administration details: Alirocumab administered as SC injection Q4W. Arm title Arm description:	Experimental Alirocumab SAR236553, REGN727 Praluent® Solution for injection Subcutaneous use of 1 mL in the abdomen, thigh, or outer area of the upper arm

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 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:

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.

^{[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.

Baseline characteristics

baselille characteristics	
Reporting groups	
Reporting group title	Cohort 1 - Alirocumab 30 mg Q2W: < 50 kg
Reporting group description:	
	50 kilograms (kg) received subcutaneous (SC) injection of ed every 2 weeks (Q2W) up to 8 weeks added to lipid modifying
Reporting group title	Cohort 1 - Alirocumab 50 mg Q2W: > = 50 kg
Reporting group description:	
Subjects with body weight greater than mg administered Q2W up to 8 weeks add	or equal to (>=) 50 kg received SC injection of alirocumab 50 ded to LMT.
Reporting group title	Cohort 2 - Alirocumab 40 mg Q2W: < 50 kg
Reporting group description:	
Subjects with body weight < 50 kg recei weeks added to LMT.	ved SC injection of alirocumab 40 mg administered Q2W up to 8
Reporting group title	Cohort 2 - Alirocumab 75 mg Q2W: > = 50 kg
Reporting group description:	
Subjects with body weight > = 50 kg rec 8 weeks added to LMT.	eived SC injection of alirocumab 75 mg administered Q2W up to
Reporting group title	Cohort 3 - Alirocumab 75 mg Q4W: < 50 kg
Reporting group description:	
Subjects with body weight < 50 kg recei weeks (Q4W) up to 8 weeks added to LN	ved SC injection of alirocumab 75 mg administered every 4 /IT.
Reporting group title	Cohort 3 - Alirocumab 150 mg Q4W: > = 50 kg
Reporting group description:	
Subjects with body weight > = 50 kg rec to Week 8 added to LMT.	eived SC injection of alirocumab 150 mg administered Q4W up
Reporting group title	Cohort 4 - Alirocumab 150 mg Q4W: < 50 kg
Reporting group description:	

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

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

Reporting group title	Cohort 1 - Alirocumab 30 mg Q2W: < 50 kg
Reporting group description:	
	n (<) 50 kilograms (kg) received subcutaneous (SC) injection of nistered every 2 weeks (Q2W) up to 8 weeks added to lipid modifying
Reporting group title	Cohort 1 - Alirocumab 50 mg Q2W: > = 50 kg
Reporting group description:	
Subjects with body weight greater mg administered Q2W up to 8 weel	than or equal to (>=) 50 kg received SC injection of alirocumab 50 ks added to LMT.
Reporting group title	Cohort 2 - Alirocumab 40 mg Q2W: < 50 kg
Reporting group description:	
Subjects with body weight < 50 kg weeks added to LMT.	received SC injection of alirocumab 40 mg administered Q2W up to 8
Reporting group title	Cohort 2 - Alirocumab 75 mg Q2W: > = 50 kg
Reporting group description:	
Subjects with body weight $>$ = 50 k 8 weeks added to LMT.	g received SC injection of alirocumab 75 mg administered Q2W up to
Reporting group title	Cohort 3 - Alirocumab 75 mg Q4W: < 50 kg
Reporting group description:	
Subjects with body weight < 50 kg weeks (Q4W) up to 8 weeks added	received SC injection of alirocumab 75 mg administered every 4 to LMT.
Reporting group title	Cohort 3 - Alirocumab 150 mg Q4W: > = 50 kg
Reporting group description:	
Subjects with body weight > = 50 k to Week 8 added to LMT.	g received SC injection of alirocumab 150 mg administered Q4W up
Reporting group title	Cohort 4 - Alirocumab 150 mg Q4W: < 50 kg
Reporting group description:	
Subjects with body weight < 50 kg 12 weeks added to LMT.	received SC injection of alirocumab 150 mg administered Q4W up to
Reporting group title	Cohort 4 - Alirocumab 300 mg Q4W: > = 50 kg
Reporting group description:	
Subjects with body weight $> = 50 \text{ kg}$ to 12 weeks added to LMT.	g received SC injection of Alirocumab 300 mg administered Q4W up
Reporting group title	Cohort 1 - Alirocumab 30 mg Q2W: < 50 kg
Reporting group description:	
Q2W up to 8 weeks added to LMT. Period 2: Subjects with body weigh Q2W from Week 16 until switch to required, then Cohort 2 dosage: if I	t < 50 kg received SC injection of alirocumab 30 mg administered t < 50 kg received SC injection of alirocumab 30 mg administered Cohort 2 dosage including dose adjustment to body weight as body weight was still < 50 kg, subjects received SC injection of W until Week 130; if body weight was > = 50 kg subjects received dministered Q2W until Week 130.
Reporting group title	Cohort 1 - Alirocumab 50 mg Q2W: > = 50 kg
Reporting group description:	Toomore 1 Am ocamab oo mg Q2w. > - 50 kg
	t >= 50 kg received SC injection of alirocumab 50 mg administered

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

Q2W from Week 16 until switch to Cohort 2 dosage then SC injection of alirocumab 75 mg administered

Q2W until Week 130.

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 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 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)	O.1 (± 17.4)	-55.9 (± 15.9)	-104.3 (± 17.4)

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 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

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 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

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 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	
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 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)

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 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)

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)

				1
End point values	Cohort 3 -	Cohort 3 -	Cohort 4 -	Cohort 4 -
	Alirocumab 75	Alirocumab 150	Alirocumab 150	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)

No statistical analyses for this end point

Secondary: 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 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 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

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	Cohort 1 - Alirocumab 50 mg Q2W:	Cohort 2 - Alirocumab 40 mg Q2W: <50	Cohort 2 - Alirocumab 75 mg Q2W:
	kg	> = 50 kg	kg	> = 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 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 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)

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 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)

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	
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 -	Cohort 3 -	Cohort 4 -	Cohort 4 -
	Alirocumab 75	Alirocumab 150	Alirocumab 150	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)

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 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

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 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 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)

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 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)

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

Combined estimates and SE were obtained by combining adjusted mean=

еŠ

End point values	Cohort 3 - Alirocumab 75 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)

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

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	

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 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)

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 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			
Clinical trial results 2015-003766-85 version 1	EU-CTR publication date: 01 Sept	tember 2019	Page 32 of 62

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.	and detainly received at reast one dose of part of a dose of the open
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 the switch of dosage added to LN	kg received SC injection of alirocumab 30 mg administered Q2W up to $\sqrt{11}$.
Reporting group title	Cohort 1 - Alirocumab 50 mg Q2W: > = 50 kg
Reporting group description:	
Subjects with body weight >= 50 the switch of dosage added to LN	O kg received SC injection of alirocumab 50 mg administered Q2W up to $M\Gamma$.
Reporting group title	Cohort 2 - Alirocumab 40 mg Q2W: < 50 kg
Reporting group description:	
Subjects with body weight < 50 the switch of dosage added to LN	kg received SC injection of alirocumab 40 mg administered Q2W up to $\overline{\mathrm{MT}}$.
Reporting group title	Cohort 2 - Alirocumab 75 mg Q2W: >= 50 kg
Reporting group description:	
Subjects with body weight $> = 50$ the switch of dosage added to LN	Okg received SC injection of alirocumab 75 mg administered Q2W up to
Reporting group title	Cohort 3 - Alirocumab 75 mg Q4W: < 50 kg
Reporting group description:	
Subjects with body weight < 50 the switch of dosage added to LN	kg received SC injection of alirocumab 75 mg administered Q4W up to MT.
Reporting group title	Cohort 3 - Alirocumab 150 mg Q4W: > = 50 kg
Reporting group description:	
Subjects with body weight >= 50 to the switch of dosage added to	O kg received SC injection of alirocumab 150 mg administered Q4W up LMT.
Reporting group title	Cohort 4 - Alirocumab 150 mg Q4W: < 50 kg
Reporting group description:	
Subjects with body weight < 50 the end of the OLE period (up to	kg received SC injection of alirocumab 150 mg administered Q4W up to 130 weeks) added to LMT.
Reporting group title	Cohort 4 - Alirocumab 300 mg Q4W: > = 50 kg
Reporting group description:	
Cubicate with body weight . E	Oka received SC injection of alirequench 200 mg administered OAW up

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.

Alirocumab 40 Q2W Post-switch Reporting group title

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 0
Epistaxis			

subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	О	0
Oranhari in gaal Dain			
Oropharyngeal Pain subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0 7 4 (0.00%)	0	0
	O	O	O
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
, ,	Ü	Ü	G
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	О
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 7 0 (10.07 %)	0
	0	'	U
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	О
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	О	О
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)	О	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 /25 000/)	0 / / /0 00%	0 / 4 /0 000/)
	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	О
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 7 4 (25.00%)	0 / 6 (0.00%)	0 7 4 (0.00%)
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 / 0 000/)	0.77.70.00%	0 / 4 /0 00%
occurrences (all)	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (an)	0	0	О
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
Dualananhritia			
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 / 0 000/)	0.77.70.00%	0 (4 (0 00%)
occurrences (all)	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (an)	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			

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	О	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	О
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)	О	1	0
1			

Road Traffic Accident subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0 00%)	0 / 5 (0.00%)
occurrences (all)	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
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)	О	О	О
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%)
	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%) O
subjects affected / exposed			
subjects affected / exposed occurrences (all) Musculoskeletal and connective tissue disorders			
subjects affected / exposed occurrences (all) Musculoskeletal and connective tissue disorders Arthritis	0	0	0
subjects affected / exposed occurrences (all) Musculoskeletal and connective tissue disorders Arthritis subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
subjects affected / exposed occurrences (all) Musculoskeletal and connective tissue disorders Arthritis subjects affected / exposed occurrences (all)	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
subjects affected / exposed occurrences (all) Musculoskeletal and connective tissue disorders Arthritis subjects affected / exposed occurrences (all) Flank Pain	0 / 6 (0.00%)	0 / 6 (0.00%)	0 0 / 5 (0.00%) 0
subjects affected / exposed occurrences (all) Musculoskeletal and connective tissue disorders Arthritis subjects affected / exposed occurrences (all) Flank Pain subjects affected / exposed	0 / 6 (0.00%) 0 / 6 (0.00%)	0 / 6 (0.00%) 0 / 6 (0.00%)	0 0 / 5 (0.00%) 0 0 / 5 (0.00%)
subjects affected / exposed occurrences (all) Musculoskeletal and connective tissue disorders Arthritis subjects affected / exposed occurrences (all) Flank Pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 / 6 (0.00%)	0 / 6 (0.00%) 0 / 6 (0.00%)	0 0 / 5 (0.00%) 0 0 / 5 (0.00%)
subjects affected / exposed occurrences (all) Musculoskeletal and connective tissue disorders Arthritis subjects affected / exposed occurrences (all) Flank Pain subjects affected / exposed occurrences (all) Muscle Spasms	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	O / 5 (0.00%) O / 5 (0.00%) O
subjects affected / exposed occurrences (all) Musculoskeletal and connective tissue disorders Arthritis subjects affected / exposed occurrences (all) Flank Pain subjects affected / exposed occurrences (all) Muscle Spasms subjects affected / exposed	0 / 6 (0.00%) 0 / 6 (0.00%) 0	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%)	0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0
subjects affected / exposed occurrences (all) Musculoskeletal and connective tissue disorders Arthritis subjects affected / exposed occurrences (all) Flank Pain subjects affected / exposed occurrences (all) Muscle Spasms subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 / 6 (0.00%) 0	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%)	0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0
subjects affected / exposed occurrences (all) Musculoskeletal and connective tissue disorders Arthritis subjects affected / exposed occurrences (all) Flank Pain subjects affected / exposed occurrences (all) Muscle Spasms subjects affected / exposed occurrences (all) Myalgia	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1	0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	О	О
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 7 3 (20.00%)
, ,	'		'
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
letabolism 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%)

Alirocumab 150 mg Alirocumab 300 mg 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	О

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	О	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)			
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 occurrences (all)	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	О	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	0.777(0.00%)	0.45 (0.00%)	0 /10 /0 00%
occurrences (all)	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
			U
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)	О	О	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 / 4 / 0 000/ \	0 / 5 (0 00%)	0 / 10 / 0 00% \
occurrences (all)	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
Coodin onlock (un)	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 7 10 (0.00%)
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 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (an)	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)	170(10.0770)		
occurrences (un)	 	1	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	О	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1 7 3 (20.00%)	0
(u.,,			
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	О	О	О
Skin and subcutaneous tissue disorders			
James and substitutions tissue districts	I	I	I

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	О
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	О	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)	О	О	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	О
Post Procedural Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	О	О
Pyelonephritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	О
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	О
Tonsillitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	О
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	1 / 10 (10.00%)
occurrences (all)	О	1	1
Urinary Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	О	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

	Alirocumab 75 Q2W	
Non-serious adverse events	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	0 / 18 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Food Allergy subjects affected / exposed	0 / 10 / 0 000/)		
	0 / 18 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Premenstrual Pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal			
disorders Asthma			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Oropharyngeal Pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Sinus Congestion			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
(any			
Psychiatric disorders			
Alcohol Abuse			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Anxiety Disorder			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Depressed Mood			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Investigations	1		
Blood Follicle Stimulating Hormone			
Decreased	1	1	I

subjects affected / exposed	0 / 18 (0.00%)
occurrences (all)	
occurrences (an)	0
Blood Luteinising Hormone Decreased	
subjects affected / exposed	0 / 18 (0.00%)
occurrences (all)	0
Low Density Lipoprotein Decreased	
	0 / 18 (0.00%)
occurrences (all)	0
Coodin onloss (all)	O
Injury, poisoning and procedural complications	
Animal Scratch	
subjects affected / exposed	0 / 18 (0.00%)
occurrences (all)	0
Arthropod Bite	
	0 / 18 (0.00%)
occurrences (all)	0
Concussion	
	0 / 18 (0.00%)
occurrences (all)	
occurrences (an)	O
Fall	
subjects affected / exposed	0 / 18 (0.00%)
occurrences (all)	0
	V
Hand Fracture	
subjects affected / exposed	1 / 18 (5.56%)
occurrences (all)	1
Ligament Sprain	
Ligament Sprain subjects affected / exposed	/10/11 110/\
·	! / 18 (11.11%)
occurrences (all)	2
Post-Traumatic Pain	
	0 / 18 (0.00%)
occurrences (all)	0
, , , , , , , , , , , , , , , , , , ,	U
Radius Fracture	
subjects affected / exposed	0 / 18 (0.00%)
occurrences (all)	0
	Č
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)	О	
Abdominal Pain		

subjects affected / exposed	1 / 18 (5.56%)	I
occurrences (all)	17 10 (3.30%)	
(,	'	
Constipation		
subjects affected / exposed	1 / 18 (5.56%)	
occurrences (all)	1	
Diarrhoea		
subjects affected / exposed	0 / 18 (0.00%)	
occurrences (all)		
occurrences (an)	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 / 10 / 0 000/)	
	0 / 18 (0.00%)	
occurrences (all)	0	
Flank Pain		
subjects affected / exposed	0 / 18 (0.00%)	
occurrences (all)	0	
` ,	J	
Muscle Spasms		
subjects affected / exposed	0 / 18 (0.00%)	
occurrences (all)	0	
Martin		
Myalgia subjects affected / exposed	0 /40 /0	
	0 / 18 (0.00%)	
occurrences (all)	0	
Tendon Pain		
I	I	I

subjects affected / exposed	1 / 18 (5.56%)	
occurrences (all)	1	
Lu for attack and the forest attacks		
Infections and infestations Abscess Limb		
subjects affected / exposed	1 (10 (5 5 (0))	
	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 / 19 (0 00%)	
	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)	О	
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		
5			
Pyelonephritis subjects affected / exposed	0 /10 /0 00%		
	0 / 18 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
±			
Tonsillitis subjects affected / exposed	1 / 10 / 5 5 4 9/)		
occurrences (all)	1 / 18 (5.56%)		
occurrences (un)			
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 Musatic Infaction			
Vulvovaginal Mycotic Infection subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1 / 18 (3.30%)		
	<u> </u>		
etabolism 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