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

## Summary

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

### Results information

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

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | DFI14223 |

### Additional study identifiers

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

Notes:

### Sponsors

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

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-001169-PIP01-11 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 03 May 2019 |
| Is this the analysis of the primary completion data? | No |

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

Notes:

## General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy:

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

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 30 June 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Norway: 1 |
| Country: Number of subjects enrolled | Spain: 5 |
| Country: Number of subjects enrolled | Sweden: 2 |
| Country: Number of subjects enrolled | Czech Republic: 11 |
| Country: Number of subjects enrolled | France: 1 |
| Country: Number of subjects enrolled | South Africa: 1 |
| Country: Number of subjects enrolled | Netherlands: 8 |
| Country: Number of subjects enrolled | Canada: 3 |
| Country: Number of subjects enrolled | Russian Federation: 4 |
| Country: Number of subjects enrolled | United States: 6 |
| Worldwide total number of subjects | 42 |
| EEA total number of subjects | 28 |

Notes:

| Subjects enrolled per age group | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 13 |
| Adolescents (12-17 years) | 29 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

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

### Pre-assignment

Screening details:

A total of 42 subjects were included in this study.

### Period 1

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

### Arms

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

Arm description:

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

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

Dosage and administration details:

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

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

Arm description:

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

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

Dosage and administration details:

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

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

Arm description:

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

| | |
|---|---|
| Arm type | Experimental |

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

Dosage and administration details:

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

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

Arm description:

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

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

Dosage and administration details:

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

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

Arm description:

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

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

Dosage and administration details:

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

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

Arm description:

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

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

Dosage and administration details:

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

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

Arm description:

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

| | |
|---|---|
| Arm type | Experimental |

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

Dosage and administration details:

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

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

Arm description:

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

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

Dosage and administration details:

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

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

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

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

## Period 2

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

## Arms

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

Arm description:

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

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

Dosage and administration details:

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

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

Arm description:

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

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

Dosage and administration details:

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

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

Arm description:

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

| | |
|---|---|
| Arm type | Experimental |

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

Dosage and administration details:

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

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

Arm description:

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

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

Dosage and administration details:

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

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

Arm description:

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

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

Dosage and administration details:

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

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

Arm description:

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

| | |
|---|---|
| Arm type | Experimental |

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

Dosage and administration details:

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

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

Arm description:

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

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

Dosage and administration details:

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

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

Arm description:

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

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

Dosage and administration details:

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

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

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

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

Notes:

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

## Baseline characteristics

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

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

| | | | |
|---|---|---|---|
| Race<br>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)<br>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<br>Units: subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 14.3 | 9.8 | 13.8 |
| standard deviation | ± 2.3 | ± 1.9 | ± 1.6 |
| Gender categorical<br>Units: subjects | | | |
| Female | 2 | 3 | 3 |
| Male | 4 | 3 | 2 |
| Race<br>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)<br>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<br>Units: subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 11.3 | 13.6 | |
| standard deviation | ± 2.2 | ± 2.1 | - |
| Gender categorical<br>Units: subjects | | | |
| Female | 1 | 2 | 19 |
| Male | 5 | 3 | 23 |

| | | | |
|---|---|---|---|
| Race<br>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)<br>Units: mmol/L | | | |
| arithmetic mean | 5.100 | 4.641 | |
| standard deviation | ± 1.136 | ± 0.926 | - |

## End points

### End points reporting groups

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

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

End point description:

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

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

| End point type | Primary |
|---|---|

End point timeframe:

Baseline, Week 8

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

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

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 8

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

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

At Week 8

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

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

At Week 8

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

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 12

Notes:

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

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

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

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

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

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 8

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

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

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

**Statistical analyses**

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 8

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

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

**Statistical analyses**

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 8

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

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

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

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

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

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

**Statistical analyses**

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 8

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

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

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

**Statistical analyses**

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 8

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

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

**Statistical analyses**

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 8

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

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 8

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

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

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 8

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

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

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 8

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

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

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 8

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

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

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Week 8

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

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

## Statistical analyses

No statistical analyses for this end point

## Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

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

| | |
|---|---|
| Assessment type | Systematic |

## Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 21.1 |

## Reporting groups

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

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

Reporting group description:

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

| | |
|---|---|
| Reporting group title | Alirocumab 40 Q2W Post-switch |

Reporting group description:

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

| | |
|---|---|
| Reporting group title | Alirocumab 75 Q2W Post-switch |

Reporting group description:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 11 August 2016 | Following amendments were made: - Clarifications regarding statin dosing requirements. - Replacement of a 2-option screening period, each of different lengths, with a single, up to 6-week (+1 week), screening period for all subjects, to allow inclusion as soon as eligibility was confirmed.<br>- 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.<br>- 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