# 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

Published: 13-06-2016
Last updated: 15-04-2024

Primary objective: To evaluate the effect of alirocumab on low-density lipoprotein cholesterol (LDL-C) levels after 8 weeks of treatment in heterozygous familial hypercholesterolemia (heFH) patients age of 8 to 17 years, with LDL-C *130 mg/dL (3.37…

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Other condition |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON47221

**Source**
ToetsingOnline

**Brief title**
Odyssey KIDS

### Condition

- Other condition

**Synonym**
Familial hypercholesterolemia, high cholesterol

### Health condition

familiaire hypercholesterolemie

### Research involving

Human

## Sponsors and support

**Primary sponsor:** Sanofi-aventis
**Source(s) of monetary or material Support:** Sanofi

## Intervention

**Keyword:** Alirocumab, Children, Dose-finding, Familial hypercholesterolemia

## Outcome measures

### Primary outcome

Percent change in calculated LDL-C

### Secondary outcome

- Absolute change in calculated LDL-C

- Percentage of participants achieving a calculated LDL-C level lower than 130

mg/dL (3.37 mmol/L)

- Percentage of participants achieving a calculated LDL-C level lower than 110

mg/dL (2.84 mmol/L)

- Percent change in Apolipoprotein B (Apo B)

- Percent change in non-high density lipoprotein cholesterol (non-HDL-C)

- Percent change in Total-C

- Percent change in Lipoprotein (a) (Lp[a])

- Percent change in triglycerides (TG)

- Percent change in HDL-C

- Percent change in Apo A-1

- Absolute change in Apo B

- Absolute change in non-HDL-C

- Absolute change in Total-C

- Absolute change in Lp(a)

- Absolute change in TG

- Absolute change in HDL-C

- Absolute change in Apo A-1

- Absolute change in ratio Apo B/Apo A-1

# Study description

**Background summary**

Familial hypercholesterolemia (FH) is an inherited disorder of lipid metabolism, characterized by severely elevated levels of low-density lipoprotein cholesterol (LDL-C) that lead to premature atherosclerosis and cardiovascular disease (CVD). FH is the most clearly documented to have important cardiovascular consequences beginning in childhood. To be effective at preventing Coronary Heart Disease, prevention must begin decades prior to the onset of symptoms.

Alirocumab is an antibody that targets a specific protein (PCSK9), which works by reducing the number of receptors on the liver that remove LDL cholesterol from the blood. By blocking PCSK9*s ability to work, more receptors are available to get rid of LDL cholesterol from the blood and, as a result, lower LDL cholesterol levels. Studies in adult patients have shown significant LDL reductions.

This study is designed to evaluate the efficacy, safety and pharmacokinetics (PK) of alirocumab in the pediatric population in order to support appropriate dose selection of alirocumab for the Phase 3 pediatric study.

**Study objective**

Primary objective: To evaluate the effect of alirocumab on low-density

lipoprotein cholesterol (LDL-C) levels after 8 weeks of treatment in heterozygous familial hypercholesterolemia (heFH) patients age of 8 to 17 years, with LDL-C *130 mg/dL (3.37 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.

Secondary objectives:
-To evaluate the safety and tolerability of alirocumab.
-To evaluate the pharmacokinetics profile of alirocumab.
-To evaluate the effects of alirocumab on other lipid parameters.

### Study design

Phase 2, open label, ascending dose

### Intervention

Cohort 1: Alirocumab SC Q2W
Cohort 2: Alirocumab SC Q2W
Cohort 3: Alirocumab SC Q4W
Cohort 4: Alirocumab SC Q4W

### Study burden and risks

The most common side effects reported with alirocumab (occurring in at least 1% of patients) include injection site reactions, itching and upper respiratory symptoms.

## Contacts

**Public**
Sanofi-aventis

Kampenringweg 45 E -
Gouda 2803 PE
NL
**Scientific**
Sanofi-aventis

Kampenringweg 45 E -
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NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

## Inclusion criteria

- Children and adolescent male and female patients aged of 8 to 17 years at the time of signed informed consent.
- Patients with a diagnosis of heterozygous familial hypercholesterolemia (he FH) through genotyping or clinical criteria.
- Patients treated with an optimal dose of statin with or without other LMT(s) or non-statin LMT(s) if statin intolerant at stable dose for at least 4 weeks prior to screening visit (Week -2).
- Patients with calculated LDL-C greater than or equal to 130 mg/dL (*3.37 mmol/L) at the screening visit (Week -2).
- Patients with body weight greater than or equal to 25 kg.
- Patients aged of 8 to 9 years to be at Tanner stage1 and patients aged of 10 to 17 years to be at least at Tanner stage 2 in their development.
- A signed informed consent indicating parental permission with or without patient assent, depending on capacity for understanding based on developmental maturity. In cases involving emancipated or mature minors with adequate decision-making capacity, or when otherwise
permitted by law, a signed informed consent directly from patients.

## Exclusion criteria

- Patient with secondary hyperlipidemia.
- Diagnosis of homozygous familial hypercholesterolemia.
- Patient who has received lipid apheresis treatment within 2 months prior to the screening period, or has plans to receive it during the study.
- Known history of type 1 or type 2 diabetes mellitus.
- Known history of thyroid disease.

- Known history of hypertension.
- Fasting triglycerides >350 mg/dL (3.95 mmol/L) at the screening visit (Week -2).
- Severe renal impairment (ie, eGFR <30 mL/min/1.73 m2 at the screening visit [Week -2]).
- ALT or AST >2 x ULN (1 repeat lab is allowed).
- CPK >3 x ULN (1 repeat lab is allowed).

# Study design

## Design

| | |
|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 05-10-2016 |
| Enrollment: | 9 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Praluent |
| Generic name: | alirocumab |
| Registration: | Yes - NL outside intended use |

# Ethics review

Approved WMO

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|---|---|
| Date: | 13-06-2016 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |

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| Approved WMO Date: | 18-08-2016 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 04-11-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 08-12-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 13-02-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 08-03-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 05-04-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 23-10-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 23-01-2018 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 09-02-2018 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO | |

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|---|---|
| Date: | 14-11-2018 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 15-11-2018 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 17-01-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 11-02-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2015-003766-85-NL |
| Other | IND105574 |
| CCMO | NL57952.018.16 |