A Randomized, Double-Blind, Placebo-Controlled Study Followed by an Open Label Treatment Period to Evaluate the Efficacy and Safety of Alirocumab in Children and Adolescents with Heterozygous Familial Hypercholesterolemia

Published: 11-06-2018
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Primary goal: To evaluate the efficacy of alirocumab administered every 2 weeks (Q2W) versus placebo after 24 weeks of double-blind (DB) treatment on low-density lipoprotein cholesterol (LDL-C) levels in children with heterozygous familial...

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON55709

Source
ToetsingOnline

Brief title
Alirocumab in Children with Heterozygous Familial Hypercholesterolemia

Condition

- Other condition

Synonym
Hetrozygous familial hypercholesterolemia, high cholesterol

Health condition

Familiaire hypercholesterolemie

Research involving
Human

Sponsors and support

Primary sponsor: Genzyme Europe BV
Source(s) of monetary or material Support: Genzyme Europe B.V.

Intervention

Keyword: Alirocumab, Children, Familial hypercholesterolemia

Outcome measures

Primary outcome

Percent change in low-density lipoprotein cholesterol (LDL-C) from baseline to

Week 24

Secondary outcome

- Percent change in LDL-C

- Percent change in Apo B

- Percent change in non-HDL-C

- Percent change in Total-C

- Proportion of patients with LDL-C level < 3.37 mmol/L

- Proportion of patients with LDL-C level < 2.84 mmol/L

- Percent change in lipoprotein (a)

- Percent change in HDL-C

- Percent change in fasting triglycerides (TG)

- Percent change in apolipoprotein A1 (Apo A-1)

- Number of patients with adverse events

- Maturing cognition (Cogstate Battery Test)

Study description

Background summary

Familial hypercholesterolemia (FH) is a hereditary disorder of lipid metabolism, characterized by severely elevated levels of low-density lipoprotein (LDL-c) leading to early onset of atherosclerosis and cardiovascular disease (CVD). It has been shown that these complications occur already in early childhood. To be treated effectively, prevention must begin decades prior to the onset of symptoms.

Alirocumab is an antibody that targets a specific protein (PCSK9) that reduces the number of LDL receptors on liver cells which remove LDL from the blood circulation. PCSK9 inhibition results in more receptors being present on the surface of liver cells resulting in lower levels of circulating LDL-C.

This study is designed to evaluate the efficacy and safety of alirocumab in the pediatric population (ages 8 to 17) with heterozygous familial hypercholesterolemia.

Study objective

Primary goal:

To evaluate the efficacy of alirocumab administered every 2 weeks (Q2W) versus placebo after 24 weeks of double-blind (DB) treatment on low-density lipoprotein cholesterol (LDL-C) levels in children with heterozygous familial hypercholesterolemia 8 to 17 years of age on top of background treatment.

Secondary goals:

-To evaluate the efficacy of alirocumab versus placebo on low-density lipoprotein cholesterol (LDL-C) levels.
-To evaluate the effects of alirocumab versus placebo on other lipid parameters.
-To evaluate the safety and tolerability of alirocumab in comparison with placebo.
-To evaluate the efficacy, safety, and tolerability of alirocumab after open label treatment.
-To evaluate the development of anti-alirocumab antibodies.

Study design

Phase 3, double-blind, placebo-controlled study, followed by open-label treatment.

Intervention

Alirocumab 40, 75 or 150 mg/ml or placebo SC Q2W
Alirocumab 75, 150 or 300 mg/ml or placebo SC Q4W

Study burden and risks

Risk and burdens related to blood collection, study procedures and possible adverse events.

Contacts

Public
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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 8 to 17 years at the time of signed informed consent., -Patients with diagnosis of heterozygous familial hypercholesterolemia (heFH) through genotyping or clinical criteria., -Patients treated with optimal dose of statin +/- other LMT(s) or non-statin LMT(s) if statin intolerant at stable dose for at least 4 weeks prior to screening lipid sampling., -Patients with calculated LDL-C greater than or equal to 130 mg/dL (>=3.37 mmol/L) at the screening visit except for patients who have previously participated in the DFI14223 study., -A signed informed consent indicating parental permission with or without patient assent.

Exclusion criteria

-Patient with body weight less than 25 kg., -Patients aged of 8 to 9 years not at Tanner stage 1 and patients aged of 10 to 17 years not at least at Tanner stage 2 in their development., -Patients 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., -Patients with uncontrolled type 1 or type 2 diabetes mellitus., -Patients with known uncontrolled thyroid disease., -Patients with uncontrolled hypertension., -Fasting triglycerides >350 mg/dL (3.95 mmol/L)., -Severe renal impairment (ie, estimated glomerular filtration rate [eGFR] <30 mL/min/1.73 m^2., -Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >2 x upper limit of normal (ULN)., -Creatinine phosphokinase (CPK) >3 x ULN.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	06-02-2019
Enrollment:	5
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	11-06-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	17-09-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	19-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO

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:	30-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	13-12-2019
Application type:	Amendment
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Approved WMO Date:	16-12-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-03-2020
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Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-03-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-02-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-02-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-03-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	01-04-2021
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
Other	2017-001903-60
EudraCT	EUCTR2017-001903-60-NL
CCMO	NL65553.018.18

Study results

Date completed:	05-08-2022
Results posted:	07-02-2023

First publication
05-12-2022