A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Evaluate the Efficacy and Safety of SAR236553/REGN727/Alirocumab in Patients With Heterozygous Familial Hypercholesterolemia Not Adequately Controlled With Their Lipid-Modifying Therapy

Published: 31-07-2012
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The objective of the study is to assess the efficacy, tolerability and safety of SAR236553/Alirocumab when administered during 1.5years in patients with heterozygote familial hypercholesterolemia, who despite of lipid lowering therapy still have...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON39858

Source
ToetsingOnline

Brief title
EFC12492 / Odessey FH1

Condition

- Metabolic and nutritional disorders congenital
- Lipid metabolism disorders

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
familial hypercholesterolemia, inherited hyperlipidemia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: heterozygous familial hypercholesterolemia, LDL-C, SAR236553/Alirocumab

Outcome measures

Primary outcome

To demonstrate the reduction of low-density lipoprotein cholesterol (LDL-C) by SAR236553/Alirocumab as add-on therapy to stable maximally tolerated daily statin therapy with or without other lipid-modifying therapy (LMT) in comparison with placebo after 24 weeks of treatment in patients with heterozygous familial hypercholesterolemia (heFH).

Secondary outcome

- To evaluate the effect of SAR236553/Alirocumab 75 mg in comparison with placebo on LDL-C after 12 weeks of treatment.

- To evaluate the effect of SAR236553/Alirocumab on other lipid parameters (ie, apolipoprotein B (Apo B), non-high-density lipoprotein cholesterol (non-HDL-C), total cholesterol (total-C), lipoprotein (a) (Lp (a)), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG) levels, apolipoprotein A-1 (Apo A-1) levels.

- To evaluate the long-term effect of SAR236553/Alirocumab on LDL-C.

- To evaluate the safety and tolerability of SAR236553/Alirocumab.

- To evaluate the development of anti-SAR236553/Alirocumab antibodies.

- To evaluate the pharmacokinetics (PK) of SAR236553/Alirocumab.

Study description

Background summary

The study will include patients with heterozygous familial hypercholesterolemia (heFH) with or without a history of MI or ischemic stroke. Familial hypercholesterolemia (FH) is an inherited disorder of lipid metabolism that predisposes a person to premature severe cardiovascular disease (CVD). Familial hypercholesterolemia has a high prevalence in Caucasian populations, were estimated 1 in 500 individuals are affected.
In the heterozygous form of FH, the cumulative risk of experiencing a coronary event by the age of 60 years without effective treament is at least 50% in men and approximately 30% in women.
In 4 observational studies, statin therapy was shown to reduce the risk of CVD by 50% to 80% in patients with FH. Unfortunately, even after treatment, the risk in heFH can still be almost 2-fold higher than the general population. In addition only a small fraction of treated heFH patients are able to reach recommended levels of LDL-C. Thus, the need for more intensive treatment in heFH patients is clear.

SAR236553/Alirocumab is a fully human monoclonal antibody that binds Propotein Convertase Subtilisin Kexin type 9 (PCSK9).

PCSK9 which is highly expressed in the liver, is involved in regulating the levels of Low-density lipoportein receptor (LDL-R) protein. Once secreted into plasma, PCSK9 binds to the LDL-R and promotes its degeneration, which leads to reduced LDL-C removal or higher LDL-C circulating levels.
Therefor blocking PCSK9 can potentially benefit patients by decreasing their plasma LDL-C levels. In addition, PCSK9 messenger ribonucleic acid (mRNA) and protein levels are increased in response to statins, potentially attenuating their cholesterol-lowering effect.

Study objective

The objective of the study is to assess the efficacy, tolerability and safety of SAR236553/Alirocumab when administered during 1.5years in patients with heterozygote familial hypercholesterolemia, who despite of lipid lowering

therapy still have high cholestrol

Study design

Randomized double blind, placebo contrtoled, mutlicenter study with parallel groups. Gerandomiseerd, dubbelblind, placebogecontroleerd, multicenter, multinationale studie met parallelle groepen.
Randomization 2:1 to treatment (every 2 weeks s.c. injections) with
1. SAR236553/Alirocumab
2. placebo,
Stratified according to prior history of myocardial infarction (MI) or ischemic stroke [Yes/No], statin treatment, and geographic region.
After randomization, patients.
Continue their maximal tolerated statins treattmnet with or without lipid modifying treatement
Study duration +/- 18months
After completion of the 18 month double-blind treatment period, patients may be offered to consent for another study (open-label extension study). Patients who consent to participate in the open-label extension study will not undergo the follow-up period.
Independent DSM

Intervention

Biweekly subcutenous injections with study drug/placebo

Study burden and risks

Riscs: adverse events of the study drug

Burden:
- 12 study visits and one follow-up visit in 18months. Patients need to come fasted to the visits
- 39 subcutanous injections, by the patient or relative. Training is foreseen and a diary needs to be completed for the administration
- Physical examininations: 4-5x
- Vital functions at every study visit
- Blooddraws (ca 30ms/draw) 12x
- Pregancy test (if relevant) 9x
- ECG 4x
- Questionnaire (Quality of life) 6x
- Optional pharmcokinetics ca. 12ml blood, 6x

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients with heterozygous familial hypercholesterolemia who are not adequately controlled with their lipid-modifying therapy.

Exclusion criteria

- Age < 18 years
- Patient without diagnosis of heFH made either by genotyping or by clinical criteria.
- LDL-C <70 mg/dL (<1.81 mmol/L) at the screening visit (Week-2) and patient with history of documented cardiovascular disease.
- LDL-C <100 mg/dL (<2.59 mmol/L) at the screening visit (Week-2) and patient without history of documented cardiovascular disease.

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:	Recruitment stopped
Start date (anticipated):	23-01-2013
Enrollment:	55
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	SAR236553/Alirocumab
Generic name:	nvt

Ethics review

Approved WMO Date:	31-07-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-12-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	16-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-06-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-06-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	10-10-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-01-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-07-2014
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	EUCTR2011-005109-56-NL
Other	IND NUMMER 105574
CCMO	NL41300.018.12

Study results

Date completed: 05-12-2014

Actual enrolment: 18

Summary results
Trial is onging in other countries