Long-term safety and tolerability of REGN727 / SAR236553 in high cardiovascular risk patients with hypercholesterolemia not adequately controlled with their lipid modifying therapy: a randomized, double-blind, placebo-controlled study (LTS11717)

Published: 15-02-2012
Last updated: 26-04-2024

Primary: long-term safety and efficacy of SAR236553 in high risk patients with an insufficiently controlled hypercholestolemia despite treatment with existing lipid modifying drugs.Secondary objectives: effect on individual lipids, development of...

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

Summary

ID

NL-OMON39801

Source
ToetsingOnline

Brief title
LTS11717

Condition

- Other condition

Synonym
cholesterol elevation, hypercholesteriolemia

Health condition

hypercholesterolemie

Research involving

Human

Sponsors and support

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

Intervention

Keyword: hypercholesterolemia, REGN727, SAR236553

Outcome measures

Primary outcome

Percent change from baseline in LDL-C at week 24. Adverse events.

Secondary outcome

E.g. % change from baseline in LDL-C at week 12, % patienst meeting the target

LDL-C value bereikt in week 24, development of antibodies, PK parameters.

Study description

Background summary

It is known that insufficiently or not controlled hypercholesterolemia leads to and increased risk of cardiovascular disease. Statins are the cornerstone of the drug treatment of hypercholesterolemia.
SAR236553 is a fully human monoclonal antibody that binds PCSK9 and blocks its effect on the LDL receptors located at the surface of liver cells; LDL receptors are in charge of the removal of LDL-cholesterol (bad cholesterol) from the blood. The substance PCSK9 is secreted into the blood and directly binds to the LDL receptors promoting their breakdown. The increased breakdown of LDL receptors leads to a reduced LDL-cholesterol removal from the blood, and therefore higher LDL-cholesterol circulating levels. Therefore, blocking PCSK9 binding to the LDL receptors through the use of SAR236553 can potentially benefit patients suffering from hypercholesterolemia by decreasing the blood

LDL-cholesterol levels.
In this study long-term safety and efficacy of SAR236553 will be investigated in high risk patients with an insufficiently controlled hypercholestolemia despite treatment with existing lipid modifying drugs.

Study objective

Primary: long-term safety and efficacy of SAR236553 in high risk patients with an insufficiently controlled hypercholestolemia despite treatment with existing lipid modifying drugs.
Secondary objectives: effect on individual lipids, development of anti-SAR236553 antibodies, PK.

Study design

Multicenter randomized double-blind phase III parallel-group placebo-controlled study.
Randomisation (2:1) to:
* SAR236553 150 mg s.c. every 2 weeks
* Placebo.
Stable background treatment with existing lipid-lowering therapy.
Screening period of max. 3 weeks. Treatment period 18 months. Follow-up 8 weeks.
Independent DSMB.
An interim analysis when 600 patients have concluded the 18 months treatment period..
Approx. 2100 patients.

Intervention

Treatment with SAR236553 or placebo.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: Max. study duration approx. 20 months. 13 visits (11 fasting). Duration 0,5-3 h.
SC injection (1 ml) every 2 weeks.
Physical examination 6x.
Colour vison test (to exclude optic nerve problems as an adeverse event) 4x.
Blood tests 11x, 395 ml in total.
5x10 ml blood for future testing in relation to the study medication.
Optional pharmacogenetic blood tests (12 ml).
Pregnancy test (if relevant) 7x.
ECG 5x.
Questionnaire QoL.

Dietary councelling.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Either A or B below and who are not adequately controlled with their lipid modifying therapy:
A) Patients with heterozygous familial hypercholesterolemia (heFH) with or without established coronary heart disease (CHD) or CHD risk equivalents
OR
B) Patients with hypercholesterolemia together with established CHD or CHD risk equivalents.
See protocol for more details

Exclusion criteria

* Age < 18 years.
* LDL-C <1.81 mmol/L.
* Statin that is not simvastatin, atorvastatin, or rusovastatin
* simvastatin, atorvastatin, or rusovastatin is not taken dialy or not taken at a registered dose.
* Daily doses above atorvastatin 80 mg, rosuvastatin 40 mg or simvastatin 40 mg (except for patients on simvastatin 80 mg for more than one year, who are eligible).
* Fasting serum TG >4.52 mmol/L)
* Use of fibrates other than fenofibrate within 6 weeks
* Known history of active optic nerve disease
* Pregnancy, inadequate anticonception, breast feeding

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):	16-02-2012
Enrollment:	145
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	SAR236553

Generic name:	SAR236553

Ethics review

Approved WMO Date:	15-02-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-04-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-08-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-03-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-06-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	30-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-01-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-05-2014
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:	15-07-2014
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
Other	clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2011-002806-59-NL
CCMO	NL39559.018.12