A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Evaluate the Efficacy and Safety of Alirocumab in Insulin Treated Patients with Type 1 or Type 2 Diabetes and With Hypercholesterolemia at High Cardiovascular Risk Not Adequately Controlled on Maximally Tolerated LDL-C Lowering Therapy.

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1) To demonstrate the superiority of alirocumab in comparison with placebo in the reduction of calculated low-density lipoproteincholesterol (LDL-C) after 24 weeks of treatment in patients with diabetes treated with insulin and with...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON42569

Source
ToetsingOnline

Brief title
LPS14355

Condition

- Coronary artery disorders
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
hypercholesterolemia-high cholesterol

Research involving
Human

Sponsors and support

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

Intervention

Keyword: diabetes, insulin, LDL-C

Outcome measures

Primary outcome

- Percent change in calculated LDL-C from baseline to Week 24 in the

intent-to-treat (ITT) population.

- Safety parameters, adverse events of special interest, product complaints,

laboratory data, vital signs.

Secondary outcome

- Percent change in calculated LDL-C from baseline to Week 24, using all LDL-C

values during the efficacy treatment period.

- Absolute change in HbA1c/FGP/insuline use from baseline to Weeks 12 and 24

Study description

Background summary

More than 380 million people worldwide have diabetes, most of whom will die from cardiovascular disease (CVD). Compared to people without diabetes, those with diabetes are at higher risk of developing CVD, develop associated clinical complications and at an earlier age, and have shortened life expectancy by about 6 to 7 years. In addition to the high human cost of disease, CVD contributes greatly to the overall healthcare expenditure in these patients. Dyslipidemia is a major risk factor for macrovascular complications in individuals with diabetes.
Especially a high level of LDL-cholesterol contributes significantly to an increased risk of CVD in diabetics compared to healthy individuals. The LDL-cholesterol is therefore selected as a primary endpoint for cholesterol, and is widely accepted as a valid surrogate endpoint.
Research showed that the number of CVDs is reduced significantly when LDL-cholesterol levels are lowered in diabetics. Guidelines recommend a values below 1.8 mmol/l in type 1 and type 2 diabetics with a high CVD risk; a value that is not reached in many patients even though therapy is maximized. Because of this issue potentially many patients experience additional CVDs. Therefore blocking PCSK9 binding to the LDL-Receptor can potentially benefit diabetics with hypercholesterolemia by decreasing their plasma LDL-C levels. In this high risk group, and besides the Odyssey Outcomes trial, the safety and efficacy of alirocumab in insulin treated patients is explored.

Study objective

1) To demonstrate the superiority of alirocumab in comparison with placebo in the reduction of calculated low-density lipoprotein
cholesterol (LDL-C) after 24 weeks of treatment in patients with diabetes treated with insulin and with hypercholesterolemia at high cardiovascular risk not adequately controlled on maximally tolerated LDL-C lowering therapy

2) To evaluate the safety and tolerability of alirocumab in patients with diabetes treated with insulin

Study design

A randomized, double-blind, placebo controlled paralell-group study.

Intervention

-Alirocumab starting dose of 75 mg every 2 weeks until week 12. After week 12 (and if LDL levels not reached) every 2 weeks 150 mg.
-placebo every 2 weeks.

Study burden and risks

The most common side effects of alirocumab reported in previous completed

studies of alirocumab in patients who received at least one dose of alirocumab include: injection site reactions, itching and flu (upper respiratory symptoms). None occurred in more than 6% of the 4700 patients.

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

I 01. Patients with Type 1 or Type 2 diabetes treated with insulin with LDL >=70 mg/dL, not adequately controlled by a stable, maximum dose/regimen of statin that is tolerated by the patient .
I 02. Patients >=18 years of age..
I 03. Patients diagnosed with Type 1 or Type 2 diabetes at least one year prior to the screening
visit (Week -3).

I 04. Glycosylated hemoglobin (HbA1c) <10% (Week -3)
I 05. Patients with documented history of CVD (including CHD and/or CHD risk equivalents) and/or at least one additional CV risk factor.

Exclusion criteria

- Plans to initiate new LMT during the course of the study or to modify the dose of the current LMT.
- Not on a stable dose of LMT for at least 4 weeks prior to the screening visit or from screening to randomization.
- Use of nutraceutical products or over-the-counter therapies that may affect lipids which have not been at a stable dose for at least 4 weeks prior to the screening visit or between screening and randomization visits.
- Use of red yeast rice products within 4 weeks of the screening visit or between screening and randomization visits.
- Not on a stable insulin dose for at least 3 months prior to screening.

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):	23-02-2016
Enrollment:	20
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:	27-10-2015
Application type:	First submission
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	04-12-2015
Application type:	First submission
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	06-01-2016
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	28-01-2016
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	25-02-2016
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	22-06-2016
Application type:	Amendment

Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	23-06-2016
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)

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	EUCTR2015-000799-92-NL
CCMO	NL55043.101.15
Other	U1111-1172-4772