A phase III, double-blind, randomized, placebo-controlled, multi-center study evaluating the efficacy and safety of dalcetrapib on lipids, lipoproteins, apolipoproteins and markers of CV risk in patients hospitalized for an acute coronary syndrome (ACS) when treatment is initiated within 1 week after an ACS (dal-ACUTE).

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

Summary

ID

NL-OMON36322

Source
ToetsingOnline

Brief title
dal-ACUTE

Condition

- Coronary artery disorders

Synonym
Coronary Heart Disease, Ischemic heart disease

Research involving
Human

Sponsors and support

Primary sponsor: Hoffmann-La Roche
Source(s) of monetary or material Support: Hoffman- La Roche

Intervention

Keyword: Coronary heart disease (CHD), dalcetrapib, Doubleblind, Phase III

Outcome measures

Primary outcome

The primary endpoint is the percent change from baseline in HDL-C levels after

4 weeks of treatment.

Baseline HDL-C is defined as the single HDL-C value taken at visit 2 (the day 1

randomization visit) or, if not available, the most recent assessment prior to

the start of study medication.

Secondary outcome

The secondary endpoints are:

The difference between dalcetrapib and placebo treatment groups in percent

change from baseline in HDL-C levels after 4 weeks of treatment - comparison of

this endpoint between the studies WC25501 and NC20971.

Percent change from baseline in the following parameters:

• HDL-C levels after 8, 12 and 20 weeks of treatment

• Blood lipids (TC and TG levels), lipoproteins (LDL-C levels), lipoprotein subfractions, apolipoprotein (Apo A1, Apo B and Apo E) levels, and ratios of these lipids, lipoproteins and apolipoproteins, measures of HDL functionality and other markers of CV risk

Study description

Background summary

In support of study NC20971, study WC25501 will provide evidence of efficacy and safety of dalcetrapib when treatment is started within 1 week after an ACS, by comparing the effect of dalcetrapib on lipid profile when treatment is started within 1 week after an ACS (in this study) to treatment started 4 to 12 weeks after an ACS (in study NC20971).

Study NC20971 is a phase III study evaluating the effects of dalcetrapib on cardiovascular (CV) risk in stable CHD patients, with a documented recent ACS in support of the indication *For the prevention of CV mortality and morbidity in adult patients with stable coronary heart disease (CHD) following a recent Acute Coronary Syndrome (ACS) event, used in addition to standard CV treatments (including lipid lowering strategies)*.

Study objective

The primary objective of this study is to evaluate the effect of dalcetrapib on HDL-C levels after 4 weeks of treatment when treatment is initiated within 1 week after an ACS.

The secondary objectives of this study are:
- To compare the effect of dalcetrapib on HDL-C levels after 4 weeks of treatment when treatment is initiated within 1 week after an ACS (in this study) with dalcetrapib initiated 4 to 12 weeks after an ACS (in study NC20971)

- To evaluate the effect of dalcetrapib on HDL-C levels after 8, 12 and 20 weeks of treatment

- To evaluate the effect of dalcetrapib on lipids, lipoproteins, lipoprotein sub-fractions, apolipoproteins, measures of HDL functionality, CETP mass and CETP activity

- To evaluate the effect of dalcetrapib on markers of CV risk

- To evaluate the safety profile of dalcetrapib

Study design

This trial will be a double-blind, randomized, placebo-controlled, parallel group, multi-center study in patients hospitalized for an acute coronary syndrome (ACS).

Patients admitted to the hospital for an ACS event who provided written informed consent will be screened for eligibility. The screening period should be as short as possible and no longer than 1 week after the ACS event, in which all pre-randomization assessments will be conducted.

Eligible patients will receive double-blind treatment with either 600 mg of dalcetrapib or matching placebo for 20 weeks on a background of contemporary, guidelines-based medical care for ACS. The double-blind treatment period will be followed by a 4- week safety follow-up.

Visits are scheduled 4, 8, 12 and 20 weeks after randomization.

Intervention

Patients will be subjected to the following interventions/precedures or define behavioural rules:
- physical examination
- Height and weight is measured
- Blood pressure and Heart rate are measured
- all blood samples should be taken in the fasting state
- a quality of live questionnaire will be assesed at each visit
- counseling on heart healthy diet and lifestile will be given
- serum or urine prenancy test

Study burden and risks

So far, 526 healthy volunteers received single doses of up to 4500 mg or multiple doses of up to 3900 mg of dalcetrapib. In addition, 1630 patients have received doses of dalcetrapib of up to 900 mg for up to one year. Approximately 16,300 patients are currently participating in studies with dalcetrapib.

The most common side effect of the study drug in these previous studies was:
• Diarrhea and stool abnormalities (10-15%)

Other common (1-10%) side effects included:
• dizziness
• headache
• sleep disorders

Of all these side effects, only diarrhea is considered to be caused by dalcetrapib.

Your study doctor or study staff will take your blood using a needle. Some problems you might have from this are: pain, bruises, dizziness or infection at the place of the puncture.

The development of a similar compound, called torcetrapib, was stopped in December 2006. This was due to the fact that in a large long-term trial including approximately 15,000 patients, there were more cardiovascular (49 in the torcetrapib versus 35 in the control group) and non-cardiovascular (40 versus 20) deaths and generally an increased cardiovascular risk in people taking torcetrapib compared to the group taking placebo. The non-cardiovascular deaths were mostly due to cancer and infections.
Torcetrapib leads to increases in blood pressure, and increased levels of aldosterone and cortisol. Aldosterone leads to increased blood pressure and in addition has direct negative effects on blood vessels which may lead to cardiovascular events. Cortisol is involved in the regulation of the immune system and high levels of it lead to a down regulation of the system. A down-regulated immune system may lead to an increase in infections and cancers. No clinical benefit has been seen in patients who received torcetrapib versus those who received placebo.
The study drug you will be taking, dalcetrapib, has a very different chemical structure than torcetrapib. In agreement with this, many pre-clinical and clinical experiments showed that dalcetrapib does not lead to increases in blood pressure. Importantly, treatment with dalcetrapib does not lead to increased levels of aldosterone and cortisol.

Blood levels for HDL-C (good cholesterol) may improve as a result of taking dalcetrapib in this study. Data from clinical trials with other HDL increasing compounds as well as data from animal studies, strongly suggest that increasing HDL-C reduces future cardiovascular risk.
The close medical attention the patient gets during the study may result in gaining new information about their health which may provide benefits for their general health and well being. Nevertheless, it is possible, that the patient will not get any benefit from participating in this study.

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

Adult patients, >/=45 years of age
patients admitted to the hospital for acute coronary syndrome (ACS), defined as the occurence of spontaneous myocardial infarction; hospitalization for ACS (electrocardiogram abnormalities withouth biomarkers elevation)

Exclusion criteria

- Women who are pregnant or breastfeeding
- Women of childbearing potential who are not using a highly effective contraceptive method at randomization
- Patients who have symptomatic congestive heart failure ([CHF], New York Heart Association

[NYHA] Class III or IV)
- Clinically significant heart disease which is anticipated to require coronary artery bypass grafting (CBAG), cardiac transplantation, surgical repair and/or replacement of valves during the double-blind treatment phase of the study

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):	28-04-2011
Enrollment:	120
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	na
Generic name:	dalcetrapib

Ethics review

Approved WMO

Date:	13-01-2011
Application type:	First submission

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-03-2011
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-03-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-03-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-04-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-04-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-05-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-05-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	16-05-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-05-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-06-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-06-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-06-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-08-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-08-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2010-022529-14-NL
CCMO	NL34955.060.10