High-Resolution Assessment of Coronary Plaques in a Global Evolocumab Randomized Study (HUYGENS)

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* Primary Objective: To evaluate the effect of evolocumab on fibrous cap thickness (FCT) in subjects with non ST elevation acute coronary syndrome (NSTE ACS) who are taking maximally tolerated statin therapy.* Secondary Objective(s): To evaluate the...

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

Summary

ID

NL-OMON48805

Source
ToetsingOnline

Brief title
20160184 HUYGENS

Condition

- Coronary artery disorders
- Lipid metabolism disorders

Synonym
angina, heart attack, high blood lipids, high cholesterol, Vessels supplying the heart with blood

Research involving
Human

Sponsors and support

Primary sponsor: Amgen

Source(s) of monetary or material Support: Amgen

Intervention

Keyword: coronary artery disease, coronary atherosclerotic plaques, maximally tolerated statin therapy, optical coherence tomography (OCT)

Outcome measures

Primary outcome

To evaluate the effect of evolocumab on fibrous cap thickness (FCT) in subjects

with non ST elevation acute coronary syndrome (NSTE ACS) who are taking

maximally tolerated statin therapy.

Secondary outcome

To evaluate the effects of evolocumab on coronary plaque morphology in subjects

with NSTE-ACS who are taking maximally tolerated statin therapy

Study description

Background summary

This is a phase 3, double blind, placebo controlled, randomized study evaluating the effect of evolocumab on coronary atherosclerotic plaques as assessed by OCT at baseline and at 50 weeks of treatment in subjects with a non-ST-segment elevation ACS (NSTE-ACS). The trial duration of approximately 1 year was chosen based on the results of several historical trials. Subjects will be randomized 1:1 into 2 treatment groups no more than 7 days after the signing of the informed consent: evolocumab 420 mg subcutaneously (SC) QM or placebo QM SC. The randomization will be stratified by current statin use (> 4 weeks or * 4 weeks duration) at screening. Investigators will up titrate statin therapy to the maximally tolerated dose, in accordance with local guidelines, for subjects prior to randomization.

Study objective

* Primary Objective: To evaluate the effect of evolocumab on fibrous cap thickness (FCT) in subjects with non ST elevation acute coronary syndrome (NSTE ACS) who are taking maximally tolerated statin therapy.

* Secondary Objective(s): To evaluate the effects of evolocumab on coronary plaque morphology in subjects with NSTE-ACS who are taking maximally tolerated statin therapy.
* Safety Objective: To evaluate the safety and tolerability of evolocumab treatment in subjects with NSTE-ACS who are taking maximally tolerated statin therapy.
* Exploratory Objective: To evaluate the effects of evolocumab on lipid parameters in subjects with NSTE-ACS who are taking maximally tolerated statin therapy. To evaluate the effects of evolocumab on features of coronary plaques in subjects with NSTE-ACS who are taking maximally tolerated statin therapy using different imaging techniques.

Study design

This is a phase 3, double-blind, placebo-controlled, randomized study evaluating the effect of evolocumab on coronary atherosclerotic plaques as assessed by OCT at baseline and at week 50 in subjects with an NSTE-ACS. The trial duration of 1 year was chosen based on the results of several historical trials. Subjects will be randomized 1:1 into 2 treatment groups no more than 7 days after the signing of the informed consent: evolocumab 420 mg subcutaneously (SC) QM or placebo SC QM. The randomization will be stratified by current statin use (> 4 weeks or * 4 weeks duration) at screening. Investigators will up-titrate statin therapy to the maximally tolerated dose, in accordance with local guidelines, for subjects prior to randomization On site visits are required on Day1, 4w, 24w and 50week, phone calls at 12w and 36w End of study (EOS, 52w)phone call for all subjects will be when the safety follow up assessment is completed. The Personal Injector will be used for IP administration
OCT and IVUS procedures will be done during screening and on W50.

Intervention

50% of the subjects will be randomized to evolocumab, 50% on placebo (1: 1 ratio).
A total of 8 visits will take place: Screening, Day 1, Week 4, Week 12 (by telephone), Week 24, Week
36 (by telephone), Week 50, Week 52 (by telephone).

One group receives 120 mg / ml of evolocumab on day 1 and every 4 weeks for 48 weeks with a 3.5 ml injector. The other group receives an identical volume of placebo on day 1 and every 4 weeks for 48 weeks using a 3.5 ml injector.

During the visits, physical examination is performed and vital signs are measured (3x), complaints / side effects and medication use are discussed (8x), blood is taken for testing in the local lab (4x, of which 3x fasting), angiogram is done with

IVUS and OCT (during the screening and at the end of the study in week 50). These angiograms will probably last 15 to 20 minutes longer. During the screening, training of the injection device will take place and, if necessary, during the planned visits.

In women of childbearing age a blood / urine sample is taken for a pregnancy test (4x).
For an overview of all procedures / tests, see Schedule of Assessments in section 2.2 of the protocol.

Study burden and risks

See answer to E9.

Contacts

Public
Amgen

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

*Clinical indication for coronary angiography during admission due to non ST segment elevation acute coronary syndrome (NSTE-ACS) with interventional treatment of culprit plaque.
*Subjects must have an eligible LDL-C level via local laboratory assessment in between admission for ACS and coronary angiogram.
*Subject must be on optimal statin therapy per local guidelines prior to randomization.
*Subjects must meet all of the criteria at the qualifying coronary angiogram procedure

Exclusion criteria

*Subject has taken a cholesterol ester transfer protein (CETP) inhibitor, (i.e., anacetrapib, dalcetrapib, evacetrapib), mipomersen , lomitapide or has undergone LDL apheresis in the last 12 months prior to LDL-C screening
*Subject has previously received evolocumab or any other therapy to inhibit PCSK9
*Baseline OCT does not meet OCT imaging criteria as determined by the Core Lab technical standards.

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):	13-11-2018
Enrollment:	43
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Repatha
Generic name:	Evolocumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-06-2018
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	01-08-2018
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	16-08-2018
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	12-09-2018
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	17-09-2018
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	15-02-2019
Application type:	Amendment

Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	06-03-2019
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	28-05-2019
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	17-06-2019
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	24-12-2019
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	15-10-2020
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	24-11-2020
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	07-12-2020
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)

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	EUCTR2017-003236-37-NL
ClinicalTrials.gov	NCT03570697
CCMO	NL66188.075.18

Study results

Date completed: 21-01-2021

Results posted: 12-11-2021

First publication
17-09-2021