# Effects of the PCSK9 Antibody AliroCuMab on Coronary Atherosclerosis in PatieNts with Acute Myocardial Infarction. A Serial, Multivessel, Intravascular Ultrasound, Near-Infrared Spectroscopy And Optical Coherence Tomography Imaging Study

Published: 13-12-2017
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Primary objective- To evaluate the effect of LDL-C lowering by means of the PCSK9 inhibitor alirocumab as compared with placebo on the change in percent atheroma volume (PAV) in non-infarct-related coronary arteries of patients who present with…

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

## Summary

### ID

NL-OMON50428

**Source**
ToetsingOnline

**Brief title**
PACMAN AMI

### Condition

- Coronary artery disorders

**Synonym**
Coronary Atherosclerosis; Cardiovascular disease

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Insel Gruppe AG - Inselspital
**Source(s) of monetary or material Support:** Inselspital,Regeneron Pharmaceuticals

## Intervention

**Keyword:** AliroCuMab, Coronary Atherosclerosis, LDL-cholesterol, PCSK9 Antibody

## Outcome measures

### Primary outcome

- Change in percent atheroma volume (PAV)

### Secondary outcome

- Change in lipid core burden index (defined by NIRS), macrophage accumulation,

and fibrous cap thickness of coronary plaques (defined by OCT)

- Change in lipid levels (cholesterol, LDL-C, HDL-C, Lp(a), triglycerides,

non-HDL-C, Apo B, Apo A-1, ratio Apo B/Apo A-1, Apo C-III), inflammatory

biomarkers (hs-CRP, TNFa, IL-1b, IL-6, MPO, cystatine, SIRT1, SIRT6) and other

selected biomarkers (hs-troponin T, NT-pro-BNP)

Safety objective

- Amount of adverse events

# Study description

### Background summary

Coronary artery disease (CAD) is the most frequent cause of mortality in the industrialized world. Hypercholesterolemia is a major risk factor for the development and progression of CAD. HMG-CoA reductase inhibitors (statins) lower plasma levels of low-density lipoprotein cholesterol (LDL-C), and they reduce cardiovascular mortality in proportion to the magnitude of LDL-C lowering. While statins currently represent the first-line, gold-standard therapy for primary and secondary prevention of cardiovascular morbidity and mortality, nearly 50% of patients in Europe and Canada treated with statins do not achieve their target levels of LDL-C or cannot tolerate effective statin doses; subsequently, substantial LDL-associated residual risk remains. Therefore, there has been increasing interest for additional pharmacologic strategies to effectively lower cholesterol and to further reduce cardiovascular events.

## Study objective

Primary objective
- To evaluate the effect of LDL-C lowering by means of the PCSK9 inhibitor alirocumab as compared with placebo on the change in percent atheroma volume (PAV) in non-infarct-related coronary arteries of patients who present with acute myocardial infarction, undergo percutaneous coronary intervention (PCI) in the infarct-related artery, and receive guideline-recommended high-intensity statin therapy.

Secondary objectives
- To evaluate the effect of the PCSK9 inhibitor alirocumab on the change in lipid core burden index (defined by NIRS), macrophage accumulation, and fibrous cap thickness of coronary plaques (defined by OCT) as compared with placebo in the non-infarct-related coronary arteries.
- To assess the effect of alirocumab on change in lipid levels (cholesterol, LDL-C, HDL-C, Lp(a), triglycerides, non-HDL-C, Apo B, Apo A-1, ratio Apo B/Apo A-1, Apo C-III), inflammatory biomarkers (hs-CRP, TNFa, IL-1b, IL-6, MPO, cystatine, SIRT1, SIRT6) and other selected biomarkers (hs-troponin T, NT-pro-BNP) and explore possible associations with changes in coronary plaque characteristics.

Safety objective
To evaluate adverse events in patients treated with alirocumab.

## Study design

This is a prospective, randomized, superiority, double-blind (assessor and patients blinded to treatment), placebo-controlled, parallel-group, multi-center study to evaluate the effect of alirocumab on coronary atherosclerotic plaque burden and composition as assessed by multi-modality intracoronary imaging at baseline and following 52 weeks of treatment in

patients presenting with acute myocardial infarction undergoing PCI. The primary endpoint will be assessed at 52 weeks post randomization (or as soon as possible, when the COVID-19 restrictions allow study visits).

### Intervention

At the start of the study and after 1 year IVUS, NIRS and OCT imaging will be performed in 2 non-infarct related coronary arteries. At 2, 4 and 24 weeks, a visit to the Erasmus MC will be performed, and at 8, 12, 36, and 48 weeks telephone calls will be performed. During the visits, the patient will be trained for self-administration of the medication. By telephone calls performing by the investigational team, potential adverse events will be registered and regularly administration of the medication will be ensured. At 52 weeks (or as soon as possible, when the COVID-19 restrictions allow study visits), a final visit will be performed during which i.e. intracoronary imaging will be performed.

### Study burden and risks

The investigational product is generally well-tolerated by healthy study subjects and patients with increased cholesterol levels in the blood. In 1% to 10% of the subjects, the following adverse events took place:
* injection site reaction (redness, itch, swelling/sensitivity)
* cough, cavity inflammation, bronchial inflammations
* myalgia
* itch
* diarrhea

In rare cases (<0.5%) the imaging techniques can damage the coronary arteries (rift, blood clot formation) that may needs to be treated with an additional stent.

## 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

- Male or female, age *18 years at screening
- Acute myocardial infarction: acute ST-segment elevation myocardial infarction (STEMI) with pain onset within *24h, or non-ST segment elevation myocardial infarction (NSTEMI), with at least one coronary segment (culprit lesion) requiring PCI
- LDL-C *70 mg/dL (*1.8 mmol/L) assessed prior to, or during PCI in patients who have been receiving any stable statin regimen within * 4 weeks prior to enrollment; OR LDL-C *125 mg/dL (*3.2 mmol/L) in patients who are statin-naïve or have not been on stable statin regimen for * 4 weeks prior to enrollment
- At least two major native coronary arteries (*target vessels*) each meeting the following criteria for intracoronary imaging immediately following the qualifying PCI procedure:
- Angiographic evidence of <50% reduction in lumen diameter by angiographic visual estimation
- Target vessel deemed to be accessible to imaging catheters and suitable for intracoronary imaging in the proximal (50mm) segment (*target segment*)
- Target vessel may not be a bypass (saphenous vein or arterial) graft or a bypassed native vessel
- Target vessel must not have undergone previous PCI within the target segment
- Target vessel is not candidate for intervention at the time of qualifying PCI or over the following 6 months in the judgment of the Investigator
- Hemodynamic stability allowing the repetitive administration of nitroglycerine
- Ability to understand the requirements of the study and to provide informed consent

- Willingness to undergo follow-up intracoronary imaging

## Exclusion criteria

- Left-main disease, defined as *50% reduction in lumen diameter of the left main coronary artery by angiographic visual estimation
- Three-vessel disease, defined as *70% reduction in lumen diameter of three major epicardial coronary arteries by angiographic visual estimation or in major branches of one or more of these arteries, irrespective of the localization (proximal 50mm or more distal localization) of the obstructive lesions
- History of coronary artery bypass surgery
- TIMI flow <2 of the infarct-related artery after PCI
- Unstable clinical status (hemodynamic or electrical instability)
- Significant coronary calcification or tortuosity deemed to preclude IVUS, NIRS and OCT evaluation
- Uncontrolled cardiac arrhythmia, defined as recurrent and symptomatic ventricular tachycardia or atrial fibrillation with rapid ventricular response not controlled by medications in the past 3 months prior to screening
- Severe renal dysfunction, defined by estimated glomerular filtration rate <30 ml/min/1.73m2
- Active liver disease or hepatic dysfunction;
- Known intolerance to rosuvastatin OR
Known statin intolerance defined by the following criteria: inability to tolerate at least 2 different statins (one statin at the lowest starting average daily dose and the other statin at any dose); intolerance associated with confirmed, intolerable statin-related adverse effect(s) or significant biomarker abnormalities; symptom or biomarker changes resolution or significant improvement upon dose decrease or discontinuation; and symptoms or biomarker changes not attributable to established predispositions such as drug-drug interactions and recognized conditions increasing the risk of statin intolerance
- Known allergy to contrast medium, heparin, aspirin, ticagrelor or prasugrel
- Known sensitivity to any substances to be administered, including known statin intolerance
- Patients who previously received alirocumab or other PCSK9 inhibitor
- Patient who received cholesterol ester transfer protein inhibitors in the past 12 months prior to screening
- Treatment with systemic steroids or systemic cyclosporine in the past 3 months
- Known active infection or major hematologic, metabolic, or endocrine dysfunction in the judgment of the Investigator
- Planned surgery within 12 months
- Patients who will not be available for study-required visits in the judgment of the Investigator
- Current enrollment in another investigational device or drug study
- History of cancer within the past 5 years, except for adequately treated

basal cell skin cancer, squamous cell skin cancer, or in situ cervical cancer
- Estimated life expectancy less than 1 year
- Female of childbearing potential (age <50 years and last menstruation within the last 12 months), who did not undergo tubal ligation, ovariectomy or hysterectomy

# Study design

## Design

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| 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

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 04-07-2018 |
| Enrollment: | 50 |
| Type: | Actual |

## Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Praluent |
| Generic name: | Alirocumab |
| Registration: | Yes - NL outside intended use |

# Ethics review

Approved WMO

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| Date: | 13-12-2017 |

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| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 02-01-2018 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 20-12-2018 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 03-01-2019 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 30-10-2019 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 09-12-2019 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 10-04-2020 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 21-04-2020 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

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| Approved WMO Date: | 29-05-2020 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 20-07-2020 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (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 | EUCTR2017-001502-15-NL |
| ClinicalTrials.gov | NCT03067844 |
| CCMO | NL61713.078.17 |