Kosteneffectiviteit van een op het CYP2C19 genotype gebaseerde behandeling met plaatjesremmende geneesmiddelen bij patiënten met een hartinfarct die gedotterd zijn.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24886

Source
Nationaal Trial Register

Brief title
POPular Genetics

Health condition

Myocardial infarction, Pharmacogenetics, antiplatelet drugs, cost-effectiveness, PCI

Sponsors and support

Primary sponsor: St. Antonius Hospital
Koekoekslaan 1
3435 CM Nieuwegein
The Netherlands
Source(s) of monetary or material Support: ZonMw

Intervention

Outcome measures

Primary outcome

The primary efficacy endpoint is the number of patients who either died, developed a recurrent myocardial infarction (MI), underwent urgent target vessel revascularisation (TVR), developed definite stent thrombosis or stroke at 30 days and at one year after PCI.

The primary safety endpoint is the number of patients with non-CABG-related major bleeding at one year after PCI.

The primary endpoints in terms of pharmacoeconomics are quality of life, direct medical costs e.g. costs for blood transfusions, drugs, hospitalization and non-medical costs e.g. costs incurred due to sickness absence.

Secondary outcome

Secondary efficacy endpoints are the number of patients who either died, died from cardiovascular death, from cerebrovascular death, developed recurrent MI, definite stent thrombosis, probable stent thrombosis, possible stent thrombosis, underwent urgent target vessel revascularisation (TVR), developed stroke or the number op patients with combinations of these endpoints at 30 days and at one year after PCI.

Secondary safety endpoints are the number of patients with (non-)CABG-related major bleeding, major bleeding, minor bleeding, life threatening bleeding, fatal bleeding, intracranial bleeding, bleed requiring transfusion or the number of patients with combinations of these endpoints at at one year after PCI.

A secondary endpoint is the number of patients in whom the antiplatelet drug is prematurely discontinued or switched to another drug.

A tertiary study parameter is the number of patients with CYP2C19 and other genetic variants.

Study description

Background summary

Rationale:

Clopidogrel is crucial as antiplatelet treatment in patients undergoing percutaneous coronary intervention (PCI) with stent implantation and during one year after PCI, to prevent atherothrombotic complications. Clopidogrel is converted into its active metabolite by CYP2C19. Carriers of the non functional CYP2C19*2 and *3 alleles have an impaired CYP2C19 capacity. Clopidogrel is less effective in CYP2C19*2 and *3 carriers. For these subjects prasugrel is an alternative.

Objective:

To assess the efficacy, safety and cost-effectiveness of the CYP2C19 genotype guided antiplatelet treatment strategy, using clopidogrel or prasugrel.

Study design:

Randomized, open label, multicenter study.

Study population:

2500 ST-segment elevation myocardial infarction (STEMI) patients undergoing immediate PCI with stent implantation. All patients will receive an oral loading dose of clopidogrel of 600 mg in the ambulance, while being transported to the intervention center.

Intervention:

The intervention group will be genotyped for the CYP2C19*2 and *3 alleles within 24 hours after PCI. Carriers will receive prasugrel at a dosage of 10 mg once daily starting on the first day after the intervention for one year. Patients older than 75 years or a body weight of less than 60 kg will receive prasugrel at a dosage of 5 mg once daily. Non-carriers will be treated with clopidogrel at a dosage of 75 mg once daily from the first day and continued for one year after PCI. The control group receives clopidogrel at the same dosage as the CYP2C19*2 or *3 non-carriers of the intervention group. The follow-up duration will be one year.

Main study parameters/endpoints:

Combined endpoint of death, myocardial infarction, urgent target vessel revascularisation, stroke, stent thrombosis; bleedings; health-care resource use; quality of life assessed by the EuroQol 5D and SF36 questionnaires (and QALY's estimated based on these questionnaires).

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

The burden for patients participating in the study is that patients will be contacted monthly to fill out a questionnaire and will be requested three times during follow up to fill out a quality of life questionnaire. In the intervention group patients who are more likely to have a poor response to clopidogrel, based on their genotype will receive prasugrel. The efficacy of prasugrel in preventing major cardiovascular events is not genotype dependent. In de TRITON TIMI 38 study prasugrel was associated with a higher risk of developing bleeding complications. However, in a post hoc analysis in STEMI patients, bleedings in prasugrel and clopidogrel treated patients were similar.

Study objective

It is hypothesized that the CYP2C19 guided antiplatelet strategy will improve treatment of patients by maximizing the efficacy in preventing serious adverse cardiac events and minimizing the risk of bleeding.

Study design

Timepoints are 30 days and 12 months following PCI.

Intervention

The intervention being investigated, includes CYP2C19 genotyping, followed by a genotype guided antiplatelet treatment strategy with either prasugrel or clopidogrel on top of acetylsalicylic acid.

Patients randomized to the intervention group who carry a non functional allele will receive prasugrel while those without such an allele receive clopidogrel.

Patients in the control group will all be treated with clopidogrel in combination with acetylsalicylic acid. Antiplatelet treatment is continued for one year after PCI.

Contacts

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Eligibility criteria

Inclusion criteria

1. More than 21 years of age with symptoms of acute myocardial infarction of more than 30 minutes but less than 12 hours;

2. Performed primary PCI with stenting for STEMI.

Exclusion criteria

1. Unable to give informed consent or have a life expectancy of less than one year;

2. Active malignancy with increase in bleeding risk, in the investigators' opinion;

3. Women who are known to be pregnant or who have given birth within the past 90 days or who are breastfeeding;

4. Having received thrombolytic therapy within the previous 24 hours or oral anticoagulants during the previous 7 days;

5. Severe renal function impairment needing dialysis;

6. Confirmed or persistent severe hypertension (Systolic Blood Pressure (SBP) > 180 mmHg and/or Diastolic Blood Pressure (DBP) >110 mmHg) at randomization;

7. Contraindication to anticoagulation or at increased bleeding risk, at the investigators' opinion;

8. History of stroke or Transient Ischemic Attack (TIA);

9. Cardiogenic shock (SBP <80mmHg for >30 mins) or needing Intra-Aortic Balloon Pump (IABP);

10. History of major surgery, severe trauma, fracture or organ biopsy within 90 days prior to randomisation;

11. Clinically significant out of range values for platelet count or haemoglobin at screening, in the investigators' opinion.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-04-2011
Enrollment:	2500
Type:	Anticipated

Ethics review

Positive opinion

Date:	09-08-2011

Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 47500
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL2872
NTR-old	NTR3017
CCMO	NL35106.100.11
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON47500

Study results

Summary results
N/A