Ticagrelor or prasugrel versus clopidogrel in elderly patients with an acute coronary syndrome and a high bleeding risk: optimization of antiplatelet treatment in high-risk elderly

Published: 06-06-2013
Last updated: 25-04-2024

To assess the safety, efficacy and net clinical benefit of clopidogrel versus the new antiplatelet drugs i.e. ticagrelor and prasugrel in patients older than 70 years.

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

Summary

ID

NL-OMON47836

Source
ToetsingOnline

Brief title
POPular AGE

Condition

- Coronary artery disorders

Synonym
coronary artery disease

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Bleeding, Elderly, NSTEMI, UA

Outcome measures

Primary outcome

The first primary endpoint is the occurrence of any bleeding episode at 1 year after randomisation and second primary endpoint is the net clinical benefit at 1 year after randomisation.

Secondary outcome

Secondary safety endpoints are bleeding events either CABG related or non-CABG related, according to TIMI (10), PLATO (2), GUSTO (11), and BARC (12) classification and composite of bleeding events within each classification at 30 days and 1 year after randomisation.

Secondary net clinical benefit endpoints are composites of death from any cause other than vascular or bleeding causes, death from vascular causes, death from bleeding causes (= fatal bleeding), MI (13), stroke, UA, TIA, other arterial thrombosis, PLATO major and minor bleeding at 30 days and 1 year after randomisation.

Secondary efficacy endpoints are death from any cause, death from cardiovascular causes, death from cerebrovascular causes MI (13), stent

thrombosis as defined by ARC (14), UR, rehospitalization for ACS, stroke, TIA or composites of these endpoints at 30 days and 1 year after randomisation.

Secondary endpoints in terms of quality of life are measurements obtained with EuroQol 5D and SF36 questionnaires and frailty by using the Groningen Frailty Indicator at one month and one year.

A secondary endpoint is the number of patients in whom the antiplatelet drug is prematurely discontinued or switched to another drug leading to a cross-over.

Tertiary endpoints would be the evaluation of genetic variants on the response to clopidogrel and prasugrel or ticagrelor in terms of efficacy and safety in a candidate gene approach, Genome Wide Association Study or (next generation) sequencing.

Tertiary endpoint would be the evaluation of frailty according to the Groningen Frailty indicator (GFI * 4 would indicate a frail patient).

Study description

Background summary

Dual antiplatelet therapy is crucial in patients with an acute coronary syndrome (ACS) to prevent artherothrombotic events. The recent guideline of the European Society of Cardiology (ESC) based on PLATO en TRITON studies, recommends ticagrelor or prasugrel, which also give more bleeding complications. However, the representation of the elderly in clinical trials is low and in a subgroup analysis of patients 75 years of age statistical

significance was not reached. The ESC guideline advises the use of the CRUSADE risk score for risk stratification. However, based on the currently available data it is not clear which antiplatelet treatment should be initiated in those patients with a high bleeding risk, who also appear to have the highest atherothrombotic risk.

Study objective

To assess the safety, efficacy and net clinical benefit of clopidogrel versus the new antiplatelet drugs i.e. ticagrelor and prasugrel in patients older than 70 years.

Study design

Randomized, controlled, open label, multicenter study

Intervention

Patients randomized to clopidogrel will receive 75 mg daily for one year. Those randomized to the new antiplatelet drugs will be treated with either ticagrelor 90 mg twice daily or prasugrel 10 mg daily (prasugrel 5 mg in patients *75 years or weight * 60 kg), according to hospital*s local standards. The follow-up duration will be 1 year

Study burden and risks

The burden for patients participating in the study is that patients will be contacted twice during the study; 3 months and 12 months after initial diagnosis to fill out a questionnaire, to get information regarding the use of antiplatelet drugs, changes in prescribed drugs and medical condition. At one month and 12 months patients will also be requested to fill out EuroQol 5D and SF36 questionnaires to asses quality of life and the Groningen Frailty Indicator to assess frailty. The patient may be contacted by telephone if this is necessary to complete follow-up data.

Contacts

Public
Sint Antonius Ziekenhuis

Koekoekslaan 1
Nieuwegein 3430 EM
NL
Scientific

Sint Antonius Ziekenhuis

Koekoekslaan 1
Nieuwegein 3430 EM
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1) At least 70 years of age.
2) Hospitalization for NSTEMI or unstable angina according to the criteria of the ESC guideline.

Exclusion criteria

1) Contraindication to P2Y12 inhibitors i.e. clopidogrel, prasugrel or ticagrelor:
- Hypersensitivity to the active substance or to any of the excipients.
- History of intracranial bleeding or active pathological bleeding such as peptic ulcer or intracranial haemorrhage.
- Moderate to severe (Child-Pugh C) hepatic dysfunction.
- Use of strong CYP3A4 inhibitors (i.e. itraconazole, voriconazole, ketoconazole, erytromycin, clarithromycin, rifampicin, nefozodone, lopinavir, carbamazepine, fenytoïne, fenobarbital, ritonavir en atazanavir).
2) Unable or unwilling to give informed consent or have a life expectancy of less than one year.
3) Having received thrombolytic therapy within the previous 24 hours.
4) Severe renal function impairment needing dialysis.
5) Confirmed or persistent severe hypertension (Systolic Blood Pressure (SBP) > 180 mmHg and/or Diastolic Blood Pressure (DBP) >110 mmHg) at randomization.
6) At increased bleeding risk, at the investigator*s opinion, i.e. because of malignancy.

7) Cardiogenic shock (SBP * 80mmHg for >30 mins) or Intra-Aortic Balloon Pump (IABP) at the time of screening.
8) History of major surgery, severe trauma, fracture or organ biopsy within 90 days prior to randomisation.
9) Clinically significant out of range values for platelet count or haemoglobin at screening, in the investigator*s opinion.
10) ACS under dual antiplatelet therapy, e.g. aspirin with a P2Y12 inhibitor; clopidogrel, prasugrel, ticagrelor.
11) Patients with a known CYP2C19 genotype at the time of randomization.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-07-2013
Enrollment:	1000
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Brilique
Generic name:	Ticagrelor
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Efient

Generic name:	Prasugrel
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Plavix
Generic name:	Clopidogrel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	06-06-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-07-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-11-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-03-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-03-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-06-2014

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-12-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-06-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-07-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-01-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-01-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-07-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-01-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	28-02-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-04-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-02-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-04-2019
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	EUCTR2013-001403-37-NL
CCMO	NL44128.100.13
Other	TC = 3991