GLOBAL LEADERS: Comparative effectiveness of 1 month of ticagrelor plus aspirin followed by ticagrelor monotherapy versus a current-day intensive dual antiplatelet therapy in all-comers patients undergoing percutaneous coronary intervention with bivalirudin and BioMatrix family drug-eluting stent use.

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

Summary

ID

NL-OMON44752

Source
ToetsingOnline

Brief title
GLOBAL LEADERS

Condition

- Coronary artery disorders

Synonym
angina pectoris, coronair artery disease

Research involving
Human

Sponsors and support

Primary sponsor: ECRI / Cardialysis
Source(s) of monetary or material Support: sponsor ECRI

Intervention

Keyword: acs, dual antiplatelet therapy, instable angina pectoris, PCI

Outcome measures

Primary outcome

The composite of all-cause mortality or non-fatal new Q-wave MI up to 2 years

post randomisation.

Secondary outcome

The composite of investigator-reported BARC3 or BARC5 bleeding according to

BARC definitions up to 2 years post randomisation.

Study description

Background summary

Atherosclerosis and coronary artery thrombosis are a major cause of premature death worldwide, and are
an important source of loss of disability-adjusted life years.1,2 ,3 Treatment goals for patients with coronary
artery disease (CAD) and ACS after PCI may improve the survival and a reduction in the risk of myocardial infarction (MI)

and symptoms of coronary disease

Study objective

To determine in all-comers patients undergoing PCI under standardised treatment (including the BioMatrix family of drug-eluting stents and bivalirudin), whether treatment with 1 month of ticagrelor and aspirin followed by 23 months of ticagrelor monotherapy is superior with respect to the composite of all-cause mortality or non-fatal new Q-wave MI compared to treatment with 12 months of standard dual anti platelet therapy (DAPT) followed by aspirin monotherapy In some participating centers patients are approached with the request to determine using the reactivity of platelets during the 3, 6, 12 and/or 18 month outpatient monitoring decrease in a blood sample

Study design

Investigator-initiated, prospective randomised, multi-centre, multi-national, openlabel
trial to be conducted in approximately 60-80 interventional cardiology centres in Europe, North America, South America and Asia-Pacific. Patients will be randomised at a 1:1 ratio to study or reference treatment strategy. Randomisation will occur at the time of the index procedure prior to PCI. Subjects will be stratified according to centre and according to the clinical presentation (Stable Coronary Artery Disease (CAD) vs. Acute Coronary Syndrome (ACS)).
All patients will be followed for a period of 2 years

May 2017:
A small sub-study of Global Leaders (GLASSY) will start mid-May

Objectives and Ethical considerations of the substudy:
The objectives of this substudy are: to assess the impact of CEC-adjudication process on the results of the study; to quantify the added value of CEC adjudication process for endpoint reporting by evaluating the concordance between IR-reported and CEC-adjudicated events; to gather mechanistic information to aid in the interpretation of the effect of the experimental treatment in the parent trial and to identify specific subgroups of patients that could particularly benefit from the experimental therapy in terms of ischemic and bleeding events.
The substudy is simply based on an independent assessment of clinical events using source documentation of the main study. There will be no additional risks or burden for the patients. Participants will also not derive immediate benefit from the results of this study; however, its findings will help to improve the quality of clinical research with consequent advantage for the entire community including patients and physicians. So far, indeed, the impact of CEC on the quality of trial results has never been assessed. GLASSY represents the first

systematic attempt to establish whether the CEC-adjudication process is essential or rather dispensable for the conduct of large randomized clinical trials. Additional potential benefits are mainly related to a better understanding of the results of the main trial through the categorization of the type of mortality, MI and bleeding events.

Intervention

Experimental treatment strategy
All patients in the treatment group will receive acetylsalicylic acid (ASA) and ticagrelor for 1 month followed by 23 months of ticagrelor monotherapy.
Reference treatment strategy
ACS patients incl. unstable angina (UA) patients: ASA and ticagrelor for 12 months followed by 12 months of ASA monotherapy.
Stable CAD patients*: ASA and clopidogrel for 12 months followed by 12 months of ASA monotherapy.
* Biomarker negative, no clinical signs and/or symptoms of ongoing myocardial ischemia.
All patients will receive a BioMatrix family drug-eluting stent during the index PCI.
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All patients will receive bivalirudin during the index procedure in countries where it is available.
Note: After 2 years, the medical treatment is left to the discretion of the physician

In a subgroup of patients (n = 2455), the platelet reactivity will be analysed at 3,6,11 and/or 18 months after the index procedure.

Study burden and risks

Risks PCI treatment:
Risks are comparable to the standard PCI treatment.

Side effects to study medication:
bleedings
allergy to study medication and shortness of breath
less protection in anti trombotic treatment in the treatment group

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

Real world, all comer patients;1. Age *18 years;;2. Presence of one or more coronary artery stenoses of 50% or more in a native coronary artery or in a saphenous venous or arterial bypass conduit suitable for coronary stent implantation in a vessel with a reference vessel diameter of at least 2.25 mm (no limitation on the number of treated lesions, and vessels, and lesion length).;3. Able to provide informed consent and willing to participate in 2 year follow-up period.

Exclusion criteria

1. Known intolerance to aspirin, P2Y12 inhibitors, bivalirudin, stainless steel or biolimus;;2. Known intake of a strong CYP3A4 inhibitor (e.g., ketoconazole, clarithromycin, nefazodone, ritonavir, and atazanavir), as co-administration may lead to a substantial increase in exposure to ticagrelor;;3. Known moderate to severe hepatic impairment (alanine-aminotransferase * 3 x ULN);;4. Planned surgery, including CABG as a staged procedure

(hybrid) within 12 months of the index procedure, unless dual antiplatelet therapy is maintained throughout the peri-surgical period;;5. Need for chronic oral anti-coagulation therapy;;6. Active major bleeding or major surgery within the last 30 days;;7. Known history of intracranial haemorrhagic stroke or intra-cranial aneurysm;;8. Known stroke (any type) within the last 30 days;;9. Known pregnancy at time of randomisation;;10. Female who is breastfeeding at the time of randomisation.;11. Currently participating in another trial and not yet at its primary endpoint.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-07-2013
Enrollment:	1800
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	aspro clear
Generic name:	ascetylsalicylacid
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	brilique
Generic name:	ticagrelor

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	plavi
Generic name:	clopidogrel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	04-06-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-06-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-12-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-01-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-03-2014
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-05-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-06-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-09-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-09-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-05-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-05-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-08-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	23-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-06-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-06-2017
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	EUCTR2012-003515-58-NL
CCMO	NL43637.078.13