A Randomized, Double-Blind, Placebo Controlled, Parallel Group, Multinational Trial, to Assess the Prevention of Thrombotic Events with Ticagrelor Compared to Placebo on a Background of Acetyl Salicylic Acid (ASA) Therapy in Patients with History of Myocardial Infarction

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

Summary

ID

NL-OMON39760

Source
ToetsingOnline

Brief title
PEGASUS - TIMI 54

Condition

- Coronary artery disorders

Synonym
atherothrombotic events, obstruction of a coronary artery

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: atherothrombotic events, long term treatment, P2Y12 ADP receptor antagonist, platelet inhibition

Outcome measures

Primary outcome

The primary efficacy variable is time to first occurrence of any event after

randomization from

the composite of cardiovascular death, non-fatal MI, or non-fatal stroke.

Secondary outcome

(i) Time to occurrence of cardiovascular death after randomization

(ii) Time to occurrence of all-cause mortality after randomization

Study description

Background summary

Atherothrombosis is associated with the main causes of mortality on a worldwide scale. Its prevalence will further increase in the future. Moreover, after the initial manifestation of atherothrombosis, patients remain at high risk for serious complications for years after their initial event. It has been proven that dual-antiplatelet therapy is beneficial compared to treatment with ASA alone for patients with acute coronary syndrome (ACS) for up to a year of therapy. Ticagrelor is a reversible, potent, oral platelet aggregation inhibitor, which works through inhibition of the adenosine diphosphate (ADP)

P2Y12 receptor. In the phase III PLATO trial, patients presenting with an acute coronary syndrome were randomized to ticagrelor (180 mg loading dose followed by 90 mg twice daily) or clopidogrel (300-600 mg loading dose followed by 75 mg daily) for up to 12 months. The trial demonstrated the superiority of ticagrelor in the prevention of both fatal and non-fatal cardiovascular events with no significant increase in major bleeding. Currently, there are no data to support dual therapy beyond 12 months. However, post hoc analysis suggests that dual antiplatelet therapy would likely provide clinical benefit for high risk population with prior myocardial infarction. .

Study objective

The current study is being conducted to determine whether long-term dual-antiplatelet therapy with ticagrelor in combination with ASA (recommended daily dose 75-100 mg) is beneficial in patients with history of MI (1-3 years ago) and additional risk factors for atherothrombosis compared with monotherapy with ASA alone.

Study design

A Randomized, Double-Blind, Placebo Controlled, Parallel Group, Phase III Trial.

Intervention

Patients will be randomised to 90 mg or 60 mg of ticagrelor orally bd or placebo for a minimum treatment duration of 12 months.

Study burden and risks

The patient is asked to visit the hospital for at least 6 times and maximum 11 times. Blood samples will be taken in this study. The total volume of blood that will be collected is 81 ml. The patient will be asked to fill out a short questionnaire on his/her quality of life at maximum 5 visits. The patient will undergo a physical examination at 2 visits. The patient will have an electrocardiogram at 2 visits. Woman of child-bearing potential have to provide a urine sample to test for pregnancy.

The study medication may cause some side effects. The taking of a blood sample may cause some discomfort and there is the possibility of bruising.

Contacts

Public

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Men and women >50 years of age.
- Person who had a heart attack within 1-3 years ago and at least one additional risk factor:
* Age *65 years
* Diabetes mellitus requiring medication
*Documented history of a second prior presumed spontaneous MI (>1 year ago)
*Documented history of angiographic evidence of multivessel coronary artery disease (CAD)
*Chronic, non-end stage renal dysfunction
- Treated with ASA,
- Females of child-bearing potential must have a negative urine pregnancy test at enrollment and
must be willing to use a medically accepted method of contraception that is considered reliable in the judgment of the investigator.
- Written informed consent prior to any study specific procedures.

Exclusion criteria

- Planned use of ADP receptor blockers (eg, clopidogrel, ticlopidine, prasugrel), dipyridamole, or cilostazol
- Planned coronary, cerebrovascular, or peripheral arterial revascularization
- Concomitant therapy with strong cytochrome P450 3A (CYP3A) inhibitors, CYP3A substrates with narrow therapeutic indices, or strong CYP3A inducers.
- Need for chronic oral anticoagulant therapy or chronic low-molecular-weight heparin
- Patients with known bleeding diathesis or coagulation disorder
- Patients with:
*A history of previous intracranial bleed at any time
*A central nervous system tumour or intracranial vascular abnormality at any time
*Intracranial or spinal cord surgery within 5 years, or
*Gastrointestinal (GI) bleed within the past 6 months, or major surgery within 30 days
- History of ischemic stroke at any time
- Patients considered to be at risk of bradycardic events
- Coronary-artery bypass grafting in the past 5 years, unless the patient has experienced a spontaneous MI subsequent to the bypass surgery
- Known severe liver disease
- Renal failure requiring dialysis
- Pregnancy or lactation
- Life expectancy < 1 year
- Participation in previous study with ticagrelor if treated with ticagrelor.

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:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-02-2011
Enrollment:	700
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Brilique
Generic name:	ticagrelor

Ethics review

Approved WMO

Date:	26-10-2010
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	06-12-2010
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	27-12-2010
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	07-01-2011
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	24-01-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	18-02-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	15-04-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	20-04-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	31-05-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	19-07-2011
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	21-07-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	19-12-2011
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	16-01-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	25-01-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	24-04-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	14-05-2012
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	14-06-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	25-06-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	12-07-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	24-07-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	10-04-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	18-04-2013
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	08-11-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	06-12-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	07-02-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	10-02-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	07-04-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	22-05-2014
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	05-09-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	10-09-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	20-05-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2009-017242-30-NL
ClinicalTrials.gov	NCT01225562
CCMO	NL32010.098.10