Multicenter, randomized, placebo controlled, double-blind, parallel group, dose-finding Phase 2 study to evaluate the efficacy and safety of BAY 2433334 in patients following an acute myocardial infarction

Published: 17-12-2019
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Primary Objective:- to evaluate whether the oral FXIa inhibitor BAY 2433334 leads to a lower incidence of CV death, MI, stroke and stent thrombosis following an acute myocardial infarction when compared to a placebo- to evaluate whether the...

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

Summary

ID

NL-OMON54974

Source
ToetsingOnline

Brief title
PACIFIC-AMI

Condition

- Myocardial disorders

Synonym
Acute Coronary Syndrom, Myocardial Infarction

Research involving

Human

Sponsors and support

Primary sponsor: Bayer
Source(s) of monetary or material Support: Bayer AG

Intervention

Keyword: ACS, Anticoagulation, Factor XIa, Myocardial Infarction

Outcome measures

Primary outcome

Primary Efficacy Endpoint: the composite of CV death, MI, stroke and stent

thrombosis

Primary Safety Endpoint: Bleeding Academic Research Consortium (BARC)

definition type 2, 3 and 5

Secondary outcome

Secondary Efficacy Endpoints:

- all cause mortality

- CV death

- MI

- stroke

- stent thrombosis

Secondary Safety Endpoints:

- all bleeding

- BARC bleeding definition type 3, 5

- BARC bleeding definition type 1, 2, 3, 5

Study description

Background summary

This study will explore a dose range of BAY 2433334 in order to determine the dose that is efficacious and safe and that can be used in a Phase 3 study in the same indication. Rivaroxaban in addition to single or dual antiplatelet therapy (acetylsalicylic acid +/- clopidogrel) is the only non-Vitamin K oral anticoagulants (NOAC) approved for secondary prevention of ACS in Europe. In addition, the COMPASS study has also shown the benefit of this combination (rivaroxaban in addition to acetylsalicylic acid) in patients with stable coronary artery disease (CAD)/peripheral artery disease (PAD). The clinical use of antiplatelet therapies together with an anticoagulant in acute coronary syndrome (ACS) is limited due to concerns about bleeding risk. The inhibition of FXIa on top of antiplatelet therapy is expected to not lead to a relevant increase in bleeding and especially major bleeding, while maintaining the efficacy benefit shown for the combination of antiplatelet therapies and rivaroxaban.

Study objective

Primary Objective:
- to evaluate whether the oral FXIa inhibitor BAY 2433334 leads to a lower incidence of CV death, MI, stroke and stent thrombosis following an acute myocardial infarction when compared to a placebo
- to evaluate whether the incidence of bleeding is similar for BAY 2433334 and placebo when treated on top of dual antiplatelet therapy

Study design

Multicenter, randomized, placebo controlled, double-blind, parallel group, dose-finding phase 2 study to evaluate the efficacy and safety of BAY 2433334 in patients following an acute myocardial infarction

Intervention

3 investigational drug arms and 1 placebo arm:
- BAY 2433334 10 mg once daily
- BAY 2433334 20 mg once daily
- BAY 2433334 50 mg once daily
- Placebo once daily

The maximum duration of study participation is planned to be 55 weeks, consisting of:
* Screening Period : * 5 days

* Treatment Period: between 26 and 52 weeks
* Safety Follow-up Period: 14 days

Study burden and risks

Visits;
Visits to the hospital between 4 and 7 times and telephone contact between 4 and 6 times. The number of hospital visits and telephone contact depends on the number of weeks that the study duration for the patient (between 26 and 52 weeks). A visit to the hospital takes approximately 1 hour. There will be 1 visit with a duration of approximately 5 hours (visit 4, week 4).

Measurements:
Vital functions: Pulse rate, No risks, Every visit to the hospital.
Vital functions: Blood pressure, No risk: Possible discomfort around the arm due to the blood pressure cuff, Every visit to the hospital.
Body weight and height: No risks, Visit 1.
Blood tests: Risks: Pain, Bruising, Weakness or dizziness, Infection. Every visit to the hospital.
Electrocardiogram (ECG): Risk: Skin irritation, Visits 1, 2, 6 and 12.

BAY 2433334 may have a therapeutic benefit, but this cannot be guaranteed. Patients have the risk of side effects.

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

1. Participants must be 45 years of age or older, at the time of signing the informed consent
2. Acute myocardial infarction (excluding MI associated with PCI or CABG revascularization procedures) with:
a.clinical symptoms of acute myocardial infarction AND
b.elevated biomarkers of myocardial necrosis (creatine kinase-muscle and brain isoenzyme [CK-MB] or cardiac troponins) AND
c.at least one of the following risk factors need to be fulfilled:
i. Age * 65 years
ii.Prior MI (before the index AMI event)
iii.Prior peripheral arterial disease
iv.Diabetes Mellitus
v.Prior coronary artery bypass grafting (CABG)
AND
d. initial angiography and revascularization procedures, either PCI or CABG, as treatment for the index event performed before randomization. (Note: a planned, staged PCI procedure can be performed after randomization)
3. Plan for dual antiplatelet therapy (ASA + P2Y12 inhibitor) after hospital discharge for the index AMI
4. Randomization during hospitalization for the index AMI event and latest within 5 days of hospital admission
5. Capable of giving signed informed consent which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol. Written informed consent has to be signed before any study-specific procedure.

Exclusion criteria

1. Hemodynamically significant ventricular arrhythmias or cardiogenic shock at time of randomization
2. Active bleeding; known bleeding disorder, history of major bleeding

(intracranial, retroperitoneal, intraocular) or clinically significant gastrointestinal bleeding within last 6 months of randomization
3. Planned use or requirement of full dose and long term anticoagulation therapy during study conduct

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-08-2020
Enrollment:	196
Type:	Actual

Ethics review

Approved WMO Date:	17-12-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-07-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	18-11-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-12-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-01-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-09-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-09-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-12-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2019-003244-79-NL
CCMO	NL72151.091.19

Study results