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

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Embolism and thrombosis
Study type	Interventional

Summary

ID

NL-OMON55288

Source
ToetsingOnline

Brief title
PACIFIC-STROKE

Condition

- Embolism and thrombosis

Synonym
ischemic stroke, stroke

Research involving

Human

Sponsors and support

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

Intervention

Keyword: FXIa inhibitor, stroke

Outcome measures

Primary outcome

Composite of symptomatic ischemic stroke and covert brain infarcts detected by MRI.

Composite of International Society on Thrombosis and Hemostasis (ISTH) major bleeding and clinically relevant non-major (CRNM) bleeding

Secondary outcome

Composite of symptomatic ischemic stroke and covert brain infarcts detected by MRI, CV death, myocardial infarction and systemic embolism

Incidence of covert brain infarcts detected by MRI

Hazard ratio of symptomatic ischemic stroke

Hazard ratio of symptomatic ischemic stroke, CV death, myocardial infarction

Hazard ratio of symptomatic ischemic and hemorrhagic stroke

Hazard ratio of disabling stroke

Hazard ratio of all-cause mortality

Hazard ratio of all bleeding

Hazard ratio of ISTH major bleeding

Hazard ratio of ISTH CRNM bleeding

Hazard ratio of ISTH minor bleeding

Hazard ratio of Intracerebral hemorrhage (nontraumatic)

Study description

Background summary

Currently, patients with non-cardioembolic ischemic stroke are treated with antiplatelet therapy. No clinical studies have proven the benefit of anticoagulation therapy in patients with non-cardioembolic stroke. However, it has been shown that patients with a stroke have increased levels of FXI and patients with FXI deficiency have a lower risk for stroke. Inhibition of FXIa is expected to lead to a benefit versus placebo regarding secondary prevention of ischemic stroke as well as to not lead to a relevant increase in bleeding and especially major bleeding.

Study objective

The main objective of the study is to explore whether the addition of BAY 2433334 will lead to a dose response in reducing symptomatic strokes and covert brain infarcts and whether this is combined with no relevant increase in bleeding when given on top of antiplatelet therapy. An additional objective is to guide dose selection for Phase 3.

Study design

Multicenter, randomized, placebo-controlled, double-blind, parallel group, dose-finding Phase 2 study to evaluate efficacy and safety of BAY 2433334 in patients following an acute non-cardioembolic ischemic stroke.

Intervention

- BAY 2433334 high dose (oral, tablet, once daily)
- BAY 2433334 medium dose (oral, tablet, once daily)
- BAY 2433334 low dose (oral, tablet, once daily)
- placebo (oral, tablet, once daily)

Study burden and risks

The safety profile of BAY 2433334 is not yet determined. The following safety and risk information is available:
- A risk for bleeding cannot be excluded.

- increases in liver enzymes was shown in animal studies.
- strong CYP3A4 inhibitors and inducers cannot be used in combination with BAY 2433334, as this increases the exposure to BAY 2433334 and leads to prolonged half-life of BAY 2433334.

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. Participant must be 45 years of age and older at the time of signing the informed consent
2. Non-cardioembolic ischemic stroke with
a. persistent signs and symptoms of stroke lasting for * 24 hours OR
b. acute brain infarction documented by computed tomography (CT) or MRI AND
c. with the intention to be treated with antiplatelet therapy during the

study conduct
3. Imaging of brain (CT or MRI) ruling out hemorrhagic stroke or another pathology that could explain symptoms (e.g. brain tumor, abscess, vascular malformation)
4. Severity of index event nearest the time of randomization:
a. Part A: minor stroke (defined as NIHSS * 7) can be enrolled
b. Part B: participants with minor or moderate stroke and NIHSS * 15 can be enrolled. Participants undergoing thrombolysis or endovascular therapy (mechanical thrombectomy) can be enrolled but at the earliest 24 hours after the intervention
5. Randomization within 48 hours after the onset of symptoms of the index event (or after patients were last known to be without symptoms in case of wake-up stroke)
6. Ability to conduct an MRI either before randomization or within 72 hours after randomization

Exclusion criteria

1. Prior ischemic stroke within last 30 days of index event
2. History of atrial fibrillation or suspicion of cardioembolic source of stroke
3. Dysphagia with inability to safely swallow study medication at time of randomization
4. Contraindication to perform brain MRI
5. Part A only: thrombolysis or endovascular therapy (mechanical thrombectomy) performed for index event
7. Active bleeding; known bleeding disorder, history of major bleeding (intracranial, retroperitoneal, intraocular) or clinically significant gastrointestinal bleeding within last 6 months of randomization

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):	06-10-2020
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	15-01-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-05-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2021

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-01-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-01-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2019-003431-33-NL
CCMO	NL72077.018.19

Study results