A multicenter, randomized, open-label, active-controlled, dose-range finding study to assess the pharmacodynamic parameters, safety and tolerability of MAA868 and its effect on thrombogenesis biomarkers compared to apixaban in patients with atrial fibrillation

Published: 09-01-2018
Last updated: 12-04-2024

The primary objective of this study is to evaluate the proportion of patients achieving FXI inhibition * 80% at trough (Day 91) after monthly dosing at 3 dose levels of MAA868.

Ethical review	Not approved
Status	Will not start
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON46376

Source
ToetsingOnline

Brief title
CMAA868A2202

Condition

- Cardiac arrhythmias

Synonym

Atrial fibrillation, Atrial flutter

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: Anticoagulant, Atrial fibrillation, Factor XI, Major bleeding events

Outcome measures

Primary outcome

FXI-inhibition * 80% at trough (Day 91) after having received MAA868 3 times

Secondary outcome

Objective 1:

To evaluate the proportion of patients achieving FXI inhibition * 80% at trough

after the first and second dose (Day 31 and Day 61) at 3 dose levels of MAA868.

Objective 2:

To evaluate the incidence of major bleeding events, clinically relevant

non-major bleeding events and total bleeding with MAA868 relative to apixaban

during the treatment period.

Objective 3:

To assess the effect of MAA868 on D-dimer and other thrombogenesis biomarkers

as indicators of efficacy at Day 31, Day 61 and Day 91 compared to apixaban.

Objective 4:

To evaluate the safety and tolerability of MAA868 compared to apixaban.

Study description

Background summary

Atrium Fibrillation is the most common cardiac arrhythmia, which effects more than 6 million people in Europe and is associated with a 4-5 fold increase in embolic stroke.
Vit K antagonists (e.g. Warfarine) and NOAC's are effective in reducing stroke and systemic embolism, however, bleeding risk continues to be high.
Factor XI holds important roles in both the intrinsic and extrinsic coagulation pathways and in brdiging the initiation and amplification phases of plasmatic hemostasis, yet plays a minor role in hemostasis after vessel injury and is therefore associated with a lower incidence of ischemic stroke, cardiovascular and venous thrombotic events.
This hypothesis is supported by the existence of people with a Factor XI deficiency. These people have reduced risk of developing thrombosis and related complications.

Study objective

The primary objective of this study is to evaluate the proportion of patients achieving FXI inhibition * 80% at trough (Day 91) after monthly dosing at 3 dose levels of MAA868.

Study design

This is a randomized, open-label, blinded endpoint evaluation, active controlled, dose-range finding study. After a screening period of 1 to 2 weeks, patients will be randomized to 1 of 4 treatment groups (low, medium or high dose MAA868 or apixaban) in a 1:1:1:1 ratio and followed during a 90-day treatment period. Randomization will be stratified by country and whether patients are anticoagulant naïve (Yes/No) at screening. Patients will be transitioned to a NOAC and/or other standard of care therapy at the investigator's discretion on Day 91 and followed up to Day 170.

Intervention

- MAA868 180 mg s.c 3x (once monthly)
- MAA868 150 mg s.c. 3x (once monthly)
- MAA868 150 mg s.c. 1x + 120 mg s.c. 2x (once mothly)

- Apixaban 5 mg b.i.d. during 90 days

Study burden and risks

Adverse effects of study medication and study procedures.
Change of anti-coagulation medication.

Physical examination: 9x
Length: 1x
Weight: 3x
Vital functions (RR/Pulse/Bodyteperature): 9x
Triple ECG: 6x
Collection of bloodsamples: 9x
Urine test (dipstick): 9x
Pregnancy test (urine), when applicable: 6x
S.c.administration of MAA868: 3x, when applicable.

Contacts

Public
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL
Scientific
Novartis

Raapopseweg 1
Arnhem 6824 DP
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Male and female patients * 55 and 85 years old
- Body weight between 50 and 130 kg inclusive
- Atrial fibrillation or atrial flutter, as documented by electrocardiography
- CHA2DS2-VASc risk score * 2 for male and female patients. Male patients with CHA2DS2VASc risk score of 1 can be included if anticoagulation therapy is warranted.
- Either anticoagulant-naïve or receiving a stable treatment of a recommended dose of a new oral anticoagulant (NOAC) over the 8 weeks prior to screening.

Exclusion criteria

- History of stroke, transient ischemic attack or systemic embolism.
- History of major bleeding during treatment with an anticoagulant or antiplatelet therapy in the last 12 months.
- History of traumatic or non-traumatic intracranial, intraspinal or intra-ocular bleeding.
- Known bleeding diathesis or any known active bleeding site at screening or baseline.
- Family history of bleeding disorder.
- Known active GI lesions predisposing to bleeding events.
- Myocardial infarction, unstable angina pectoris or coronary artery bypass graft (CABG) surgery within 12 months prior to the screening period.
- Known hemodynamically significant valvular heart disease.
- Uncontrolled hypertension defined as SBP/DBP * 160/100 mmHg at the screening visit.
- Heart failure NYHA class IV in the 3 months prior to the screening visit.
- Dual antiplatelet therapy. Treatment with a P2Y12 inhibitor or low dose aspirin (* 100 mg/d) is allowed but not both.
- Severe renal impairment (creatinine clearance 30 mL/min) at the screening visit.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	40
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Eliquis
Generic name:	apixaban
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	MAA868
Generic name:	MAA868

Ethics review

Approved WMO

Date:	09-01-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	28-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Not approved

Date:	31-05-2018
Application type:	First submission
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	EUCTR2017-002741-29-NL
ClinicalTrials.gov	NCT03398434
CCMO	NL63967.018.17