Protocol CV185030: A Phase 3, Active (Warfarin) Controlled, Randomized, Double-Blind, Parallel-Arm Study to Evaluate Efficacy and Safety of Apixaban In Preventing Stroke and Systemic Embolism in Patients with Nonvalvular Atrial Fibrillation

Published: 22-05-2007
Last updated: 11-05-2024

Primary objective: To determine if apixaban is noninferior to warfarin (INR target range 2.0-3.0) in the combined endpoint of stroke (ischemic or hemorrhagic) and systemic embolism, in subjects with AF and at lease one additional risk factor for...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON35379

Source
ToetsingOnline

Brief title
ARISTOTLE

Condition

- Cardiac arrhythmias

Synonym
atrial fibrillation

Research involving
Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Sponsor/farmaceut

Intervention

Keyword: atrial fibrillation, embolism, stroke

Outcome measures

Primary outcome

Primary efficacy endpoint: The primary efficacy endpoint is the time to first occurrence of confirmed stroke (ischemic or non-ischemic) or systemic embolism, regardless of whether the subject is receiving treatment at the time of event.

Primary safety endpoint: The primary safety endpoint will be time to first occurrence of confirmed major bleeding during the treatment period or 30 days post-treatment if the event is a SAE.

Secondary outcome

The secondary efficacy endpoints will be: time to first occurrence of confirmed: ischemic stroke, hemorrhagic stroke, systemic embolism, all cause death and the composite of the combinations of all of these indications.

Secondary safety endpoints is a composite of confirmed major bleeding and confirmed clinically relevant non-major bleeding.

Study description

Background summary

Apixaban is a potent, predictable and long-acting anticoagulant. In addition no therapeutic monitoring is needed for safe dosage. Oral administration is possible without an effect from food. Apixaban is easy to dose and showed a low toxicity.
Research hypothesis: Apixaban is noninferior to warfarin for prevention of stroke (ischemic or hemorrhagic) or systemic embolism in subjects with atrial fibrillation (AF) and additional risk factor(s) for stroke.

Study objective

Primary objective: To determine if apixaban is noninferior to warfarin (INR target range 2.0-3.0) in the combined endpoint of stroke (ischemic or hemorrhagic) and systemic embolism, in subjects with AF and at lease one additional risk factor for stroke.

Study design

Randomized, double-blind, active-controlled study with a double dummy design.

Intervention

Group 1: twice daily 5 m Apixaban and Warfarin placebo
Group 2: Warfarin dose titrated to a target INR range of 2.0 - 3.0 and twice daily Apixaban-placebo.

Patients with a higher risk of bleeding will receive a lower dose of Apixaban (2,5 mg twice daily).

Study burden and risks

Patient will have to visit the hospital 67 times in total for blood sampling, physical exam, once a year an ECG and to discuss adverse events and concomitant medication.

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) Age >= 18 years
2) In atrial fibrillation or atrial flutter not due to reversible cause and documented by ECG at the time of enrollment OR If not in atrial fibrillation/flutter at the time of enrollment, must have atrial fibrillation/flutter documented on two separate occasions, not due to a reversible cause at least 2 weeks apart in the 12 months prior to enrollment.
3) One or more of the following risk factor(s) for stroke: a) Age 75 years or older, b) prior stroke, TIA or systemic embolus, c) Either symptomatic congestive heart failure within 3 months or left ventricular dysfunction with an LV ejection fraction (LVEF) <= 40%, d) Diabetes mellitus, e) hypertension requiring pharmacological treatment.

Exclusion criteria

1) Atrial fibrillation or flutter due to reversible causes.
2) Clinically significant mitral stenosis
3) Increased bleeding risk that is believed to be a contraindication to oral anticoagulation.
4) Conditions other than atrial fibrillation that require chronic anticoagulation.
5) Persistent, uncontrolled hypertension (systolic BP > 180 mmHg of diastolic BP > 100 mm Hg).
6) Active infective endocarditis.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-02-2008
Enrollment:	252
Type:	Actual

Medical products/devices used

Product type:	Medicine
Product type:	Medicine
Brand name:	nvt
Generic name:	Warfarine

Ethics review

Approved WMO Date:	22-05-2007
Application type:	First submission
Review commission:	METC Twente (Enschede)
Approved WMO Date:	06-08-2007
Application type:	Amendment
Review commission:	METC Twente (Enschede)

Approved WMO Date:	15-10-2007
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	24-10-2007
Application type:	First submission
Review commission:	METC Twente (Enschede)
Approved WMO Date:	20-12-2007
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	27-03-2008
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	15-05-2008
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	27-05-2008
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	19-11-2008
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	08-12-2008
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	10-02-2009
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO	

Date:	12-05-2009
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	06-10-2009
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	11-11-2009
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	25-03-2010
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	13-04-2010
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	21-06-2010
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	16-08-2010
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	06-10-2010
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	03-01-2011
Application type:	Amendment
Review commission:	METC Twente (Enschede)

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	EUCTR2006-002147-91-NL
CCMO	NL16777.044.07