A randomized, double blind, placebo controlled, parallel group trial for assessing the clinical benefit of Dronedarone 400mg BID on top of standard therapy in patients with permanent atrial fibrillation and additional risk factors

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

Summary

ID

NL-OMON34262

Source
ToetsingOnline

Brief title
PALLAS

Condition

- Cardiac arrhythmias

Synonym
Atrial fibrillation & atrial flutter

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi-aventis
Source(s) of monetary or material Support: sanofi-aventis

Intervention

Keyword: Atrial fibrillation, Benefit, Dronedarone, Risk factors

Outcome measures

Primary outcome

Coprimary Endpoints

• Composite endpoint of first stroke, systemic arterial embolism, myocardial infarction or cardiovascular death

• Composite endpoint of first unplanned cardiovascular hospitalization or death from any cause

All deaths, strokes, systemic arterial embolisms and myocardial infarctions, all heart failure hospitalizations as well as all other unplanned cardiovascular hospitalizations up to the first not refuted unplanned cardiovascular hospitalization will be adjudicated by a blinded committee.

Secondary outcome

Secondary Endpoint

• Cardiovascular death

Study description

Background summary

Atrial fibrillation (AF) is the most frequent sustained arrhythmia, affecting 6% of the people older than 70 years and the overall incidence rises with age. AF is associated with a 1.5-1.9- fold increase in mortality risk and significant morbidity causing symptom. It is common practice to restore sinus rhythm by pharmacological means or by electrical cardioversion, after which patients often receive antiarrhythmic treatment to reduce the change of AF recurrence. Amiodarone (Cordarone*), an anti-arrhytmic drug with a complex electrophysiological profile is a very effective therapy for the maintenance of sinus rhythm post-conversion. Dronedarone is very similar to amiodarone, but without the iodine molecule so less amiodarone related side effects can be expected.
Given the trend for a beneficial effect of dronedarone in the AF/AFL population derived from the data of former studies (EURIDIS/ ADONIS) on the combined endpoint of hospitalisation for cardiovascular reasons or any death it is expected that treatment with dronedarone can similarly decrease this combined endpoint in high risk patients with a history of AF/AFL.

Study objective

The primary objective of this trial is to demonstrate the efficacy of Dronedarone in preventing major cardiovascular events (stroke, systemic arterial embolism, myocardial infarction or cardiovascular death) or unplanned cardiovascular hospitalization or death from any cause in patients with permanent atrial fibrillation and additional risk factors.

Study design

Prospective, randomized, double blind, parallel group, international, multicenter trial evaluating the effects of dronedarone 400 mg BID versus placebo (ratio 1:1) in patients with permanent atrial fibrillation and additional risk factors.

Intervention

Dronedarone: 400 mg, one tablet twice a day with the morning and evening meals
Placebo, one tablet twice a day with the morning and evening meals

Study burden and risks

Patients will be followed according to schedule (page 8-9 of the protocol). A 2D electrocardiography will be done at baseline and a 12-lead ECG maximum 11 times. Besides at maximum 6 visits, bloodsamples will be taken for biochemistry parameters. Patients may experience dronedarone related 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

Permanent AF defined by the presence of all of the following criteria:
- Availability of one 12-lead ECG not more than 14 days prior to randomization showing that the patient is in AF or atrial flutter
- Availability of documentation (including either rhythm strips or medical report of the rhythm) showing that the patient was in AF or atrial flutter at least 6 months prior to randomization
- No evidence of sinus rhythm in the period between these two documentations of AF
- Patient and physician decision to allow AF to continue without further efforts to restore sinus rhythm
Patients aged 65 years or older with at least one of the following risk criteria:
- Coronary artery disease
- Prior stroke or Transient Ischemic Attack (TIA)

- Symptomatic heart failure
- Left ventricular ejection fraction less or equal to 0.40
- Peripheral arterial occlusive disease
- Aged 75 years or older with both hypertension and diabetes mellitus

Exclusion criteria

- Paroxysmal AF
- Persistent AF without a decision to allow AF to continue without further efforts to restore sinus rhythm
- Heart failure of New-York Heart Association (NYHA) class IV or recent unstable NYHA class III

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:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-09-2010
Enrollment:	544
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Multaq
Generic name:	Dronedarone

Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	15-06-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-07-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-09-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-09-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-09-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-09-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-10-2010
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-10-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-11-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-11-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-11-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-12-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-12-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-12-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	27-12-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-01-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-02-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-02-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-02-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-06-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2010-019791-73-NL
ClinicalTrials.gov	NCT01151137
CCMO	NL32603.060.10