The effect of the addition of dronedarone to, versus increase of, existing conventional rate control medication on ventricular rate during persistent atrial fibrillation (AFRODITE study)

Published: 18-01-2009
Last updated: 04-05-2024

Primary:To assess whether the addition of dronedarone (Multaq®) to existing conventional rate control therapy leads to a reduced ventricular rate after 1 week in patients with a high HR at rest during AF in comparison to an increase of conventional...

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

Summary

ID

NL-OMON36263

Source
ToetsingOnline

Brief title
AFRODITE

Condition

- Cardiac arrhythmias

Synonym
atrial fibrillation; irregular heart beat

Research involving
Human

Sponsors and support

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

Intervention

Keyword: add-on, atrial fibrillation, dronedarone, standard therapy

Outcome measures

Primary outcome

Ventricular rate after 1 week.

Secondary outcome

- Ventricular rate after 3 months.

- Number of registered AF episodes.

- Number of symptomatic AF episodes.

- Severity of AF and AF-like symptoms.

- Adverse events.

- Rate of premature study discontinuation (*going off study prematurely*).

- Number of symptomatic episodes of bradycardia.

- Incidence of low heart rate (<60 bpm).

Study description

Background summary

Previous studies have shown no evident difference in benefit between rate or rhythm control strategies in the management of AF. In current treatment guidelines it is recommended to start with rate control therapy and switch to rhythm control in case of rate control fails or cannot be intensified. Adverse events and treatment discontinuation are common with conventional rhythm control therapy.
If AF patients are inadequately controlled (i.e. HR at rest > 80 bpm) on rate

control treatment, adjustment, i.e.a dose increase or a switch to rhythm control is indicated. The physician*s preference may be influenced by treatment duration, number of rate control agents and/or severity of symptoms.
The combination of rhythm and rate control properties with good tolerability and a lack of proarrhythmic effects suggests that dronedarone may address several of the shortcomings of current treatment options. The effects of adding dronedarone to conventional rate control in comparison to a dose increase of conventional therapy in insufficiently controlled AF patients are not yet documented. These data will help to position this promising new drug in the existing treatment options for AF.
Therefore the current study will address the effects on ventricular rate during AF of the addition of dronedarone to the existing rate control treatment with a beta blocker and/or a calcium antagonist in comparison to dose increase of the existing treatment in patients with insufficiently controlled persistent AF.

Study objective

Primary:
To assess whether the addition of dronedarone (Multaq®) to existing conventional rate control therapy leads to a reduced ventricular rate after 1 week in patients with a high HR at rest during AF in comparison to an increase of conventional therapy.
Secondary:
To compare both study arms with regard to:
- Ventricular rate after 3 months.
- Number of registered AF episodes.
- Number of symptomatic AF episodes.
- Severity of AF and AF-like symptoms.
- Adverse events.
- Rate of premature study discontinuation (*going off study prematurely*).
- Number of symptomatic episodes of bradycardia.
- Incidence of low heart rate (<60 bpm).

Study design

Randomized, multicenter, parallel group open label study in the Netherlands.
Accepted existing conventional rate control medication at study entry:
• beta blocker or
• calcium antagonist or
• beta blocker plus calcium antagonist or
• beta blocker plus digoxin or
• calcium antagonist plus digoxin.

Randomisation (1:1) to
Arm A (experimental arm): Addition of dronedarone 400 mg BID to the unchanged existing conventional rate control medication.

Arm B (control arm, standard treatment): Increase of conventional rate control medication, i.e.: dose increase of existing beta-blocker or calcium antagonist or digoxin. At this stage the dose of no more than one drug should be increased. In week 1 no further treatment adjustment or cardioversion.
After 1st week possibility to adjust standard treatment (beta blocker, calcium antagonist and/or digoxin) in both arms. In arm A the dose of dronedarone shall not be changed. Cardioversion accepted, however patient should go off study if a 2nd cardioversion is necessary.

Duration of study: 3 months.
596 patients.

Intervention

Dronedarone or intensified standard treatment.

Study burden and risks

Risk: Adverse events of study medication.
Burden: 5 visits in 3 months. Weekly completion of questionnaire re. AF-related symptoms. 5 bloodsamples to be taken of max 10 ml each.

Contacts

Public
Sanofi-aventis

Kampenringweg 45 D-E
2803 PE Gouda
Nederland
Scientific
Sanofi-aventis

Kampenringweg 45 D-E
2803 PE Gouda
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Paroxysmal AF (according to ACC/AHA/ESC 2006 definition) with HR >80 bpm at rest despite treatment with <=2 rate control agents (i.e. beta blocker and/or calcium antagonist). Patients using digoxin are eligible.
• Documented AF in the past 24 hours.
• Treated with the following rate control medication:
- beta blocker or
- calcium antagonist or
- beta blocker plus calcium antagonist or
- beta blocker plus digoxin or
- calcium antagonist plus digoxin.
• > 45 years of age.
• Anticoagulant treatment in line with local guidelines.

Exclusion criteria

• Incapacitated patients.
• Permanent AF (according to ACC/AHA/ESC 2006 definition).
• Use of class I or III AADs in the past 3 months.
• Patients scheduled for cardioversion or pulmonary vein ablation.
• Unstable NYHA class III and all class IV HF.
• AV block grade 2 or 3.
• Known severe renal impairment (serum creatinine >180 µmol/l).
• Known severe hepatic impairment (AST, ALT >3x ULN).
• Contra-indication for dronedarone.
• Participation in a clinical drug study in the 3 months prior to inclusion.
• Women of childbearing potential, who do not use adequate contraception (in the opinion of the investigator).
• Lactating women.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-04-2010
Enrollment:	596
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Multaq
Generic name:	dronedarone
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	18-01-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	10-02-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	11-02-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-05-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-06-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-06-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-06-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-06-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-07-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-08-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	17-08-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-08-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-09-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-12-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-01-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-02-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-02-2011
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	EUCTR2009-018215-53-NL
ClinicalTrials.gov	NCT01047566
CCMO	NL31164.060.09