A randomized, double blind, placebo-controlled, parallel, international multicenter study assessing the efficacy of S066913 in patients with paroxysmal atrial fibrillation.
Double-blind, International study AssessinG efficacy of S066913 in paRoxysmal Atrial Fibrillation -IKur inhibitor (DIAGRAF - IKUR)

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

Summary

ID

NL-OMON41862

Source
ToetsingOnline

Brief title
DIAGRAF - IKUR

Condition

- Cardiac arrhythmias

Synonym
intermittent heart rate disturbance, paroxysmal atrial fibrillation

Research involving
Human

Sponsors and support

Primary sponsor: Institut de Recherches Internationales Servier I.R.I.S
Source(s) of monetary or material Support: ADIR

Intervention

Keyword: IKUR blocker, Paroxysmal atrial fibrillation

Outcome measures

Primary outcome

-The absolute change from baseline of AF/AT burden

Baseline will be the 4-week ICM recording before inclusion visit.

Secondary outcome

-The absolute change from baseline of AF burden

-Mean duration of longest AF/AT episodes

-Mean number of AF/AT episodes

-Incidence of persistent AF

-Percentage of asymptomatic patients (whatever rhythm) and asymptomatic

patients (symptoms in sinus rhythm excluded)

-Percentage of patients who have * 30% (* 50%) reduction from baseline in AF/AT

burden

-Mean ventricular rate in AF

These endpoints will be studied over the full 4-week treatment period. Another

analysis will be performed considering only the last 3-week treatment period

Study description

Background summary

AF is the most common sustained cardiac arrhythmia (33.5 million people worldwide, near 5 million new cases each year), and its prevalence will increase with the aging population. AF is associated with an increased risk of stroke incidence and mortality. The disease is progressive and can progress to permanent AF. Currently available AAD's are moderately effective in restoring and maintainain sinus rhythm. Moreover, they can produce serious adverse effects and although efficient in reducing stroke risk, are not associated with improvement in mortality. While effective, catheter ablation conveys a relevant risk of major complications. S066913 potently and selectively inhibits the IKur channel in the atria, by increasing the AERP (atrial effective refractory period). Aymptomatic atrial tachyarrhythmias occur frequently and the stroke risk is at least as high as it is for symptomatic patients. As correlation of symptoms with the AF episodes is limited, it is not possible to rely on symptoms to detect AF or to measure the effect of a rhythm control treatment. Conventional methods used for PAF detection have limited sensitivity due to the infrequent measurements. Insertable continuous monitoring (ICM) devices have been equipped with AF detection and measurement capabilities and can be subcutaneously inserted under local anaesthesia. The use of these highly sensitive and specific ICM's has demonstrated that continuous monitoring was much more accurate than conventional monitoring to detect AF recurrences post ablation.

Study objective

The aim of this study is to evaluate the efficacy of three doses of S 066913 (5 mg, 25 mg and 100 mg o.d.) versus placebo administered for 4 weeks on atrial fibrillation and/or atrial tachycardia burden (AF/AT burden) in patients with paroxysmal atrial fibrillation (PAF) who are potentially eligible for atrial fibrillation (AF) ablation and are implanted with insertable cardiac monitoring (ICM) device.
The safety and pharmacokinetic profile of S 066913 will also be evaluated.

Study design

Target population: patients with PAF who are potentially eligible for AF ablation.

Randomized, double blind, placebo-controlled, parallel, international multicenter study to evaluate the efficacy of S 066913 on AF/AT burden.

Intervention

During the selection visit or during the following days, the ICM will be implanted subcutaneously under local anaesthesia. The ICM can remain implanted after the study until it's breakdown.
oral administration of S066193 or placebo

Study burden and risks

ICM implantation may be associated with potential risks and discomforts. A little bleeding during the procedure and bruising over the ICM are common and usually of no consequence. There is about 2% (2 in every 100 patients) probability of the ICM causing potential risks. They include, but are not limited to: *Infection at the implant site. To minimise the risk, antibiotics can be used before and after the procedure.
*A hematoma over the ICM. Occasionally this needs to be drained.
*Pain at the implant site.
*Movement of the ICM from its initial position or coming through the skin.
*Rejection of the ICM by the body, which may involve symptoms such as swelling, redness, or other irritation at, or near, the implant site.
Taking blood samples may cause some discomfort, bruising or bleeding from the site of sampling and may cause a blood clot or bruising.

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

Adult patients (except women of childbearing potential) potentially eligible for atrial fibrillation ablation, In sinus rhythm at selection visit or within 7 days after selection visit. With 1 documented episodes of AF in within 18 months before selection and at least 2 other episodes of AF within 30 days prior to selection (symptomatic or asymptomatic). Eligible for and agreeing to receive ICM implantation following local guidelines and practice, or patients already implanted with an ICM device of the same type as used in the study,
Informed consent obtained.
During baseline period, AF/AT burden must be * 1% and * 70% and at least 3 episodes of AF.

Exclusion criteria

Main non-selection criteria
* AF secondary to a reversible cause,
* persistent or permanent AF,
* Patient with more than one anti-arrhythmic drug stopped due to lack of efficacy (rather than intolerance or side effect), provided they were administered at recommended anti-arrhythmic dose,
* Patients previously treated with amiodarone that was stopped because of lack of efficacy, or amiodarone treatment within 3 months prior to selection,
* Corrected QT interval duration (Fridericia*s formula) > 450 ms for male, 470 ms for female,
* High degree atrio-ventricular block (2nd degree or complete),
* Any history of sustained ventricular tachycardia, or resuscitated sudden death,
* Severe chronic heart failure,
* Recent acute coronary syndrome or revascularization.
* women with childbearing potential
*Main non-inclusion criteria
* Unreliable ICM recording

* Sustained ventricular tachycardia, asystole, or sustained bradycardia according to ICM interrogation

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):	14-04-2015
Enrollment:	34
Type:	Actual

Medical products/devices used

Generic name:	Insertable Cardiac Monitor - Reveal Linq
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	11-11-2014
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	30-01-2015

Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	06-02-2015
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	17-02-2015
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	06-03-2015
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	19-03-2015
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	22-04-2015
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	11-05-2015
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	05-08-2015
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	07-08-2015
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)

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	EUCTR2014-002333-63-NL
CCMO	NL50607.075.14