Effects of ivabradine on vascular function in individuals at increased risk of developing cardiovascular disease and with impaired endothelial function;An international, multicentre, randomised, double-blind, placebo-controlled study over 12 weeks.

Published: 28-06-2013
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The purpose of this study is to demonstrate the beneficial effect of ivabradine on endothelial function in individuals with risk factors for cardiovascular disease and a resting HR * 75 bpm.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Interventional

Summary

ID

NL-OMON40596

Source
ToetsingOnline

Brief title
Effects of ivabradine on vasular function

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
impaired endothelial function

Research involving
Human

Sponsors and support

Primary sponsor: Servier R&D Benelux
Source(s) of monetary or material Support: Institut de Recherches Internationales Servier

Intervention

Keyword: ivabradine, vascular function

Outcome measures

Primary outcome

Absolute change from baseline over 12 week treatment period in FMD of the

brachial artery

Secondary outcome

Biomarkers of endothelial function and cardiovascular risk : change from

baseline over 12 week treatment period in each biomarker.

Resting heart rate (bpm) from 12 lead ECG : change from baseline over 12 week

treatment period

Study description

Background summary

There is a clear association between endothelial dysfunction and both the presence of ,and the development of atherosclerosis which may in part be explained by the reduced release of NO by the endothelium. Whilst at the same time there appears to be an association between HR, HR reduction, and the development of atherosclerotic cardiovascular disease both in animals and in humans with established CAD. By studying the effect of ivabradine on endothelial function as measured by FMD and on biomarkers of endothelial function and cardiovascular risk it is expected to explain, at least in part, the mechanism by which this drug has a positive effect on atherosclerotic CVD.

By performing the study in patients who have not yet developed clinical CVD, but who are at high risk due to both recognized risk factors (hypertension, type II diabetes mellitus, hyperlipidaemia or cigarette smoking) and an impaired FMD at baseline, we explore the hypothesis that HR reduction with ivabradine at an early stage in the atherosclerotic disease process might improve vascular health.

Study objective

The purpose of this study is to demonstrate the beneficial effect of ivabradine on endothelial function in individuals with risk factors for cardiovascular disease and a resting HR * 75 bpm.

Study design

Multicenter, international, randomised, double blind, placebo-controlled in 2 parallel and balanced groups.
Following a selection visit (ASSE) , a pre-treatment period of 2 weeks and an inclusion visit (W000); the patients will be centrally randomly assigned to one of the 2 treatment arms.
Starting 7.5 mg, the dose will be adapted after 2 weeks and after 4 weeks according to the tolerability and the heart rate value. The treatment period will last 12 weeks. FMD will be performed before treatment and at the end of treatment period. Moreover, intra-patient variability will be assessed in a random subgroup of 20% of patients from all participating centres at baseline and at W012

Intervention

-12 lead ECG (2 ECG with 5 min interval)after at least 5 minutes rest at each visit except the last one. -- ---FMD measurement at ASSE and W012 . To assess the intra-patient variability, in a subset of patients FMD will be repeated before the first medication intake and after 12 weeks of treatment.
-blood sampling for routine lab tests at ASSE and W012. Blood sampling for biomarkers at W000 and W012.

Study burden and risks

Cfr E2 and E9

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

- Men or postmenopausal women of any ethnic origin aged between 21 and 74 years
- In sinus rhythm with resting HR at least 75 bpm
- At increased risk of subsequent cardiovascular disease (documented by the presence of at least two cardiovascular risk factors such as diabetes, hypertension, smoking, hypercholesterolemia) and impaired FMD * 5.0 %

Exclusion criteria

- Previous diagnosis of coronary heart disease
- Previous diagnosis of heart failure or current clinical signs or symptoms in keeping with a diagnosis of heart failure
- History of cerebrovascular or peripheral arterial disease
- Uncontrolled hypertension
- Chronic infectious or inflammatory disease
- Chronic Obstructive Pulmonary Disease (COPD) treated with inhaled bronchodilators
- Malignancy
- Current therapy with nicorandil, nitrate, insulin

- Contra-indication to ivabradine

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):	24-01-2014
Enrollment:	200
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	procoralan
Generic name:	ivabradine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	28-06-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	26-08-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-09-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-03-2014
Application type:	Amendment
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	EUCTR2012-000215-89-NL
CCMO	NL45222.018.13
Other	www.clinicaltrialsregister.eu