ISRCTN30654443 https://doi.org/10.1186/ISRCTN30654443

Efficacy of ivabradine in combination with beta-blockers vs up-titration of beta-blockers in daily practice

Submission date
22/12/2017

Recruitment status
No longer recruiting

Registration date
24/01/2018

Overall study status
Completed

Last Edited
08/03/2018

Condition category
Circulatory System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Angina is chest pain that occurs when the blood supply to the muscles of the heart is restricted. It affects more than a hundred million patients in the world, and although treatments exist the disease is not always optimally controlled. Heart rate reduction is important part of treatment. This study compares the effectiveness and tolerability of the combination of beta-blockers with ivabradine versus increased dose of beta-blockers up to the maximum tolerated dose.

Who can participate?
Patients aged 18 and over with stable angina undergoing regular treatment with beta-blockers

What does the study involve?
Patients are randomly allocated to either standard therapy with increased dose of beta-blockers up to the maximum tolerated dose, or ivabradine is added to their current beta-blockers dose. There are five clinic visits: at the start of the study (Visit 0), 2 weeks (Visit 1), 4 weeks (Visit 2), 8 weeks (Visit 3) and 16 weeks (Visit 4).

What are the possible benefits and risks of participating?
The results of a previous study demonstrated the effectiveness and good tolerability of this combination. At the same time tolerability problems which could limit increasing the dose of beta-blockers are well known in clinical practice.

Where is the study run from?
Sechenov First Moscow State Medical University (Russia)

When is the study starting and how long is it expected to run for?
August 2008 to January 2011

Who is funding the study?
Servier Affaires Medicales (France)

Who is the main contact?
Prof. Glezer Maria

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Efficacy of ivabradine in combination with beta-blockers vs up-titration of beta-blockers in daily practice

Acronym
Control-2

Study objectives
Heart rate (HR) reduction is an integral part of anti-anginal therapy, but many patients do not reach the guidelines-recommended target of <60 bpm despite high use of beta-blockers (BB). Failure to up-titrate BB doses may be partly to blame. Randomised controlled studies showed that addition of ivabradine to a beta-blocker in patients with stable angina reduced angina symptoms and improved exercise capacity compared with beat-blocker alone. The larger experience in patients from daily practice will help to understanding about the broader potential for combination treatment with ivabradine and BBs.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethic approval was obtained before recruitment of the first participants

Study design
Multicentre open randomised prospective study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Stable angina

Interventions
For this trial, there wasn't a central randomization procedure. Each investigator was provided with a table of randomization. Consecutive patients were allocated to standard therapy with BB up-titration to the maximal tolerated dose or ivabradine was added to their current BB dose, in a 1:4 ratio of patients. Up-titration of BB was carried out according to achieved resting HR and tolerability as, in contrast to heart failure, there is no recommended target dose or recommended BB molecule in treating stable angina, and thus a wide variety of agents and doses are commonly used. Five clinic visits were performed: baseline (Visit 0), 2 weeks (Visit 1), 4 weeks (Visit 2), 8 weeks (Visit 3) and 16 weeks (Visit 4).

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Ivabradine

Primary outcome measure
Measured at baseline (Visit 0), 2 weeks (Visit 1), 4 weeks (Visit 2), 8 weeks (Visit 3) and 16 weeks (Visit 4):
1. Change in heart rate during the 16-week treatment period
2. Change in CCS class of angina
3. Number of angina attacks with standard therapy vs ivabradine

4. Proportion of patients who were angina-free between study visits
5. Patient self-reported health status, measured using the visual analogue scale (VAS)

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
01/08/2008

Completion date
30/01/2011

Eligibility

Key inclusion criteria
1. Adult patients (≥18 years)
2. Documented angina of effort, Canadian Cardiovascular Society (CCS) class II-III, which has been stable for at least three months, with ≥3 attacks per week
3. In sinus rhythm with HR ≥60 bpm
4. Undergoing regular treatment of stable angina with a BB in a dose which was below the maximum for angina treatment

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
1104

Key exclusion criteria
1. Chronic heart failure of NYHA class III-IV
2. Non-sinus rhythm
3. Blood pressure >180/100 mm Hg at rest
4. Treatment with verapamil or diltiazem

Date of first enrolment
02/11/2009

Date of final enrolment
30/12/2009

Locations

Countries of recruitment
Russian Federation

Study participating centre
Sechenov First Moscow State Medical University
Department of Preventive and Emergency Cardiology
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Sponsor information

Organisation
Servier Affaires Medicales

Sponsor details
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Sponsor type
Industry

ROR
https://ror.org/034e7c066

Funder(s)

Funder type
Industry

Funder Name
Servier Affaires Medicales

Results and Publications

Publication and dissemination plan

Intention to publish date
22/11/2011

Individual participant data (IPD) sharing plan
The datasets generated during the current study are not publicly available but are available from the corresponding author on reasonable request.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results			Yes	No
Results article	results	01/03/2018		Yes	No