

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

<b>Submission date</b> 22/12/2017	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 24/01/2018	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 08/03/2018	<b>Condition category</b> Circulatory System	<input type="checkbox"/> 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

Prof Glezer Maria

### Contact details

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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 beta-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)**

Ethical 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 ( $\geq 18$  years)
2. Documented angina of effort, Canadian Cardiovascular Society (CCS) class II-III, which has been stable for at least three months, with  $\geq 3$  attacks per week
3. In sinus rhythm with HR  $\geq 60$  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

2-4 Bolshaya Pirogovskaya st

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119991

**Sponsor information****Organisation**

Servier Affaires Medicales

**Sponsor details**

35 rue de Verdun

Suresnes

France

92284

**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?
<a href="#">Results article</a>	results			Yes	No
<a href="#">Results article</a>	results	01/03/2018		Yes	No