Evaluation of the anti-anginal efficacy and safety of oral administration of ivabradine compared to placebo on top of a background therapy with a calcium antagonist (amlodipine or nifedipine) in patients with stable angina pectoris: A 6-week, randomised, double-blind, parallel-group, international, multicentre study

Submission date	Recruitment status No longer recruiting	Prospectively registered			
26/12/2007		☐ Protocol			
Registration date 18/07/2008	Overall study status Completed	Statistical analysis plan			
		[X] Results			
<b>Last Edited</b> 21/04/2020	Condition category Circulatory System	[] Individual participant data			
L 1/07/LULU	Circulatory Dystern				

### Plain English summary of protocol

Not provided at time of registration and not expected to be available in the future

# **Contact information**

### Type(s)

Scientific

#### Contact name

Prof Gabriel Kamensky

#### Contact details

Faculty Hospital Ruzinov Department of Non-Invasive Cardiology Ruzinovska 6 Bratislava Slovakia SR-82606

### Additional identifiers

Clinical Trials Information System (CTIS)

#### Protocol serial number

CL3-16257-068

# Study information

#### Scientific Title

Evaluation of the anti-anginal efficacy and safety of oral administration of ivabradine compared to placebo on top of a background therapy with a calcium antagonist (amlodipine or nifedipine) in patients with stable angina pectoris. A 6-week randomised double-blind parallel-group international multicentre study.

#### Study objectives

To demonstrate that over a 6-week treatment period ivabradine is more efficacious than placebo when given in combination with calcium antagonists (amlodipine or nifedipine) in patients with stable chronic effort angina pectoris.

As of 23/07/2012 the anticipated end date for this trial has been updated from 30/01/2012 to 31/01/2013

As of 03/03/2011 the anticipated end date for this trial has been updated from 15/11/2009 to 30/01/2012.

#### Ethics approval required

Old ethics approval format

### Ethics approval(s)

First Latvian Ethics Committee, 14/09/2007

### Study design

Randomised, double-blind, parallel-group, international, multi-centre study

### Primary study design

Interventional

### Study type(s)

Treatment

### Health condition(s) or problem(s) studied

Angina pectoris

#### **Interventions**

All participants will be given either:

a. 5 mg/day amlodipine (oral) for 6 weeks or

b. 30 mg/day nifedipine GastroIntestinal Therapeutic System (GITS) (oral) for 6 weeks

In addition, they will be given either ivabradine or placebo according to random allocation: Group 1: 5 mg twice a day (bid) ivabradine for 2 weeks then uptitration to 7.5 mg bid (except if HR< 60 bpm and/or symptomatic bradycardia) for 4 weeks
Group 2: Placebo daily for 6 weeks

#### Intervention Type

Other

#### Phase

**Not Specified** 

#### Primary outcome(s)

Response to treatment, evaluated over a 6-week treatment period, will be defined as a decrease of at least 3 angina attacks per week and/or an increase in the time to 1 mm ST segment depression of at least 60 s during a treadmill Exercise Tolerance Test (ETT), performed according to a modified Bruce protocol at the trough of ivabradine activity (i.e.  $12 \pm 1$  hours post-dosing) and  $24 \pm 2$  hours after amlodipine or nifedipine administration on centrally read values.

ETT will be performed at SEL, W0, and W6 (trough and peak of ivabradine activity) visits and the following parameters will be measured:

- 1. Total Exercise Duration (TED, sec)\*
- 2. Time to onset of 1 mm ST segment depression (TST 1 mm, sec)\*
- 3. Time to onset of angina pain (TAO, sec)\*\*
- 4. Time to Limiting Angina (TLA, sec)\*\*
- 5. Heart Rate at rest and at peak of exercise (HR, bpm)\*
- 6. Rate Pressure Product at rest and at peak of exercise (RPP, bpm x mmHg)\*
- \* Evaluated by Core Reading Centre
- \*\* Evaluated by investigator

#### Key secondary outcome(s))

Changes in other classical exercise tolerance test parameters (secondary efficacy criteria):

- 1. Change over a 6-week treatment period in all the ETT criteria (TED, TST 1mm, TAO, TLA, HR and RPP at rest and at peak exercise):
- 1.1. At the trough of ivabradine activity (i.e.  $12 \pm 1$  hours post-dosing) and  $24 \pm 2$  hours after nifedipine or amlodipine administration
- 1.2. At the peak of ivabradine activity (i.e. 3  $\pm$  1 hours post-dosing) and 3  $\pm$  1 hours after nifedipine or amlodipine administration
- 2. Response to TST 1 mm criterion defined as an increase over a 6-week treatment period in the time to 1 mm ST segment depression of at least 60 sec, at the trough of ivabradine activity (i.e.  $12 \pm 1$  hours post-dosing) and  $24 \pm 2$  hours after amlodipine or nifedipine on centrally read values

#### Completion date

31/01/2013

## **Eligibility**

### Key inclusion criteria

- 1. Stable angina pectoris
- 2. Patients already treated with amlodipine or nifedipine
- 3. Sinus rhythm: heart rate 60 beats per minute

### Participant type(s)

Patient

### Healthy volunteers allowed

# No Age group **Not Specified** Sex All Total final enrolment 1277 Key exclusion criteria Heart rate <60 beats per minute Date of first enrolment 15/12/2007 Date of final enrolment 31/01/2013 Locations Argentina Armenia

Countries of recruitment

Brazil

Bulgaria

Chile

Estonia

Hungary

India

Korea, South

Lithuania

Mexico

Moldova

Peru

**Philippines** 

Study participating centre Faculty Hospital Ruzinov Bratislava Slovakia SR-82606
Sponsor information
Organisation Institut de Recherches Internationales Servier (France)
ROR https://ror.org/034e7c066
Funder(s)
Funder type Industry

Institut de Recherches Internationales Servier (France)

**Results and Publications** 

Individual participant data (IPD) sharing plan

**Poland** 

Romania

Serbia

Slovakia

Tunisia

Ukraine

Funder Name

**Russian Federation** 

The datasets generated during and/or analysed during the current study will be available upon request from https://clinicaltrials.servier.com if a Marketing Authorisation has been granted after 1st January 2014.

### IPD sharing plan summary

Available on request

### **Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results				No	No
Basic results			21/04/2020	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes