

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 26/12/2007	Recruitment status No longer recruiting	☐ Prospectively registered ☐ Protocol
Registration date 18/07/2008	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 21/04/2020	Condition category Circulatory System	☐ Individual participant data

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

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Additional identifiers

Clinical Trials Information System (CTIS)

2006-006246-34

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 ± 1 hours post-dosing) and 24 ± 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 ± 1 hours post-dosing) and 24 ± 2 hours after nifedipine or amlodipine administration

- 1.2. At the peak of ivabradine activity (i.e. 3 ± 1 hours post-dosing) and 3 ± 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 ± 1 hours post-dosing) and 24 ± 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

Countries of recruitment

Argentina

Armenia

Brazil

Bulgaria

Chile

Estonia

Hungary

India

Korea, South

Lithuania

Mexico

Moldova

Peru

Philippines

Poland

Romania

Russian Federation

Serbia

Slovakia

Tunisia

Ukraine

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

Funder Name

Institut de Recherches Internationales Servier (France)

Results and Publications

Individual participant data (IPD) sharing plan

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