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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

Registration date
18/07/2008

Overall study status
Completed

Last Edited
21/04/2020

Condition category
Circulatory System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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

Primary study design
Interventional

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

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
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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