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Determination of the efficacious and safe dose of ivabradine in paediatric patients with dilated cardiomyopathy and symptomatic chronic heart failure from ages 6 months to 18 years

Submission date
22/09/2011

Recruitment status
No longer recruiting

Registration date
10/11/2011

Overall study status
Completed

Last Edited
18/04/2018

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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

CL2-16257-090

Study information

Scientific Title
Determination of the efficacious and safe dose of ivabradine in paediatric patients with dilated cardiomyopathy and symptomatic chronic heart failure from ages 6 months to 18 years. A randomised, double-blind, multicentre, placebo controlled, phase II/III dose-finding study with a PK/PD characterisation and a 1 year efficacy/safety evaluation.

Study objectives
Determination of the efficacious and safe dose of ivabradine in paediatric patients with dilated cardiomyopathy and symptomatic chronic heart failure aged from 6 months to less than 18 years.

Ethics approval required
Old ethics approval format

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

Study design
Randomised double-blind placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

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
Paediatric dilated cardiomyopathy and symptomatic chronic heart failure

Interventions
During the titration period:
[6-12] months: ivabradine, oral liquid paediatric formulation, the starting dose 0.02 mg/kg twice daily or placebo, then 4 titrations according to HR matching with placebo, i.e. 0.05 mg/kg, 0.10 mg/kg, 0.15 mg/kg and 0.20 mg/kg twice daily or placebo.

[1-3] and [3-18] years with weight < 40 kg: ivabradine, oral liquid paediatric formulation, at the starting dose 0.05 mg/kg twice daily or placebo, then 4 titrations according to HR matching with placebo, i.e. 0.10 mg/kg, 0.15 mg/kg, 0.20 mg/kg and 0.30 mg/kg twice daily or placebo.

[3-18] years with weight >= 40 kg: ivabradine adult tablet formulation, at the starting dose 2.5 mg twice daily or placebo, then 4 titrations according to HR matching with placebo, i.e. 5 mg, 7.5 mg, 10 mg and 15 mg twice daily or placebo.

During the maintenance period: ivabradine, oral liquid paediatric formulation (or adult tablet formulation), at the target dose, twice daily or placebo.
During 1 year treatment period: ivabradine, oral liquid paediatric formulation (or adult tablet formulation), at the dose defined during the maintenance period and adapted according to the weight at each visit, twice daily or placebo.

Intervention Type
Drug

Phase
Phase II/III

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

Primary outcome measure
1. Characterization pharmacokinetics (PK) and PK/Pharmacodynamics (PD) at D014 and M000
2. Target HR achievement: HR measurements during titration period (D000, D014, D028, D042, D056, M000)

Secondary outcome measures
1. Echocardiographic parameters over the study
2. Heart failure symptoms severity over the study
3. Cardiovascular biomarker NT- proBNP over the study
4. Safety over the study

Overall study start date
15/10/2011

Completion date
30/09/2013

Eligibility

Key inclusion criteria
1. Patients of both gender aged from 6 months to 18 years old
2. Patients with dilated cardiomyopathy (DCM) receiving their usual treatment for chronic heart failure (CHF) at the optimal dose
3. Patients in sinus rhythm
4. Resting heart rate (HR) complying with the following criteria:
4.1. HR >= 105 bpm in the age-subset [6-12] months
4.2. HR >= 95 bpm in the age-subset [1-3] years

4.3. HR >= 75 bpm in the age-subset [3-5] years
4.4. HR >= 70 bpm in the age-subset [5-18] years
5. CHF class II to IV NYHA or Ross classification, stable for at least 1 month prior to selection
6. Left ventricular (LV) dysfunction with left ventricular ejection fraction (LVEF) <= 45% documented by echocardiography LV dysfunction consecutive to idiopathic dilated cardiomyopathy (DCM), post-viral myocarditis DCM or ischaemic DCM

Participant type(s)
Patient

Age group
Child

Lower age limit
6 Months

Upper age limit
18 Years

Sex
Both

Target number of participants
90

Key exclusion criteria
1. Class I NYHA or Ross Classification (asymptomatic patients)
2. Patients actively listed for transplantation at time of entry into the study or anticipated to undergo heart transplantation or corrective heartsurgery during the 1 year following entry into the study
3. History of symptomatic or sustained (≥ 30 sec) ventricular arrhythmiaunless a cardioverter defibrillator was implanted
4. Patients with structural valvular disease or severe functional valvulardisease requiring surgery
5. Significant systemic ventricular outflow obstruction
6. DCM secondary to muscular dystrophies, hemoglobinopathies, HIV,carnitine deficiency, anthracyclines
7. Patients requiring unauthorised concomitant treatment
8. Serum creatinine >2.0 mg/dL or >180 µmol/L (blood sampleperformed at ASSE visit)
9. AST and/or ALT > 3 upper normal limits (blood sample performed at ASSE visit)
10. Unstable cardiovascular condition at selection or inclusion

Date of first enrolment
15/10/2011

Date of final enrolment
30/09/2013

Locations

Countries of recruitment

Australia

Belgium

Brazil

Bulgaria

Canada

Denmark

Finland

France

Germany

Hungary

India

Italy

Mexico

Poland

Portugal

Romania

Russian Federation

Spain

Sweden

United Kingdom

Study participating centre
Service de Cardiologie Pédiatrique
Paris Cedex 15
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Sponsor information

Organisation
Institut de Recherches Internationales Servier (France)

Sponsor details
50 rue Carnot
Suresnes
France
92284

Sponsor type
Industry

Website
http://www.servier.com/

ROR
https://ror.org/034e7c066

Funder(s)

Funder type
Industry

Funder Name
Institut de Recherches Internationales Servier (France)

Results and Publications

Publication and dissemination plan
Publication plan:
Summary results are published in https://clinicaltrials.servier.com.

Intention to publish date

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