

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	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
Registration date 10/11/2011	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
Last Edited 18/04/2018	Condition category Circulatory System	<input type="checkbox"/> 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

Contact name

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Contact details

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Additional identifiers

Protocol serial number

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

Study type(s)

Treatment

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 \geq 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(s)

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)

Key secondary outcome(s)

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

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 \geq 105 bpm in the age-subset [6-12] months
 - 4.2. HR \geq 95 bpm in the age-subset [1-3] years
 - 4.3. HR \geq 75 bpm in the age-subset [3-5] years
 - 4.4. HR \geq 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) \leq 45% documented by echocardiography LV dysfunction consecutive to idiopathic dilated cardiomyopathy (DCM), post-viral myocarditis DCM or ischaemic DCM

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Child

Lower age limit

6 months

Upper age limit

18 years

Sex

All

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 arrhythmia unless a cardioverter defibrillator was implanted
4. Patients with structural valvular disease or severe functional valvular disease 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 $\mu\text{mol/L}$ (blood sample performed 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**

United Kingdom

Australia

Belgium

Brazil

Bulgaria

Canada

Denmark

Finland

France

Germany

Hungary

India

Italy

Mexico

Poland

Portugal

Romania

Russian Federation

Spain

Sweden

Study participating centre
Service de Cardiologie Pédiatrique
Paris Cedex 15
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75743

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