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An observational study of chronic heart failure patients receiving ivabradine

Submission date 20/10/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 08/11/2016	**Overall study status** Completed	
Last Edited 16/06/2023	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Heart failure means that the heart has become too weak or stiff and is unable to pump blood around the body. The annual mortality (death) rate of heart failure patients is over 20% despite receiving treatment. Higher heart rate is a risk factor for poor outcome, but heart rate reduction is often insufficient in such patients. The drug ivabradine (Corlentor®) improves heart function as well as long-term survival in chronic heart failure patients with reduced left ventricular ejection fraction (i.e. the amount of blood pumped out of the heart) through specifically heart rate reduction, and is recommended in the heart failure treatment guidelines of Europe, America and China. Since Corlentor® was just approved by Chinese food and drug administration (CFDA) in April 2015, more clinical information needs to be collected during practice in China. The aim of this study is to assess how well Corlentor® works and its safety in Chinese heart failure patients.

Who can participate?
Patients aged over 18 with chronic heart failure and reduced left ventricular ejection fraction whose resting heart rate is 75 beats per minute or over, and who have been prescribed Corlentor® before entering the study

What does the study involve?
All patients are asked to come to follow-up visits after four weeks and then after another five months. During these visits a routine practice investigation is carried out. A quality of life questionnaire is completed and the safety and tolerability of Corlentor® is measured and evaluated during the follow-up visits. The dosage of Corlentor® can be adapted or even discontinued if needed during the follow-up period according to heart rate reduction, but the follow-up visits continue as scheduled regardless of whether the Corlentor® is taken or not.

What are the possible benefits and risks of participating?
Corlentor® may relieve heart failure symptoms, improve heart function and quality of life, and reduce the re-hospitalization and/or death rate. Close follow-up by investigators during the study may also provide additional benefit to the participants. Corlentor® has been used worldwide since 2005 and was approved in China in 2015, and the possible side effects include phosphenes (visual disturbances) and bradycardia (slow heart rate).

Where is the study run from?
About 80 hospitals all over China, with Zhongshang Hospital Fudan University as the leading site.

When is the study starting and how long is it expected to run for?
December 2016 to June 2021

Who is funding the study?
Servier (Tianjin) Pharmaceutical Co., Ltd (China)

Who is the main contact?
Dr Qiaohui Kang, qiaohui.kang@servier.com

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
IC4-16257-004-CHN

Study information

Scientific Title
POSITIVE: POSt-authorization drug Intensive surveillance monitoring sTudy of IVabradine efficacy and safety in patients with chronic heart failurE

Acronym

POSITIVE

Study objectives
To assess the efficacy and safety of Corlentor®(ivabradine) in Chinese chronic heart failure patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics committee of Zhongshan Hospital Fudan University, 12/09/2016, ref: B2016-118

Study design
Prospective multicentre single-arm observational study

Primary study design
Observational

Secondary study design
Single-arm study

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
Chronic heart failure

Interventions
This study enrolls patients who have already been administered the study drug in line with the indication described on the label based on the doctor’s decision. After that, the investigator collects information during the follow-up period (1-month and 6-month visits). The study drug dose is adjusted or discontinued based on the doctor’s judgement during the follow-up period. Follow-up continues until the 6-month visit regardless of the study drug use.

The study drug (Corlentor®) should be used following the description of the label. 5 mg bid is the recommended starting dose, but the starting dose can be changed based on the patient’s situation and adjusted during the follow-up period. It is recommended on the label that a 2.5 mg bid starting dose should be considered in patients aged over 75, with dose adjustment based on the patient's heart rate (because the direct efficacy of Corlentor® is heart rate reduction), and the maximum dose should not exceed 7.5 mg bid during long-term use.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Heart rate change after Corlentor® administration, measured using office daytime resting heart rate (heart rate and rhythm from the 12-lead ECG will also be considered for double-confirm if available) at the 1-month and 6-month visit

Secondary outcome measures
Measured at the 1-month and 6-month visit:
1. Heart failure symptoms, measured based on the inquisition and physical examination carried out by cardiologists
2. Left ventricular function, measured by echocardiogram
3. Heart failure biomarker (BNP and/or NT-proBNP), assessed with a routine laboratory test
4. Quality of life, assessed by KCCQ questionnaire
5. Safety and tolerability of Corlentor®, measured through monitoring adverse drug reactions and changes of laboratory indicators after administration of the drug

Overall study start date
31/12/2016

Completion date
30/06/2021

Eligibility

Key inclusion criteria
1. Male or female, outpatients or inpatients, over 18 (inclusive) years old
2. Sinus rhythm
3. Resting heart rate ≥75 bpm as measured by 12-lead ECG prior to enrollment
4. Chronic heart failure patients with systolic dysfunction (the left ventricular ejection fraction (LVEF) was ≤ 40 % in the last 3 months)
5. Patients whose cardiac function classification according to the New York Heart Association (NYHA) standard are class 2-4
6. Patients who have received standard treatment (including β-blockers) for heart failure, or are intolerable or contraindicated to β-blockers
7. Patients who meet the indication of Corlentor® and are starting to receive Corlentor® treatment
8. Patients who have signed the informed consent forms

Participant type(s)
Patient

Age group
Adult

Lower age limit

18 Years

Sex
Both

Target number of participants
3300

Total final enrolment
1003

Key exclusion criteria
1. Patients who have received the treatment with Corlentor® within 2 weeks
2. Recent (<1 month) occurrence of acute myocardial infarction
3. Acute heart failure and cardiogenic shock
4. Sick sinus syndrome or sino-atrial block
5. Third-degree atrioventricular block
6. Severe hypotension (<90/50 mmHg)
7. Severe liver dysfunction (Child-Pugh score ≥10)
8. End-stage renal failure (Plasma creatinine clearance <15 ml/min)
9. Pregnancy, lactation and women of child-bearing potential not using appropriate contraceptive measures
10. Patients unable to visit as scheduled

Date of first enrolment
31/12/2016

Date of final enrolment
17/07/2020

Locations

Countries of recruitment
China

Study participating centre
Zhongshang Hospital Fudan University (leading site)
Shanghai
China
200032

Study participating centre
72 sites in China
China
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Sponsor information

Organisation
Servier (Tianjin) Pharmaceutical Co., Ltd

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Sponsor type
Industry

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ROR
https://ror.org/00fan0f25

Funder(s)

Funder type
Industry

Funder Name
Servier (Tianjin) Pharmaceutical Co., Ltd

Results and Publications

Publication and dissemination plan
Current publication and dissemination plan as of 09/06/2021:
Planned publication in a high impact peer reviewed journal

Previous publication and dissemination plan:
To be confirmed at a later date

Intention to publish date
30/06/2024

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study are available from Prof. Junbo Ge (ge.junbo@zs-hospital.sh.cn) on reasonable request.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Interim results article		08/12/2021	09/12/2021	Yes	No