Prospective, Double-Blind, Multicenter Study Evaluating the Safety of Repeat Doses of IV Serelaxin in Subjects with Chronic Heart Failure

Published: 21-07-2014
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Primary:Assess the safety of repeat doses of serelaxin in chronic heart failureSecondary:- Assess the incidence rate of adverse events of special interest, indicative of hypersensitivity reactions- Assess the safety and tolerability of repeated…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON40917

Source
ToetsingOnline

Brief title
RELAX-REPEAT

Condition

- Heart failures

Synonym
Chronic Heartfailure

Research involving
Human

Sponsors and support

Primary sponsor: Novartis

Source(s) of monetary or material Support: Sponsor/opdrachtgever van dit onderzoek; Novartis Pharma B.V.

Intervention

Keyword: Anti-serelaxin antibodies, Chronic Heartfailure, Safety, Serelaxin

Outcome measures

Primary outcome

Percentage of participants with chronic heart failure who develop antiserelaxin antibodies following repeat administration of IV continuous infusions of serelaxin up to 48 hours

Secondary outcome

- Percentage of participants with chronic heart failure who develop antiserelaxin antibodies
- Antibody levels in subjects with chronic heart failure who develop antiserelaxin antibodies (neutralizing, non-neutralizing or both)
- Number of patients with adverse events
- Percentage of participants with chronic heart failure who develop antiserelaxin antibodies neutralizing or non-neutralizing
- Pharmacokinetics of RLX030: Area under the plasma concentration time curve from time zero up to 48 hours post dose (AUC 0-48), actual concentrations over time,
- Pharmacokinetics of RLX030: Cmax steady state (Cmaxss) concentration, clearance of serelaxin

Study description

Background summary

The purpose and rationale of this study is to evaluate the safety of repeat 48 hour IV serelaxin (RLX030A) dosing through the detection of anti-serelaxin antibodies and any related adverse events. Data from this study will be collected from a stable CHF subject population and used to support registration of serelaxin as a treatment to improve outcomes in subjects with acute heart failure.

Study objective

Primary:
Assess the safety of repeat doses of serelaxin in chronic heart failure

Secondary:
- Assess the incidence rate of adverse events of special interest, indicative of hypersensitivity reactions
- Assess the safety and tolerability of repeated infusions of serelaxin relative to placebo, in subjects with chronic heart failure
- Characterize the pharmacokinetics of serelaxin during and after administration of repeated infusions

Study design

This is a multicenter, randomized, double-blind, parallel group, placebo-controlled, 2-arm trial to evaluate the safety of repeated serelaxin exposure in subjects with stable, chronic heart failure (CHF NYHA Class II * III)

Intervention

IV infusion with serelaxin/placebo for 48 hours; 3x.

Study burden and risks

Burden and risks of participation is the chance of side effects from the study medication and inconveniences of blood sampling and the infusion.

The known side effects of the study medication include reducing blood pressure, anemia and menstrual disorders (longer, heavier, irregular / more frequent bleeding). Reduction of blood pressure and anemia can cause symptoms such as dizziness or fainting. Reduction of potassium in the blood is also observed during treatment with serelaxin. A decrease of potassium in the blood can lead

to symptoms such as muscle weakness, muscle cramps, and a disturbed heart rhythm.
In addition, antibodies are observed after treatment with serelaxin. Up to now, no adverse effects of antibodies seen. Serelaxin is a protein. That means there is a risk of severe allergic reactions. These are allergic reactions such as a greatly reduced blood pressure and respiratory problems.

Risks and discomforts are expected to be minor and acceptable.

3x IV infusion requiring hospitalization for 53 hours. At least 6 visits and more frequent blood sampling, measurement of weight, respiratory rate, blood pressure, pulse and body temperature and performing physical examination than standard. Total duration is estimated at a minimum of 172 hours.

There is no standard therapy denies.

There is no therapeutic effect is expected during this study, however, this study may provide useful information for the future.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Body weight of * 160 kg
- Subjects with compensated CHF (NYHA Class II * III) at time of screening with a prior documented history of chronic heart failure
- NT-proBNP >300 pg/ml (according to central measurement) at visit 1
- Subjects treated with appropriate and guideline-indicated CHF standard of care
- Ability to comply with all requirements, including ability to receive at least a 48 hour infusion plus follow-up time required for each dosing visit.

Exclusion criteria

- Current acute decompensated HF
- Any major solid organ transplant recipient or planned anticipated organ transplant within 1 year
- Documented history of untreated ventricular arrhythmia with syncopal episodes, ventricular tachycardia, or ventricular fibrillation without ICD (implantable cardioverter defibrillator) with significant hemodynamic consequences within the 3 months prior to screening
- Presence of hemodynamically significant mitral and /or aortic valve disease, except mitral regurgitation secondary to left ventricular dilatation: including significant left ventricular outflow obstruction (e.g., obstructive hypertrophic cardiomyopathy, severe aortic stenosis)
- Subjects with severe renal impairment defined as prerandomization eGFR < 30 ml/min/1.73m2 calculated using the sMDRD equation and/or those receiving current or planned dialysis or ultrafiltration

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-11-2014
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Serelaxin
Generic name:	Relaxin

Ethics review

Approved WMO Date:	21-07-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-09-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-09-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2013-002781-39-NL
ClinicalTrials.gov	NCT01982292
CCMO	NL49578.042.14