A Phase I, Single-Centre, Randomized, Double-Blind, Placebo Controlled, Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of ARA 290 Administered Intravenously to Healthy Subjects, and extension in renal patients

Published: 18-07-2008
Last updated: 06-05-2024

The present study will investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of ARA 290 administered intravenously to healthy subjects, and of intravenously and subcutaneously administered ARA 290 to renally impaired subjects.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Allergic conditions
Study type	Observational invasive

Summary

ID

NL-OMON33878

Source
ToetsingOnline

Brief title
ARA 290 multiple dose

Condition

- Allergic conditions
- Glucose metabolism disorders (incl diabetes mellitus)

- Renal disorders (excl nephropathies)

Synonym
allergic reaction, histamine-induced skin response

Research involving
Human

Sponsors and support

Primary sponsor: Araim Pharmaceuticals, Inc
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: erythropoietin, healthy volunteers, histamine, tissue protection

Outcome measures

Primary outcome

The safety and tolerability of ARA 290 after multiple dosing.

The pharmacokinetics of ARA 290 after multiple dosing.

The suppression of histamine-induced wheal and flare by multiple doses of ARA 290 (part 1).

Renal and endothelial function after a single iv or sc dose of ARA 290 (part 2).

Secondary outcome

The effects of multiple doses of ARA 290 on renal function, by measuring creatinin clearance, protein excretion, endothelin-1 excretion, and fractional sodium excretion.

The effects of multiple doses of ARA 290 on insulin resistance as measured by fasting insulin and glucose.

Study description

Background summary

ARA 290 is an 11-amino acid, linear peptide that is being developed as a tissue protective peptide. ARA 290 mimics the tissue protective pharmacology of erythropoietin (EPO) but is not erythropoietic.

ARA 290 and related peptides have been shown to be active in preclinical models of stroke, renal ischemia-reperfusion, renal and neuronal cisplatinum toxicity, diabetic neuropathy and retinopathy, sciatic nerve crush injury, wound healing, and in suppressing the wheal induced by intradermally administered histamine

Study objective

The present study will investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of ARA 290 administered intravenously to healthy subjects, and of intravenously and subcutaneously administered ARA 290 to renally impaired subjects.

Study design

This is a:
1) single-centre, randomized, double-blind, placebo controlled, multiple ascending dose study.
Dosing group will consist of two groups of seven healthy subjects (5 active treatment and 2 placebo per group, total of 14 subjects).
2) single-centre, randomized, double-blind, placebo controlled, single dose study (iv versus sc) in 1 cohort of 6 renally impaired subjects.

Study burden and risks

Unexpected adverse reactions.
Clinical significant findings during screening.
Hematoma following venapunctures.

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

1. Subjects must be 18-65 years of age (inclusive);
2. Body Mass Index (BMI) between 18 and 30 kg/m2 (inclusive) and body weight between 50 kg and 90 kg (inclusive);
3. History of good physical and mental health;
4. Subject has no clinically significant abnormality on the electrocardiogram performed;
5. Subject is a non-smoker or has not used nicotine/nicotine-containing products for at least 3 months;
6. Subject is able to read and understand the written consent form, complete study-related procedures, and communicate with the study staff;
7. Subject is willing to comply with study restrictions.;Renal patients: creatinin clearance between 30 and 60 mL/min, other criteria comparable to healthy volunteers.

Exclusion criteria

1. Clinically relevant abnormal laboratory results, ECG, vital signs, or physical findings;
2. Subject has a semi recumbent systolic blood pressure of >150 mmHg and or diastolic blood pressure of > 90 mmHg;
3. Subject has an estimated creatinin clearance <80 mL/min based on the Cockcroft-Gault equation.

4. Positive test for hepatitis B, C or HIV;
5. Positive pregnancy test;
6. Male subjects must consent to use a medically acceptable method of contraception throughout the entire study period and for 3 months after the study is completed. Female subjects must be either post-menopausal (last menstrual period > 2 years ago and FSH > 25 IU/L), surgically sterilized (> 6 months ago), or hysterectomized;
7. History of alcoholism or substance abuse within three years prior to screening;
8. Positive drug or alcohol test;
9. Male subjects habitually using more than 21 units of alcohol per week and female subjects using more than 14 units of alcohol per week;
10. Subject is unable to refrain from or anticipates the use of prescription medication in the period beginning one week prior to administration of the initial dose of the study drug until the post study visit;
11. Subject has a history of severe allergies, or has had an anaphylactic reaction or significant intolerability to prescription or non-prescription drugs or food;
12. Subjects that received a vaccination or immunization within the last month;
13. Participation in an investigational drug trial in the 3 months prior to administration of the initial dose of study drug;
14. Subject who has undergone major surgery within three months prior to screening;
15. Donation or loss of blood (> 500 mL) within 3 months prior to screening;
16. Subjects who have a reaction to the negative control of the histamine test when tested on Day -1;
17. Any abnormalities on the back of the subject which would interfere with the histamine skin prick test as judged by the investigator (e.g. persons with dermatographism, eczema, tattoos or with dark skin-tones which would inhibit clear determination of wheal and flare for histamine assay);
18. Inadequate venous accessibility as judged by clinicians (physician or nurse).
19. Any other condition that in the opinion of the investigator would complicate or compromise the study, or the well being of the subject.;Renal patients: criteria comparable with healthy volunteers, except for conditions related to chronic kidney disease.

Study design

Design

Study type:	Observational invasive
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):	25-09-2008
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	18-07-2008
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	13-08-2008
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	11-03-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2008-004617-10-NL
CCMO	NL24175.058.08