A Single-Centre, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of ARA 290 Administered Intravenously to End-Stage Renal Disease Patients

Published: 18-09-2009
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The present study will investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of ARA 290 administered intravenously to patients with ESRD.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional

Summary

ID

NL-OMON33202

Source
ToetsingOnline

Brief title
ARA 290 ESRD

Condition

- Renal disorders (excl nephropathies)

Synonym
end-stage renal disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: erythropoietin, ESRD, tissue protection

Outcome measures

Primary outcome

The study endpoints are safety and tolerability parameters (12-lead ECG, haematology, blood biochemistry including hs-CRP, adverse events), pharmacokinetics of ARA 290 (venous blood samples at 3, 6 and 12 min). Blood sampling for hs-CRP will be performed at the start of each hemodialysis session. If a reduction in hs-CRP is seen in this study, blood samples that will be collected in the study may be subjected to additional analyses to further characterize the anti-inflammatory effects of ARA 290.

Secondary outcome

N/A

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 patients with ESRD.

Study design

Single-centre, randomized, double-blind, placebo-gecontrolled study with multiple doses of ARA 290. Both cohorts will consist of 6 adult patients with ESRD (4 active treatment and 2 placebo). If there is a clear effect (defined as a decrease in hs-CRP >50% from baseline) dose-escalation will be reconsidered and will follow only after an extension of the number of patients that will be dosed with 0.7 mg ARA 290 (in a 1:2 placebo:active fashion) to unambiguously confirm the effects observed in the first 6 patients.

Intervention

Intravenous administration of ARA 290 or placebo (6 doses).

Study burden and risks

Unexpected adverse reactions.

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

• Be able to read and understand the written consent form, complete study-related procedures, and communicate with the study staff;
• Willing to comply with study restrictions;
• Between 18 and 65 years of age (inclusive).
• Body Mass Index (BMI) between 18 and 30 kg/m2 (inclusive);
• Diagnosis of clinically stable ESRD, as determined by the investigator;
• Requiring regular dialysis therapy for at least 12 weeks prior to first administration of study agent;
• Receiving treatment with IV or SC erythropoietin receptor agonist for a minimum of 8 weeks prior to administration of study agent, requiring doses to remedy EPO-resistance, with evidence of stable hemoglobin levels;
• Baseline hemoglobin values between 9.0 and 12.0 g/dL (5.6 - 7.5 mmol/L) before entering the study;
• CRP levels of at least 7 mg/L;
• Normal serum folate and vitamin B12 levels at screening;
• Having a creatinine clearance below 15 mL/min (chronic kidney disease stage 5), based on the Cockcroft-Gault equation

Exclusion criteria

• Clinically relevant abnormal history of physical and mental health other than conditions related to chronic kidney disease of patient, as determined by medical history taking (as judged by the investigator);
• Clinically relevant abnormal laboratory results, ECG, vital signs, or physical findings other than conditions related to chronic kidney disease of patient (as judged by the investigator);
• Subject has uncontrolled hypertension;
• Subject is unable to refrain from the use of disallowed concomitant medication from one

week prior to the first study drug administration until follow-up assessments;
• Subject has a history of severe allergies, or has had an anaphylactic reaction or significant intolerability to prescription or non-prescription drugs or food;
• Subject has a history of syncopal episodes;
• Subjects that received a vaccination or immunization within the last month;
• Participation in an investigational drug trial in the 3 months prior to administration of the initial dose of study drug or more than 4 times per year;
• Subject has undergone major surgery within six months prior to screening;
• Any other condition that in the opinion of the investigator would complicate or compromise the study, or the well being of the subject.

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):	12-01-2010
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO

Date:	18-09-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Approved WMO Date:	21-10-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	26-04-2010
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	15-12-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	23-01-2012
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	EUCTR2009-014838-14-NL
CCMO	NL29277.058.09