A phase II study of ARA 290 as therapeutic strategy in no-option critical limb ischemia patients.

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A proof of concept study to test whether ARA 290 improves wound healing and reduces neuropathic pain in no-option patients with CLI

Ethical review	Approved WMO
Status	Will not start
Health condition type	Skin and subcutaneous tissue therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON34878

Source
ToetsingOnline

Brief title
ARA 290 as therapeutic strategy in critical limb ischemia patients.

Condition

- Skin and subcutaneous tissue therapeutic procedures
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Critical limb ischemia

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,ARAIM Pharmaceuticals

Intervention

Keyword: ARA 290, Critial limb ischemia, Erytropoeitin

Outcome measures

Primary outcome

Wond healing

Pedal pain

Local inflammation

Secondary outcome

Systemic inflammation

Safety

Study description

Background summary

Critical Limb Ischemia (CLI) is the end-stage of lower extremity peripheral artery disease in which severe obstruction of blood flow results in ischemic rest pain, ulcers/gangrene and a significant risk for limb loss. CLI is responsible for an estimated 220,000-240,000 amputations yearly in the United States and Europe, and is a source of significant mortality, morbidity, disability and social and economic costs. The annual costs of CLI have recently been estimated to be > $10 billion for the United States alone. Current strategies for CLI are revascularization, restoring blood supply to the ischemic area. Unfortunately, in a substantial proportion of patients (i.e. patients with diabetes mellitus(1) or patients requiring distal repair in the absence of an adequate vein graft) the prospects of intervention are notably poor, and in patients with small vessel disease and occlusion of the tibial arteries intervention may even be impossible. Prognosis for these patients in terms of quality of life, life expectancy and costs is poor, and these patients can only be treated by a below- or above-knee amputation.
Erythropoietin (EPO) is a well-known stimulator of erythrocyte production and widely used in the treatment of anemia caused by kidney disease, cancer, or chronic inflammation Over the past decade, it has become evident that erythropoietin, besides its effect on hematopoiesis, possesses many other biological activities that can generally be summarized as counteracting the

actions of proinflammatory cytokines and their deleterious effects in tissue injury). In these nonhematopoietic activities, EPO is locally produced in the immediate vicinity of the injury.
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 but is devoid of its haematopoietic effects. In preclinical models of tissue damage ARA 290 has been shown to exhibit general anti-inflammatory activities, to promote wound healing in various animal models of impaired wound healing, and to promote neuroregeneration (including a profound reduction of neuropathic pain in animal models of this pathology). These observations suggest that activation of the tissue protective erythropoietin receptor may promote tissue homeostasis in CLI, thereby limiting tissue loss and pain.

Study objective

A proof of concept study to test whether ARA 290 improves wound healing and reduces neuropathic pain in no-option patients with CLI

Study design

A randomized placebo controlled study of ARA 290 or placebo in no option critical limb ischemia patients

Intervention

ARA 290 or placebo

Study burden and risks

The clinical experience with ARA 290 is very limited. Thus far no side effects have been upserved in phase I studies (multiple doses up to 2 mg per dose).

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

Critical limb ischemia
No option for conventional revascularization
Written informed consent
Expected life expectancy > 1 year

Exclusion criteria

Overt diabetic disease
Clinically relevant abnormal history of physical and mental health other than conditions related to CLI, 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 CLI (as judged by the investigator)
Subject has a history of severe allergies, or has had an anaphylactic reaction or significant intolerability to prescription or non-prescription drugs or food
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
Use of erythropoietin, systemic corticosteroids (e.g. prednisone etc.) and other immune modulatory drugs

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:	Will not start
Start date (anticipated):	01-05-2010
Enrollment:	12
Type:	Anticipated

Ethics review

Approved WMO Date:	29-04-2010
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	23-07-2010
Application type:	First submission
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	EUCTR2010-018584-41-NL
CCMO	NL31947.058.10