Allogeneic mesenchymal Stromal cells for Angiogenesis and neovascularization in no-option Ischemic Limbs

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Primary Objective: To investigate whether intramuscular administration of allogeneic MSCs is safe and potentially effectiveSecondary Objective: To investigate the potential of various markers related to inflammation, angiogenesis, and...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Interventional

Summary

ID

NL-OMON45407

Source
ToetsingOnline

Brief title
SAIL Trial

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
PAOD Fontaine 3-4, Severe Limb Ischemia (SLI)

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Angiogenesis, Clinical trial, Mesenchymal stromal cells, Severe limb ischemia

Outcome measures

Primary outcome

Primary outcome is therapy success at 6 months, which is a composite outcome measure considering mortality, limb status, clinical status (Rutherford classification) and changes in pain score.

Secondary outcome

Secondary outcomes are the incidence of major (amputation through or above the ankle joint) and minor (distal from the ankle joint) amputations, mortality, changes in the number and extent of leg ulcers, ulcer healing, clinical classification, pain-free walking distance (PFWD), ankle-brachial (ABI) and toe-brachial index (TBI), and quality of life (EuroQoL 5-D (EQ5D) and SF-36).
In addition to biochemical parameters we will assess markers for endothelial activation and injury, inflammation, oxidative stress, circulating progenitor cells, cytokines and growth factors and immunological responses.

Study description

Background summary

Severe limb ischemia (SLI) has major impact on quality of life, morbidity and mortality. Many patients are not eligible for revascularization, leaving amputation as only option. Mesenchymal stem or stromal cells (MSC), because of their immunomodulatory and vasculoregenerative properties, may provide a novel therapy for SLI. Allogeneic MSC therapy is attractive as it may be used as *off-the-shelf* available treatment and allows testing and selection of isolates before administration.

Study objective

Primary Objective: To investigate whether intramuscular administration of allogeneic MSCs is safe and potentially effective
Secondary Objective: To investigate the potential of various markers related to inflammation, angiogenesis, and neovascularization to predict therapeutic efficacy and prognosis.

Study design

A randomized, double-blinded, placebo-controlled clinical trial with 6 months follow-up. Randomization will be performed by the Cell Therapy Facility of the UMC Utrecht by means of a computerized table. Subjects will be allocated to receive either MSC or placebo in a 1:1 fashion. The treatment (MSC) or placebo will be administered by intramuscular injections in the most affected leg.

Intervention

Intramuscular allogeneic BM-MSC injection: MSCs will be extracted from BM of healthy volunteers, expanded with human platelet lysate, and stored. Patients will be randomized (1:1) to receive intramuscular injections (30 sites) of either placebo, or 150*106 allogeneic BM-MSC in the most affected limb. Blinded syringes are provided and cell suspensions will be injected intramuscularly by an experienced operator into multiple sites (30 sites, 1-1.5cm in depth, volume of 1.0mL placebo or MSC per site) in the ischemic lower extremity.

Study burden and risks

Burden: Subjects will be screened during an inclusion visit (t=0). They will be physically examined and blood samples will be taken (40mL). Baseline measurements will be performed, including treadmill test, ABI, TBI, digital photographs and measurements of any existing ulcers. An appointment for the intervention will be made. There are 3 follow-up visits. At the first follow-up visit, 1 week after the intervention, blood will be drawn and patients will be screened for potential side-effects. Subsequent visits will take place at 2 and 6 months follow-up and include physical examination, treadmill test, ABI, TBI, digital photographs and measurements of any existing ulcers. Quality of life questionnaires (EuroQoL 5-D (EQ5D) and SF-36) will be administered at baseline and 2 and 6 months follow-up. Patients are subjected to venepuncture four times during which blood will be drawn (40 mL at inclusion and after 1 week and 20 mL at each subsequent follow-up visit). After completion of the trial patients will be contacted every year for 5 years to assess status of hard clinical outcomes during long-term follow-up, i.e. limb status and mortality. In case of death, the general practitioner will be contacted. Patients will also be asked to fill out the quality of life (EuroQoL 5-D (EQ5D) and SF-36) questionnaires every year, until 5 years after completion of the trial.

Safety: An independent Data and Safety Monitoring Board (DSMB) will review the status and conduct of the clinical trial, evaluate all causes of death and cardiovascular events and make recommendations to the clinical research group concerning the trial*s continuation and modification. If in interim analyses important clinical differences between groups become evident, the trial will be stopped and patients will be offered the best treatment available. All patients will be carefully monitored for side effects due to intramuscular injections, changes in clinical parameters (temperature, blood pressure, heart rate) and changes in renal, hepatic and metabolic parameters.

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

-age >18 years

-severe peripheral artery disease (PAD) (Fontaine class III or IV) (Rutherford 4 or 5)
-persistent, recurring rest pain requiring analgesia, and/or non-healing ulcers present for >4 weeks without evidence of improvement in response to conventional therapies
-ankle brachial index (ABI) <0.6 or "non-compressible/ unreliable"
-not eligible for surgical or endovascular revascularization
-written informed consent.

Exclusion criteria

-history of neoplasm or malignancy in the past 10 years
-serious known concomitant disease with life expectancy <1 year
-Rutherford 6 in which amputation on the short term (within 1-2 weeks) is inevitable
-Pregnancy or unwillingness to use birth control measures such as oral contraceptives or other (hormonal, uterine implant, barrier method) precautions during study
-uncontrolled infection with systemic symptoms
-follow-up impossible

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
Enrollment:	60
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cels allogenic

Ethics review

Approved WMO Date:	25-01-2017
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2016-003488-20-NL
CCMO	NL59038.000.16
Other	volgt