Intravenous Administration of In Vitro Expanded Mesenchymal Stem Cells in Patients with Pulmonary Arterial Hypertension due to Systemic Sclerosis; A Safety and Feasibility Study

Published: 22-12-2014
Last updated: 22-04-2024

The main objective is assessment of safety and feasibility of intravenous administration of autologous, in vitro expanded, mesenchymal stem cells in patients with pulmonary arterial hypertension due to systemic sclerosis. The secondary objective is...

Ethical review	Not approved
Status	Will not start
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON41219

Source
ToetsingOnline

Brief title
Cell therapy in pulmonary arterial hypertension due to systemic sclerosis.

Condition

- Heart failures
- Pulmonary vascular disorders

Synonym
increased pulmonary artery pressure, pulmonary arterial hypertension

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cell therapy, Mesenchymal Stem Cells, Pulmonary Arterial Hypertension, Systemic Sclerosis

Outcome measures

Primary outcome

The administration of autologous bone marrow-derived in vitro expanded mesenchymal stem cells will be considered feasible if all the procedures in the protocol can be performed as described. Safety will be reflected as the rate of (serious) adverse events in the study population during a follow up of 3 months.

Secondary outcome

Preliminary efficacy will be described as change in quality of life, functional class, exercise capacity, pro-brain natriuretic peptide levels, electrocardiographic and echocardiographic characteristics, and pulmonary function and pulmonary pressure measurements before and after the procedure.

Study description

Background summary

In patients with systemic sclerosis, pulmonary arterial hypertension has a poor prognosis with a one-year mortality rate of 30%. Despite optimal pharmacological treatment, patients experience daily complaints. Hence, new treatment regiments are needed. In preclinical studies it is suggested that intravenous administration of autologous bone marrow-derived mesenchymal stem

cells can be a potential treatment option.

Study objective

The main objective is assessment of safety and feasibility of intravenous administration of autologous, in vitro expanded, mesenchymal stem cells in patients with pulmonary arterial hypertension due to systemic sclerosis. The secondary objective is preliminary assessment of efficacy.

Study design

In the proposed pilot study 7 patients with systemic sclerosis and pulmonary arterial hypertension will be enrolled. 100 millilitres of bone marrow will be aspirated from the iliac crest. Mesenchymal stem cells will be separated with ficol density gradient and expanded ex vivo. After approximately 9 weeks a dose of .5-2*10^6 cells/ kg bodyweight will be administrated intravenously.

Intervention

Bone marrow will be aspirated from the iliac crest. Expanded mesenchymal stem cells will be administrated intravenously and reach the pulmonary circulation through the the right side of the heart.

Study burden and risks

Because of the poor prognosis with a one-year mortality rate of 30% in patients with systemic sclerosis and pulmonary arterial hypertension, there is a need for new treatment options. Since pre-clinical studies suggest a positive effect and previous studies did not show severe die effects in human after peripheral administartion of MSC's, it seems justifiable to investigate whether this patient population might benefit from this treatment.

Risks:
On beelding and infection after invasive procedures
Rontgen radiation exposure (catheterization, X-thorax en CT-thorax)
Complications catheterization (Nederlandse hartstichting)

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

- Pulmonary arterial hypertension, defined as a mean pulmonary artery pressure (mPAP) *25mmHg at rest with a pulmonary capillary wedge pressure (PCWP) of <15 mmHg.
- Systemic sclerosis, diagnosed according to the criteria for the classification of systemic sclerosis by The American College of Rheumatology
- Optimal medical PAH treatment
- Age * 18 years and life expectancy more than 3 months
- Able and willing to undergo catheterisation and echocardiography
- Written informed consent
- Pulmonary and haemodynamic stable for at least 3 months
- NYHA functioning class *2

Exclusion criteria

- Evidence of cancer in past 5 years (except low grade and fully resolved non-melanoma skin malignancy)
- Concurrent participation in a study using an experimental drug or an experimental procedure within 2 months before the administration procedure.
- Suspected presence of pulmonary hypertension caused by left heart disease resulting in an increased wedge pressure (group II,Nice 2013(8))

- Suspected presence of pulmonary hypertension due to pulmonary disease and/or hypoxia (group III, Nice 2013 (8)), as assessed by our PAH working group.
- Other severe concurrent illnesses (including active infection).
- Bleeding diathesis, infection with the human immunodeficiency virus (HIV) or pregnancy.
- Any other condition that, in the opinion of the investigator, could pose a significant threat to the subject if the investigational therapy would be initiated.
- Inability to undergo cardiac catheterization.
- Inability to follow the protocol and comply with follow-up requirements.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	8
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cells autologous

Ethics review

Not approved

Date:	16-12-2014
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	EUCTR2014-003133-26-NL
CCMO	NL50143.000.14