Stem Cell therapy in IschEmic Non-treatable Cardiac disease - SCIENCE

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON47824

Source
ToetsingOnline

Brief title
SCIENCE

Condition

- Heart failures

Synonym
ischaemic heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Rigshospitalet Copenhagen University Hospital, Capital Region of Denmark
Source(s) of monetary or material Support: Europese unie grant No 643478; Horizon 2020

Intervention

Keyword: Allogeneic adipose tissue-derived stromal/stem cell therapy, chronic, ischaemic heart failure, old myocard infarction

Outcome measures

Primary outcome

The primary endpoint is change in left ventricle end-systolic volume (LVESV) at 6 months follow-up between CSCC_ASC and placebo treated measured by echocardiography.

Secondary outcome

The secondary endpoints are safety evaluated by development of allogeneic antibodies and laboratory safety measurements 1, 3, 6 and 12 months after treatment and changes in left ventricular ejection fraction (LVEF), end-diastolic volume and myocardial mass at 6 months follow-up. The changes in left ventricle function will be measured by echocardiography (ECHO) or computed tomography (CT). LVESV is a widely used measure of the functional status of the left ventricle and is superior to LVEF for prediction of survival in patients with LVEF below 50%. Other secondary endpoints are changes in NYHA, CCS, Kansas City Cardiomyopathy Questionnaire, Seattle Angina Questionnaire, 6 min walking test, additional echocardiographic measures (Global strain %, left atrium volume, e*, s*) and NT-pro-BNP. In addition, safety of allogeneic CSCC_ASCs with respect to incidence and severity of serious adverse events and suspected unrelated serious adverse events will be evaluated at 12 months follow-up. A combined endpoint of

1. death, hospitalization for worsening heart failure including inserting of a

bi-ventricular pacemaker, hospitalization because of ventricular tachycardia or fibrillation 1, 2 and 3 years after treatment

2. death, hospitalization for any cardiovascular reason, hospitalization for worsening heart failure including inserting of a bi-ventricular pacemaker, hospitalization because of ventricular tachycardia or fibrillation 1, 2 and 3 years after treatment.

Study description

Background summary

Ischemic heart disease (IHD) caused by coronary artery disease is the most common cause of death with more than 17 million deaths worldwide each year and a major cause of hospital admissions in industrialized countries. ((World Health Organization, 2011)
It is an increasing economic health problem due to increasing morbidity in an ageing population. Classical therapies have reduced mortality of IHD significantly, but left an increasing number of patients with chronic IHD and/or heart failure without further treatment options.
Thus, there is an unmet need for novel, effective treatments for chronic IHD and heart failure to improve patient*s survival and quality of life and reduce health care costs. Stem cell therapy is emerging as a viable therapeutic option in this patient group as well as in several debilitating diseases for which no cure is currently available.
To implement and disseminate a new clinical therapy with stem cells to all potential candidates, safety and efficacy has to go hand-in-hand with feasibility, - it has to be logistically easy to request and perform the treatment. There are however many logistical obstacles in the present used clinical models for stem cell therapies within cardiology.
At the moment, most frequently autologous stem cells are used for the treatment of patients with ischemic heart disease. Yet the properties and proliferation rate of the obtained cells differ considerably from patient to patient. Therefore, it is difficult to treat patients with a standardized number of cells in the clinical studies. Moreover, it is logistically difficult to schedule the treatment procedure due to large variations in cell production time.
The Advanced Therapy Medicinal Product (ATMP) regulation has increased considerably within the last years. Presently, only few hospitals within the European Union have cell culture facilities approved for ATMP production.

Combined with the use of autologous treatment this leads to administratively, logistical and cost extensive transportation issues.
The project proposes a new stem cell treatment concept (intra-myocardial injections of allogeneic adipose derived stem cells (ASCs) manufactured in concordance with ATMP regulations), which is logistically easy to implement in clinical practice by elimination of the many hurdles identified during production of autologous stem cell medicinal products and conduction of clinical trials, e.g. the manual handling of cell production, transportation back and forth of tissues and cells, mismatch between readiness of the cell product and the patient*s clinical condition, availability of patients, trained personal and catheterization facilities.
We expect that intra-myocardial injection of allogeneic adipose derived stem cells (ASCs), will increase quality of life and survival for patients with chronic IHD and/or heart failure end reduces health care costs.
The SCIENCE project aims at allogeneic ASC therapy as an established and approved hospital standard care for patients with severe heart failure due to coronary artery disease. The project builds on proven safety and efficacy of mesenchymal stromal cell therapy in clinical phase I and II trials with patients with coronary heart disease and heart failure performed by members of the consortium (Friis 2011, Haack-Sørensen 2013, Mathiasen 2012, 2013, Qayyum 2012, Tendera 2009, Gyöngyösi 2009, Vrtovec 2013, 2013, Heeger 2012).
The idea behind this study is also to show that stem cell therapy is not just effective and safe but also an accessible, feasible and economically sound therapeutic option for patients with IHD and severe heart failure.

Study objective

The idea behind this study is to show that stem cell therapy is not just effective and safe but also an accessible, feasible and economically sound therapeutic option for patients with IHD and severe heart failure

The present aim is to perform at clinical double-blind placebo-controlled CSCC_ASC multicentre study in heart failure patients in Europe to investigate the regenerative capacity of the CSCC_ASC treatment.

The overall aim is to establish the relevant clinical documentation of the regenerative capacity of CSCC_ASC treatment in patients with heart failure from two supplementary clinical trials which then can be forwarded to the European Medicines Agency for a final approval of allogeneic CSCC_ASC therapy as standard care therapy in patients with ischemic heart failure in European Countries.

Study design

Patients will be randomized (2:1) to either CSCC_ASC or placebo (saline).

Treatment group:
NOGA mapping guided injection of 100 million allogeneic adipose derived stem cells (CSCC_ASC) with MYOSTAR injection catheter

Control group:
NOGA mapping guided injection of placebo (saline) with MYOSTAR injection catheter

Intervention

Treatment group:
NOGA mapping guided injection of 100 million allogeneic adipose derived stem cells (CSCC_ASC) with MYOSTAR injection catheter

Control group:
NOGA mapping guided injection of placebo (saline) with MYOSTAR injection catheter

Study burden and risks

Burden:
Patients have the following additional investigations:
5 transthoraric ultrasound examination of the heart
2 CT and/or MRI of the heart
5 NYHA and CCS classification
5 Kansas City Cardiomyopathy Questionnaire, Seattle Angina Questionnaire and EQ-5d Questionnaire
Routine investigations like physical examination and ECG
8 times bloodtesting (ca 20 mL each)
5 times 6 min walktest,
5 times registration of serious adverse events en suspected unrelated serious adverse events
1 NOGA mapping guided injection of allogeneic adipose derived stem cells (CSCC_ASC)/placebo with MYOSTAR injection catheter

Risk:
Based on conducted clinical trials with allogeneic mesenchymal stem cells and ASCs it is not expected that there will be any side-effects to the use of the allogeneic CSCC_ASC product.
Other risks to the patient are associated with the procedures performed (mentioned above) and are considered low.

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

Inclusion criteria:
1. 30 to 80 years of age
2. Signed informed consent
3. Chronic stable ischemic heart disease
4. Symptomatic Heart failure (NYHA II-III)
5. LVEF <=45% on echocardiography, CT or MRI scan.
6. Plasma NT-pro-BNP > 300 pg/ml (> 35 pmol/L)
7. Maximal tolerable heart failure medication
8. Medication unchanged two months prior to inclusion/signature of informed consent. Changes in diuretics accepted.
9. No option for percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG)
10. Patients who have had PCI or CABG within six months of inclusion must have a new angiography less than one month before inclusion or at least four months after the intervention to rule out early restenosis

11. Patients cannot be included until three months after implantation of a cardiac resynchronisation therapy device (CRTD) and 1 month after an ICD unit

Exclusion criteria

Exclusion criteria
1. Heart Failure (NYHA I or IV)
2. Acute coronary syndrome with elevation of CKMB or troponins, stroke or transitory cerebral ischemia within six weeks of inclusion. Constant elevated troponin due to renal failure, heart failure etc. do not exclude the patient.
3. Other revascularisation treatment within four months of treatment
4. If clinically indicated the patient should have a coronary angiography before inclusion
5. Moderate to severe aortic stenosis (valve area < 1.3 cm2) or valvular disease with option for surgery or interventional therapy.
6. Aortic valve replacement with an artificial heart valve. However, a trans-septal treatment approach can be considered in these patients.
7. If the patient is expected to be candidate for MitraClip therapy of mitral regurgitation in the 12 months follow-up period.
8.. Diminished functional capacity for other reasons such as: obstructive pulmonary disease (COPD) with forced expiratory volume (FEV) <1 L/min, moderate to severe claudication or morbid obesity
9. Clinical significant anaemia (haemoglobin < 6 mmol/L), leukopenia (leucocytes < 2 109/L), leucocytosis (leucocytes >14 109/L) or thrombocytopenia (thrombocytes < 50 109/L)
10. Reduced kidney function (eGFR < 30 ml/min)
11. Left ventricular thrombus
12. Anticoagulation treatment that cannot be paused during cell injections. Patients can continue with platelet inhibitor treatment
13. Patients with reduced immune response
14. History with malignant disease within five years of inclusion or suspected malignity - except treated skin cancer other than melanoma
15. Pregnant women
16. Other experimental treatment within four weeks of baseline tests
17. Participation in another intervention trial
18. Life expectancy less than one year
19. Known hypersensitivity to DMSO, penicillin and streptomycin

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-04-2017
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cels allogenic

Ethics review

Approved WMO Date:	28-10-2015
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-01-2017
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-09-2017
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-09-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	30-08-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-12-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-11-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-01-2020
Application type:	Amendment
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	EUCTR2015-002929-19-NL
CCMO	NL54174.000.15