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INtramyocardial application of STEM cells in combination with transmyocardial laser revascularisation in coronary artery bypass graft patients

Submission date
08/05/2007

Registration date
15/06/2007

Last Edited
08/07/2014

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Circulatory System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2005-004051-35

Protocol serial number
Instem_HHU_2005

Study information

Scientific Title

Acronym
INSTEM-Trial

Study objectives
Conditions studied: Patients with poor distal vessels, total arterial occlusion, or unacceptable procedural risks due to concomitant medical conditions. Up to 15% of the patients with this end-stage coronary artery disease suffer from disabling anginal symptoms regardless of maximal pharmacotherapy and conventional revascularisations.

A prospective study to assess safety and efficacy of stem cell application with regard to regional myocardial improvement in patients with Coronary Artery Bypass Graft (CABG) and Transmyocardial Laser Revascularisation (TMLR).

Please note as of 24/01/2012, the anticipated start date has ben modified from 26/05/2007 to 04 /05/2007. The anticipated end date was modified from 01/01/2010 to 04/01/2012.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval received from the local ethics committee (Ethikommission der medizinischen Fakultät der Heinrich-Heine-Universität) on the 5th April 2006 (ref: MC-LKP-85).

Study design
Phase II, open, prospective, single-arm, four centre (Düsseldorf, Lübeck, Hannover und Heidelberg) clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Coronary artery bypass graft

Interventions
The aim of the intraoperative stem cell transplantation is to repopulate diseased myocardium with cells that could restore contractility. Results of experimental studies have shown that bone marrow derived stem cells can be used to regenerate cardiomyocytes and induce angiogenesis after myocardial infarction, resulting in improvement of myocardial function. The bone marrow aspiration and the operative procedure will be performed under one general anesthesia. The number of channels of TMLR must be at least 10 holes per territory and will be documented. The stem cells must be injected within the surrounding of these laser channels.

Intervention Type
Other

Phase
Phase II

Primary outcome(s)
Safety: occurrence of Major Adverse Cardiac Event (MACE) assessed at three months after surgical study treatment. MACE will be assessed by the investigator for relationship to the interventions under the investigation in this trial.

Key secondary outcome(s))
Secondary endpoints (assessed at 3, 6 and 12 months follow-up):
1. MACE assessed at 6 and 12 months follow-up
2. Cardiac Adverse Events (AEs) defined in the Common Toxicity Criteria (CTC) (assessed form onset of surgery up to 12 months follow-up)
3. Severity of angina and extent of treatment in comparison to baseline (Canadian Cardiovascular Society [CCS] classification) (assessed at 3, 6 and 12 months follow-up)
4. Quality of Life in comparison to baseline (increase of exercise tolerance in Seattle Angina Questionnaire) (assessed at 3, 6 and 12 months follow-up)
5. Baseline Regional cardiac function by cardiac MRI is assessed and in comparison to cardiac MRI at six months follow-up (in case of an contraindication against cardiac MRI the cardiac function is assessed by cardiac CT)

Completion date
04/01/2012

Eligibility

Key inclusion criteria
1. 18 years (male or female gender)
2. Presence of at least two vessel coronary artery disease with at least one vessel that is not amenable to CABG, according to the angiogram, this vessel must serve an area of viable myocardium
3. Area of interest defined as part of free left ventricular wall with reduced contractility as shown either in ventriculographia during angiography and/or preoperative echo
4. Demonstration of reduced perfusion in the area of interest by cardiac Magnetic Resonance Imaging (MRI) or Computed Tomography (CT)
5. Global ejection fraction greater than 15% and less than 35%
6. Signed informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Any condition that in the belief of the treating physician prevents successful stem cell collection or application (e.g. systemic infection, puncture for stem cell collection impossible)
2. Any condition that may adversely affect bone marrow (such as malignancy or prior irradiation to the pelvic bone)
3. Mitral valve insufficiency greater than II
4. History of ventricular arrhythmia, not controlled by medication and/or Automatic Implantable Cardioverter Defibrillator (AICD) required
5. Need of additional heart surgery (i.e. valve replacement)
6. Emergency or salvage operation defined as within 48 hours of diagnosis
7. Evidence of left ventricular thrombus
8. Previous heart surgery within the last six months (excluding implantation of pacemaker)
9. History of symptomatic carotid disease (e.g. any Transient Ischaemic Attack [TIA], Prolonged Ischaemic Neurological Deficit [PRIND], stroke) within the last three months prior to study intervention
10. Increased Creatine Kinase (CK) (greater than three times normal) in patients with unstable angina
11. End Stage Renal Disease (ESRD) defined as serum creatinine level greater than 3.5 mg/dL, or dialysis (renal replacement therapy)
12. Concurrent active chemotherapy for cancer
13. Life expectancy less than two years
14. Platelet count less than 100000/µl
15. Pregnancy
16. Participation in other clinical trials in the last 30 days
17. Active hepatitis-infection
18. Human Immunodeficiency Virus (HIV)-infection
19. Anaemia
20. Haemorrhagic diathesis in medical history
21. Sensitivity and incompatibility against used drugs or excipients
22. Disseminated intravascular coagulation in medical history
23. Clinically active infection at the time of operation
24. Patient not able to attend follow-up as specified in the protocol
25. No informed consent

Date of first enrolment
04/05/2007

Date of final enrolment
04/01/2012

Locations

Countries of recruitment
Germany

Study participating centre

Department of Thoracic and Cardiovascular Surgery
Duesseldorf
Germany
40225

Sponsor information

Organisation
Heinrich-Heine-University (Germany)

ROR
https://ror.org/024z2rq82

Funder(s)

Funder type
University/education

Funder Name
Heinrich-Heine-University (Germany)

Funder Name
PLC Medical Systems (USA)

Funder Name
Miltenyi Biotec (Germany) - stem cell kit supply

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
	results				

Results article	07/07/2014	Yes	No