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A multicentre randomized double blind placebo controlled trial of myocardial angiogenesis using VEGF165 intramyocardial gene delivery in patients with severe angina pectoris

Submission date
05/09/2005

Recruitment status
No longer recruiting

Registration date
05/09/2005

Overall study status
Completed

Last Edited
18/04/2008

Condition category
Circulatory System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
UCT-51532

Study information

Scientific Title

Acronym
Northern trial

Study objectives
To demonstrate the clinical efficacy and safety of vascular endothelial growth factor (VEGF165) when delivered by direct myocardial injection through the NOGA navigational catheter, to improve myocardial perfusion in patients with severe angina pectoris for whom conventional percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) are either not possible or not ideal. Secondary objective will be to determine the effects of VEGF gene therapy on angina symptoms, patient-perceived quality of life and exercise capacity.

Ethics approval required
Old ethics approval format

Ethics approval(s)
St. Michael's Hospital Research Ethics Board Office of Research Administration, 12/06/2002

Study design
Multicentre randomized double blind placebo controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Coronary artery disease with severe angina

Interventions
Randomisation NOGA Catheter Mapping and Administration of Gene Therapy. The NOGA catheter will be passed into the left ventricle across the aortic valve and endocardial mapping

carried out. Once the endocardial map is complete, an injection catheter will be introduced into the left ventricle. Patients will be randomly assigned to receive 2 mg of either plasmid DNA encoding the gene for VEGF 165 suspended in phosphate buffered saline or placebo (phosphate buffered saline) in 10 divided injection sites spaced at least 1 cm apart. Injections will be targeted to regions of ischaemia identified by nuclear imaging which correlate with electro-mechanical NOGA map.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Myocardial perfusion - Rest and Stress perfusion Scores (SRS), changes in Summed Stress Scores (SSS) from baseline to 12 weeks follow-up between placebo and VEGF treated groups; this analysis will be repeated at 6 months.

Secondary outcome measures
1. Symptom evaluation (Canadian Cardiovascular Society [CCS] class Seattle Angina Questionnaire)
2. Patient-perceived Quality of Life (36-item Short Form health survey [SF-36] questionnaire)
3. Exercise performance
4. Major Adverse Cardiac Events

Overall study start date
01/08/2002

Completion date
31/12/2006

Eligibility

Key inclusion criteria
1. Canadian Cardiovascular Class III or IV angina, despite treatment with maximal medical therapy (at least 2 of either long acting nitrates, beta-blockers or calcium channel blockers, and either aspirin or clopidogrel) for at least 4 weeks
2. Adequate secondary prevention medication and risk factor management optimized
3. Ischemic defects on myocardial stress SPECT imaging (include patients with a non-reversible defect having evidence of viability [echo, or other suggestion of wall motion])
4. Left Ventricular Ejection Fraction (LVEF) greater than or equal to 20%
5. Aged less than or equal to 75 years, either sex
6. Adequate feeder coronary vessels to the territories targeted for injection
7. LV wall thickness greater than 0.9 cm in target region (by echo)
8. Coronary angiography performed within the past 12 months
9. Coronary angiogram shows at least one inflow vessel without a proximal lesion greater than 70%

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
120

Key exclusion criteria
1. Pregnancy, lactation, or any childbearing potential
2. Evidence of or a known history of cancer within the past 10 years (except for low grade and fully resolved non-melanoma skin cancer)
3. History or diagnosis of age-related macular degeneration (age-related eye disease study [AREDS]) class 3 or higher
4. Abnormal retinal vascularity (mild, moderate, or sever non-proliferative retinopathy or proliferative retinopathy, or hypertensive hemorrhages or exudates)
5. History of diagnosis of rheumatoid arthritis
6. History of an explained gastrointestinal hemorrhage within the last 5 years
7. Hypervascular dermatologic disease (spider angioma, psoriasis etc.)
8. Serum creatinine, Liver Function Tests (LFTs), or Prothrobin (PT)/Partial Thromboplastin Time (PTT) greater than two times normal
9. Creatine Phosphokinase (CPK) greater than two times Upper Limit of Normal (ULN)
10. Haematocrit (HCT) 30% or Haemoglobin (Hb) less than 100 g/l, platelet count less than 75,000
11. Bleeding diathesis
12. Other severe concurrent illness
13. Ejection Fraction (EF) less than 20%
14. New York Heart Association (NYHA) class greater than 2
15. Single vessel disease involving either the left main or proximal left anterior descending artery for patients in Group 2
16. Recent (within 4 weeks) Myocardial Infarction (MI) (Creatine Kinase Myocardial Bands [CK-MB] greater than 3 x ULN)
17. Uncontrolled hypertension (Systolic Blood Pressure [SBP] greater than 200, or Diastolic Blood Pressure [DBP] greater than 110 mmHg)
18. Persistent atrial fibrillation (must be in NSR at time of NOGA mapping)
19. Frequent, recurrent or sustained ventricular arrhythmias
20. Left ventricular thrombus visualised by either echocardiography or contrast LV angiography
21. Primary valvular heart disease (i.e. AS, MS associated with chest pain)
22. Important aortic valve sclerosis or aortic valve sclerosis or aortic stenosis moderate in severity or greater, which might impede easy catheter access to the left ventricle across the aortic valve
23. Important ilio-femoral peripheral vascular disease limiting catheter access
24. Concurrent enrollment in a study using an experimental drug or procedure
25. Inability to undergo repeat nuclear testing
26. Inability to receive dipyridamole (severe asthma, bronchospasm)
27. Inability to follow the protocol and comply with follow-up
28. Inability to record an adequate NOGA map with at least 50 points and a well defined target area
29. Inability to provide informed consent

Date of first enrolment
01/08/2002

Date of final enrolment
31/12/2006

Locations

Countries of recruitment
Canada

Study participating centre
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Sponsor information

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Sponsor type
Not defined

ROR
https://ror.org/04skqfp25

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research (CIHR) (Canada) - http://www.cihr-irsc.gc.ca (ref: UCT-51532)

Funder Name
Heart and Stroke Foundation (Canada)

Funder Name
Johnson & Johnson (Canada) - 'in-kind' only

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration