

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	☐ Prospectively registered
Registration date 05/09/2005	Overall study status Completed	☐ Protocol
Last Edited 18/04/2008	Condition category Circulatory System	☐ 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

Contact name

Dr Duncan John Stewart

Contact details

St. Michael's Hospital

Division of Cardiology

30 Bond Street

Suite 6-050k Queen Wing

Toronto

Canada

M5B 1W8

+1 416 8645724

stewartd@smh.toronto.on.ca

Additional identifiers

Protocol serial number

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

Study type(s)

Treatment

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(s)

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.

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Adult

Sex

All

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 severe 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 Prothrombin (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

St. Michael's Hospital

Toronto

Canada

M5B 1W8

Sponsor information

Organisation

St. Michael's Hospital, Toronto (Canada)

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

Individual participant data (IPD) sharing plan**IPD sharing plan summary**

Not provided at time of registration