The effect of intracoronary reinfusion of bone marrow-derived mononuclear cells (BMMNC) on all causemortality in acute myocardial infarction

Published: 13-11-2015
Last updated: 19-04-2024

To demonstrate that a single intracoronary infusion of autologous bone marrow-derived mononuclear cells in addition to state of the art treatment is safe and reduces allcause mortality in patients with reduced left ventricular ejection fraction (

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Myocardial disorders
Study type	Interventional

Summary

ID

NL-OMON46907

Source
ToetsingOnline

Brief title
BAMI

Condition

- Myocardial disorders

Synonym
Acute myocardial infarction, heart infarction, ST-elevated myocard infarct

Research involving
Human

Sponsors and support

Primary sponsor: Queen Mary and Westfield College

Source(s) of monetary or material Support: Queen Mary and Westfield College;EC FP 7 programme

Intervention

Keyword: Acute Myocardial Infarction, Bone marrow-derived mononuclear cells

Outcome measures

Primary outcome

Time from randomisation to all-cause death

Secondary outcome

Secondary efficacy endpoints:

• Time from randomisation to cardiac death

• Time from randomisation to cardiovascular death or

rehospitalisation due to heart failure

• Time from randomisation to cardiovascular

rehospitalisation for:

Recurrent MI

Coronary revascularisation procedures

Heart Failure

Unplanned implantation of ICD/CRT device after the

initial hospitalisation discharge

Stroke

Safety endpoints:

• Incidence of adverse events

• Incidence of bleeding by BARC definitions

• Incidence of syncopes

• Incidence of arrhythmias (A-fib/VT)

• Incidence of neoplastic diseases

Study description

Background summary

The long term prognosis of patients suffering from acute myocardial infarction (AMI) has progressively improved since the introduction of reperfusion therapies and in particular primary angioplasty. In the setting of ST-elevation myocardial infarction (STEMI), the immediate reopening of acutely occluded coronary arteries via primary angioplasty is the treatment of choice to salvage ischemic myocardium. However, the
sudden re-initiation of blood flow can lead to a local acute inflammatory response with further endothelial and myocardial damage. This phenomenon, described as 'reperfusion injury', may explain why, despite optimum myocardial reperfusion, the short-term mortality after AMI approaches 7% [1] and the incidence of heart failure approaches 15-20%. Despite the use of full conventional treatment, including ACE inhibitors, beta-blockers, aldosterone inhibitors and diuretics, in the context of randomised controlled trials yearly mortality rates of patients with post-infarction heart failure are still in the range of 10-13% and rehospitalisation for worsening of heart failure occurs at a yearly rate of 6-8 %. Registry data indicate a more dismal outcome in real world clinical experience. A major reason for the high morbidity and mortality is that the heart has an inadequate regenerative response to the myocardial necrosis sustained following AMI; cell death from the ischemic damage can lead to
progressive ventricular dilation and dysfunction through the processes of adverse left ventricular remodelling.

However, the discovery of tissue resident cardiac stem cells in the mammalian heart has challenged the long held belief that the heart is a terminally-differentiated organ and opens up the possibility of using bone marrow derived stem cells to repair the heart. Indeed, recent experimental studies documented that bone marrow-derived cell (BMC) injection into the infarcted heart stimulates the formation of newly formed
cardiac myocytes, although the origin of these myocytes is still a matter of debate. Numerous pre-clinical studies provided high degree of evidence that bone marrowderived cells do contribute to cardiac repair after acute myocardial injury, limit infarct expansion and improve cardiac function most likely via a paracrine mechanism of action. Pre-clinical evidence is corroborated by several small to intermediate size clinical trials demonstrating beneficial effects of

bone marrow derived cells on top of the state-of-the-art reperfusion treatment.

Study objective

To demonstrate that a single intracoronary infusion of autologous bone marrow-derived mononuclear cells in addition to state of the art treatment is safe and reduces allcause mortality in patients with reduced left ventricular ejection fraction (<=45%) after successful reperfusion for acute myocardial infarction when compared to a control group.

Study design

Multinational, multicentre, randomised, open-label, controlled, parallel-group phase III study.
Group 1: optimal standard of care
Group 2: intracoronary infusion of BM-MNCs 2 to 8 days after successful reperfusion for acute myocardial infarction
added on top of optimal standard of care.
Patients will be randomised to treatment or control group in a 1:1 ratio.
Randomisation will be stratified according to country.

Intervention

Bone marrow-derived progenitor cells will be obtained from bone marrow. Intracoronary infusion of BMMNCs will be performed via conventional percutaneous intracoronary intervention techniques using an over-the-wire balloon ("low pressure balloon inflation") between 2 to 8 days after initial acute reperfusion therapy. Patients in the control group will not undergo any of the described interventions and will not receive the therapy. All patients will be treated with optimal post myocardial infarction pharmacological treatment.

Study burden and risks

In previous investigations where the BM-MNC investigational medicinal product (IMP) manufactured as in the BAMI study has been used (bone marrow-derived progenitor cells *t2c001*), no BM-MNC associated adverse reactions were reported.
Aspiration of bone marrow: infection, nerve damage
Hartcatherisation: heart tamponade, hematoma, infection, exposure to radiation
Patients will be tested for HIV, syphilis, hepatitis.

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

1. Signed and dated informed consent
2. Men and women of any ethnic origin aged >= 18 years
3. Patients with acute STelevation (including new LBBB)
myocardial infarction as defined by the universal definition of AMI.
4. Successful acute reperfusion therapy (residual stenosis visually <50% and TIMI flow >=2) within 24 hours of symptom
onset or thrombolysis within 12 hours of symptom onset followed by successful percutaneous coronary intervention
(PCI) within 24 hours after thrombolysis
5. Left ventricular ejection fraction <= 45% with significant regional wall motion abnormality assessed by quantitative
echocardiography (central, independent core lab analysis) 3 to 6 days after reperfusion

therapy
6. Open coronary artery suitable for cell infusion supplying the target area of abnormal wall motion

Exclusion criteria

1. Participation in another clinical trial within 30 days prior to randomisation
2. Previously received stem/progenitor cell therapy
3. Pregnant or nursing women
4. Mental condition rendering the patient unable to understand the nature, scope and possible consequences of the study or to follow the protocol
5. Necessity to revascularise additional vessels, outside the target coronary artery at the time of BMMNC infusion (additional revascularisations after primary PCI and before BMMNC cell infusion are allowed), unless clinically indicated and according to latest guidelines. This decision should be madfe at the time of the index procedure and explicitly stated at the time.
6. Cardiogenic shock requiring mechanical support
7. Platelet count <100,000/µl, or hemoglobin <8.5 g/dl
8. Impaired renal function, i.e. serum creatinine >2.5 mg/dl
9. Persistent fever or diarrhea not responsive to treatment within 4 weeks prior screening
10. Clinically significant bleeding within 3 months prior screening
11. Uncontrolled hypertension (systolic >180 mmHg and diastolic >120 mmHg)
12. Life expectancy of less than 2 years from any noncardiac
cause or neoplastic disease

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	25-03-2016
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cells autologous

Ethics review

Approved WMO Date:	13-11-2015
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-12-2015
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-02-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-04-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-05-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-08-2017

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-01-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-03-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-04-2019
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	EUCTR2012-001495-11-NL
CCMO	NL53394.000.15