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A Phase III randomized, double-blinded, placebo-controlled trial to investigate the impact of intra-coronary transfusion of G-CSF mobilized autologous circulating hematopoietic stem/progenitor cells (CPC) therapy in patients with diffuse coronary artery disease who are not candidates for coronary artery intervention

Submission date 14/06/2018	**Recruitment status** Recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 26/06/2018	**Overall study status** Ongoing	[ ] Statistical analysis plan [ ] Results
Last Edited 08/01/2024	**Condition category** Circulatory System	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Heart disease is the second leading cause of death worldwide. Although the treatment of this disease has been extensively investigated, effective treatment options are still limited. Therefore, it is of utmost important for clinicians to find an effective treatment for these diseases. A type of stem cells found in the blood, known as G-CSF mobilized autologous circulating hematopoietic stem/progenitor cells (CPCs), have been shown to improve heart disease outcomes. The aim of this study is to find out whether CPCs can improve heart function for patients with heart disease who are not candidates for coronary artery interventions (PCI or CABG).

Who can participate?
Patients aged 20-80 years-old with heart disease who are not candidates for PCI or CABG

What does the study involve?
Participants are randomly allocated into the experimental group or the control group. The experimental group are treated with CPCs. The control group are treated with plasma (blood). All participants are followed up for one year after the treatment to assess their heart function.

What are the possible benefits and risks of participating?
The possible benefits are improvement of heart function and quality of life. The risks include arrhythmia, increased risk of angina or heart failure, stroke, claudication (pain in the legs due to reduced blood flow), hemorrhage, anemia, renal insufficiency (kidney failure) and electrolyte

imbalance. The possible side effects from the CPC therapy include deterioration of brain function, recurrent stroke, heart problems, blockage of arteries, bleeding, anemia, deterioration of kidney function, gastrointestinal (gut) complications, electrolyte (minerals in the body) imbalance, sepsis (blood poisoning) and cancer.

Where is the study run from?
Kaohsiung Chang Gung Memorial Hospital (Taiwan)

When is the study starting and how long is it expected to run for?
November 2017 to August 2026

Who is funding the study?
Chang Gung Medical Research Program Grant (Taiwan)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
TFDA No. 106IND02037

Study information

Scientific Title

Application of G-CSF mobilized autologous circulating hematopoietic stem/progenitor cells (CPC) for patients with diffuse coronary artery disease (CAD) who are non-candidates for coronary artery intervention: a phase III clinical trial for evaluation of efficacy

Acronym
CPC for patients with CAD

Study objectives
G-CSF mobilized autologous circulating hematopoietic stem/progenitor cells (CPC) may be a therapeutic option for patients with diffuse Coronary Artery Disease (CAD) and non candidates for coronary artery intervention.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 20/09/2023, Chang Gung Medical Foundation, Institutional Review Board (199, TUNG HWA NORTH ROAD, TAIPEI, 10507, Taiwan; +886 (03) 3196200; dog111443@cgmh.org.tw), ref: 201700248A0C505

2. Taiwan FDA, 22/05/2018, No. 106IND02037

Study design
Prospective single-center interventional trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Diffuse Coronary Artery Disease (CAD) and non candidates for coronary artery intervention

Interventions
Patients are randomised into the experimental group and the control group (2:1) based on an automatically generated random number table.

Experimental group: G-CSF mobilized autologous circulating hematopoietic stem/progenitor cells (CPC): 3.0 x 10(7) cells/kg (n=64)
Control group: plasma from subjects (n=32)

All subjects will be followed up for one year after the treatment.

Intervention Type
Biological/Vaccine

Phase
Phase III

Drug/device/biological/vaccine name(s)
Hematopoietic stem/progenitor cells (CPC)

Primary outcome measure
Left ventricular ejection fraction (LVEF) examined by 3D echo and cardiac MRI at baseline (D6) and 12 months

Secondary outcome measures
1. The incidence of death monitored from baseline (D6) to 12 months during one-year follow-up
2. The incidence of major cardiac events (i.e., defined as the occurrence of myocardial infarction, congestive heart failure, or refractory angina) monitored from baseline (D6) to 12 months during one-year follow-up
3. Heart failure evaluated according to NYHA functional class. The left ventricular ejection fraction (LVEF) is measured by cardiac ultrasonography at baseline and each revisit (1 week, 1 month, 3 months, 6 months, 9 months, and 12 months) to evaluate the left ventricular systolic function. The heart function of subjects (NYHA Functional Class) from mild to severe is divided from Class I to Class IV for assessing the improvement of heart failure
4. The symptom severity of angina pectoris assessed according to the Canadian cardiovascular society grading system at baseline and each revisit (1 week, 1 month, 3 months, 6 months, 9 months, and 12 months). Exertion-induced angina from mild to severe is divided from Class I to Class IV for assessing the improvement of angina pectoris

Overall study start date
30/11/2017

Completion date
20/08/2026

Eligibility

Key inclusion criteria
Age between 20-80 y/o, coronary syndrome, subjects with severe diffuse coronary artery disease who have been diagnosed by cardiac catheterization, not suitable for cardiac catheterization or surgical coronary artery bypass surgery after cardiac internist and surgeons evaluate, and receiving optimal medical therapy, including antiplatelet therapy (aspirin or clopidogrel), ACEI /ARB, beta-blocker, calcium channel blocker, nitrates, etc. The symptom of chest pain is still evaluated as Canadian Cardiovascular Society class II-IV Angina. LVEF ≤55 % examined by 3D echo (i.e. LVEF ≥60 % indicates normal. After stem cell treatment, the LVEF is improved up to 5

%, unchanged or continually deteriorated. Therefore, the criteria of enrollment of LVEF is ≤55 %). Patients are willing to accept the G-CSF mobilized autologous circulating hematopoietic stem /progenitor cells (CPC) treatment through cardiac catheterization, and are willing to join this study follow-up.
The severe diffuse coronary artery disease is defined as follows:
1. Clinical symptoms of angina (Canadian Cardiovascular Society class II-IV)
2. Tl-201 scan presents reversible ischemic changes (results should be adopted within 6 months)
3. Highly diffuse vascular lesions show in angiography results (continuous normal segmental vessels length no longer than 10 mm), and the degree of stenosis more than 75% (results can be adopted within 6 months)
4. Due to vascular occlusion showed diffuse and too small, not to be suitable for PCI (angioplasty nowhere to be implemented) or CABG (which can be accessed at no normal blood vessels) analyzed by PCI and CABG experts. The vessel must be severe diffuse stenosis (unsuitable for CABG)

Participant type(s)
Patient

Age group
Adult

Lower age limit
20 Years

Upper age limit
80 Years

Sex
Both

Target number of participants
96 subjects (64 subjects for treatment group and 32 subjects for control group)

Key exclusion criteria
1. Age <20 y/o or >80 y/o
2. Pregnant or breastfeeding women
3. No adventitious agents, ex. HIV infection, HBV and HCV carriers (HBsAg+ or anti-HCV +) (subjects without examination of HIV, HBV and HCV are excluded)
4. Myocardial infarction within 3 months, stent placement within 3 months
5. Severe aortic or mitral stenosis
6. Asthma and not suitable for cardiac catheterization treatment (including NYHA functional class IV)
7. Malignant or hematologic disease. Severe disease with life span less than one year
8. Chronic kidney disease (CCr <20 ml/min) and patients receiving dialysis
9. Under immunosuppressive medications
10. Autoimmune diseases
11. Contraindication to G-CSF
12. The subject previously received cell therapy
13. Participating in another clinical study and planning to participate in another clinical study during the course of this study

Date of first enrolment
01/06/2018

Date of final enrolment
01/08/2026

Locations

Countries of recruitment
Taiwan

Study participating centre
Kaohsiung Chang Gung Memorial Hospital
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Sponsor information

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00k194y12

Funder(s)

Funder type
Hospital/treatment centre

Funder Name

Chang Gung Medical Research Program Grant

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal

Intention to publish date
31/12/2026

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date