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The therapeutic effect of autologous peripheral blood-derived stem cell therapy on acute brain infarcts

Submission date 07/04/2018	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 23/04/2018	**Overall study status** Ongoing	
Last Edited 02/12/2024	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Stroke is a leading cause of death and disability worldwide, and is the third highest cause of death in Taiwan. About 85% of strokes are ischemic strokes, which happen when the arteries that supply the brain with oxygen (the carotid arteries) become narrowed (stenosis) or blocked (occluded) by a sticky substance called plaque that builds up on the artery walls (atherosclerosis), causing reduced blood flow (ischemia) to the brain. Atherosclerosis in the carotid arteries is one of the biggest causes of recurrent stroke, and so reducing carotid stenosis is an important part of stroke prevention. There is growing evidence that stem cell therapy using endothelial progenitor cells (EPCs) (stem cells from bone marrow) can help to regenerate the lining of blood vessels. Previous studies have shown that increasing levels of EPCs circulating in the blood is related to improvement in the recovery of those with ischemic stroke. Currently, there is little research looking at the safety and effectiveness of using EPC therapy for treating ischemic stroke.
This study aims to find out whether EPC therapy is an effective treatment for patients with brain ischemia following an ischemic stroke.

Who can participate?
Adults aged between 45 and 80 with acute ischemic stroke

What does the study involve?
All participants receive eight injections of granulocyte-colony stimulating factor (a protein which stimulates the bone marrow to produce stem cells and release them into the bloodstream) every 12 hours for four days. On the fifth day, patients have a tube placed into the right femoral vein (main vein in the thigh) so that circulating EPCs can be collected. These EPCs are then injected back into the patients into the internal carotid artery (in the neck). Patients are then followed up for five years through a combination of interviews and medical record reviews, in order to find out how effective the treatment has been.

What are the possible benefits and risks of participating?
Participants may benefit from improvement to their disability. There are risks of side effects

from the EPC therapy, including 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?
January 2018 to April 2026

Who is funding the study?
1. National Science Council (Taiwan)
2. Chang Gung Medical research Program (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
Chang Gung Memorial Hospital No. 201700116A0C601

Study information

Scientific Title
An investigation of the therapeutic impact of intra-carotid arterial transfusion of autologous peripheral blood-derived stem cell/progenitor cell (CD34+) therapy on acute ischemic stroke --- a phase II randomized controlled clinical trial

Study objectives
Intra-carotid arterial transfusion of autologous peripheral blood-derived stem cell/progenitor cell (CD34+) therapy might have a therapeutic potential for patients with acute brain infarcts through increase in brain perfusion mediated by angiogenesis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Chang Gung Medical Foundation Institutional Review Board, 14/11/2017, ref: 201700116A0C601

Study design
Prospective single-center interventional trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Patients with acute ischemic stroke and stationary condition in the convalescent phase

Interventions
For the primary objective of the study, an estimated sample size of 58 study patients in each group is based on the effective size with an α = 0.05, a power of 80%, an improvement of 1.5 in NIHSS score in control vs. 4.0 with EPC therapy and the SD was 4.5. A 10% dropout rate is assumed. Therefore, a total of 116 patients are enrolled within 3 years and randomly allocated into EPC-treatment group (n = 58) and Placebo group (n = 58). Regarding randomization process, random number generated by computers are sealed in envelopes. The envelopes are opened in consecutive order by technicians at core lab who are blinded to case randomization. EPC treatment or not is administered according to randomization results. The ratio of EPC to placebo is 1:1.
Participants in the EPC treatment group receive subcutaneous injection of granulocyte-colony stimulating factor (G-CSF) 5μg/kg twice daily for 4 consecutive days within 7 days after acute stroke. Endothelial progenitor cells (EPCs) are collected at day 5 for 3-4 hours from double

lumen sheath inserted at right femoral vein using a machine (COBE Spectra 6.1). The collected EPCs are immediately transfused back to patients themselves with a dose of 3.0x107 EPCs once through internal carotid artery of infarct side using a 6F JR guiding catheter via right radial arterial approach.
Partiicpants in the control group receive guideline-directed standard therapy for ischemic stroke except for cell-based therapy.
All of the data is collected with a blinded method. Decoding the random number needs to be allowed by leader principal investigator. The duration of treatment and follow-up is at least one year and the follow-up period and details in placebo group are the same to those in EPC-treatment group. The participants are followed up at Neurology and Cardiovascular outpatient clinics for safety and efficacy monitoring for 5 years.

Intervention Type
Procedure/Surgery

Primary outcome measure
Events of all-cause mortality and recurrent ischemic stroke are recorded at 90 days and 1 year

Secondary outcome measures
1. Post-therapy 90-day combined endpoint of recurrent stroke or death
2. Post-therapy disability is evaluated with modified Rankin Scale score and Barthel Index; WAIS-III and CASI National Institutes of Health Stroke Scale (NIHSS) within 1, 3, and 30 days (±14 days) and 90 days (±14 days):
3. Post-therapy brain reperfusion status is measured by using brain Magnetic resonance imaging [Arterial Spin Labeling (ASL) and Dynamic Contrast Enhancement] at 24-72 hours and 90 days (±14 days)
4. Post-therapy brain perfusion defect evaluation is measured using radionuclear medicine image [brain Tc-99m scan] 24-72 hours and 90 days (±14 days)
5. Any adverse events are recorded within 5 years post-therapy

Overall study start date
01/01/2018

Completion date
30/04/2026

Eligibility

Key inclusion criteria
1. Suffer from acute ischemic stroke within 14 ± 7 days
2. Evidence of brain ischemia on nuclear medicine examination
3. NIHSS score between 8 and 21
4. Already on standard medical therapy based upon stroke guideline, e.g., antiplatelet, antihypertensive, and statin.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
A total of 116 participants with acute ischemic stroke (58 participants treated with intra-carotid PBSC therapy, the other 58 participants treated with standard guideline-directed medical therapy, e.g., antiplatelet and antihypertensive agents)

Total final enrolment
28

Key exclusion criteria
1. Age less than 45 years old or more than 80 years old
2. Patients received t-PA and anticoagulation
3. Non-middle cerebral artery territory stroke or hemorrhagic stroke
4. Pregnant women
5. Patients with active infectious disease or autoimmune disorder
6. Myocardial infarction (MI) within 3 months
7. Severe aortic stenosis or mitral stenosis
8. Congestive heart failure, New York Heart Association functional class IV
9. Malignancy or other severe disease with life span less than one year
10. Chronic kidney disease with CCr<20ml/min and end stage renal disease
11. Join other clinical trials
12. Patients cannot receive regular follow-up
13. Other brain disease (tumor, degenerative disease, infective disease)

Date of first enrolment
01/05/2018

Date of final enrolment
30/04/2021

Locations

Countries of recruitment
Taiwan

Study participating centre
Kaohsiung Chang Gung Memorial Hospital
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Sponsor information

Organisation
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Sponsor type
Hospital/treatment centre

Website
https://www.cgmh.org.tw

ROR
https://ror.org/02verss31

Funder(s)

Funder type
Research council

Funder Name
National Science Council

Funder Name
Chang Gung Medical Research Program

Results and Publications

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

Intention to publish date
30/04/2027

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Dr. Pei-Hsun Sung, e12281@cgmh.org.tw

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		20/11/2024	02/12/2024	Yes	No