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Preventing cognitive decline and dementia from cerebral small vessel disease

Submission date
14/05/2015

Recruitment status
No longer recruiting

Registration date
05/07/2015

Overall study status
Completed

Last Edited
17/08/2023

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
About 35,000 people each year in the UK have a type of stroke, called 'lacunar' or 'small vessel' stroke, which is different to other common types of stroke and for which there is no proven treatment. There is some evidence to suggest that small vessel stroke is caused by damage to the lining of the tiny blood vessels in the brain that stops the vessels functioning normally and damages the brain. This damage not only causes stroke, but it also causes problems with thinking and walking. It is possible that damage to the small blood vessels of the brain causes up to 40% of all dementias. Some drugs that are commonly used in other blood vessel diseases may help improve vessel function and prevent worsening of small vessel damage in the brain; however, the drugs need to be tested for this condition first. One such drug yet to be tested in the UK is cilostazol, although it has been tested in the Far East, but not on dementia. Another drug widely used in the UK in heart disease but not stroke is called isosorbide mononitrate. The aim of this small study is to find out how patients feel about testing the effects of cilostazol and isosorbide mononitrate on blood vessel function. The study will use detailed scanning and blood vessel measurements, and find out if both drugs might be better than just one. The results of this study will be used to inform a future large clinical study to investigate whether these drugs prevent worsening of small vessel disease.

Who can participate?
Adults who have had a mild ischaemic stroke in the past 4 years

What does the study involve?
Participants are randomly allocated into one of four groups. Each group is given different medication - one group receives cilostazol, one receives isosorbide mononitrate, one receives both drugs to start immediately and the other group gets both drugs but delay the start for three weeks. Participants are monitored for side effects and tolerability of the medication, the safety of the medication in combination with usual post-stroke medication and the effects of the medications on measurements of how well blood vessels are working in the brain and the rest of the body. During the 10-week study period the drugs are switched, so half of the participants eventually take both of the drugs. All participants also take both of the drugs in combination at some point during the study. The measurements are repeated up to 3 times to see what effect this has.

What are the possible benefits and risks of participating?
The aim of this study is to show that these medications are safe to use in people after a stroke. The main risks are associated with the side effects of the medications, which are well known as they have been used extensively to treat other conditions. The most common side effect is a headache but this normally settles after a few days.

Where is the study run from?
1. University of Edinburgh (UK)
2. University of Nottingham (UK)

When is the study starting and how long is it expected to run for?
October 2015 to October 2017

Who is funding the study?
Alzheimer's Society (UK)

Who is the main contact?
1. Dr Julia Boyd (public)
Julia.boyd@ed.ac.uk
2. Prof J Wardlaw (scientific)
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-001953-33

ClinicalTrials.gov (NCT)
NCT02481323

Protocol serial number
PrevSVD-2015

Study information

Scientific Title
Preventing cognitive decline and dementia from cerebral Small Vessel Disease (Prevent-SVD): a phase II pilot, factorial, randomised, open label blinded end-point trial to investigate short-term effects of cilostazol and isosorbide mononitrate on tolerability, safety, and vascular function in patients with small vessel disease associated stroke. (Lacunar Intervention Trial 1 (LACI-1))

Acronym
Prevent-SVD

Study objectives
Cilostazol and ISMN will be tolerable to participants in full dose and will improve endothelial function in participants with clinically-evident SVD, as determined using cerebrovascular reactivity and systemic arterial compliance measures.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Scotland A REC, 09/11/2015, ref: 15/SS/0154

Study design
Two-centre dose-escalation factorial placebo-controlled prospective blinded intermediary endpoint trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Stroke due to cerebral small vessel disease

Interventions
Participants will be randomised to one of four groups to take one or other drug or both starting immediately or both with a delayed start, the dose of each drug initially being started at low dose and then increased per week to target dose:
1. Cilostazol 50 to 100mg twice daily
2. Isosorbide mononitrate 25mg twice daily

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
1. Cilostazol 2. Isosorbide mononitrate

Primary outcome(s)
Number of patients reaching target dose judged on direct questioning, medication diary and tablet count

Key secondary outcome(s))
1. Symptoms of headache, palpitations, or loose stools (all present/absent and if present then degree of interference with daily life), dizziness (dizziness scale), nausea (nausea scale) assessed every two weeks during the trial
2. Safety (bleeding, recurrent vascular events, death) assessed at the end of the trial
3. Effect on blood pressure measured three times standing and sitting with an omron bp device assessed in weeks 3 and 8
4. Effect on platelet function measured with a specialised platelet function assay (platelet solutions) assessed in weeks 3 and 8
5. Effect on cerebrovascular reactivity measured with magnetic resonance imaging and carbon dioxide breathing challenge assessed in week 8
6. Effect on arterial stiffness measured using pulse wave velocity and pulse wave analysis assessed in week 3 and week 8

Completion date
31/10/2017

Eligibility

Key inclusion criteria
1. Mild symptomatic ischaemic stroke compatible with a lacunar ischaemic stroke in the past four years with brain magnetic resonance imaging or CT brain scanning that confirmed the relevant infarct or excluded other cause for symptoms

2. Age >35 years
3. Independent in activities of daily living (modified Rankin ≤2)
4. Able to give consent (Montreal Cognitive Assessment score 26-30)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
57

Key exclusion criteria
1. Other significant acute neurological illness since suffering stroke
2. Age <35
3. Requiring assistance with activities of daily living (Modified Rankin ≥3)
4. Active cardiac disease (myocardial infarction in past 6 months, active angina, symptomatic cardiac failure)
5. Carotid stenosis >50% NASCET
6. Contraindication to trial drugs
7. Current use of trial drugs
8. Unable to swallow
9. Bleeding tendency
10. Unlikely to comply with trial medication
11. Planned surgery during the trial period
12. History of intracranial haemorrhage
13. Other life threatening illness
14. History of drug overdose or attempted suicide or significant active mental illness
15. Pregnancy

Date of first enrolment
01/11/2015

Date of final enrolment
31/08/2017

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
University of Edinburgh
Stroke Service NHS Lothian
Western General Hospital
Edinburgh & The Royal Infirmary of Edinburgh
Edinburgh
United Kingdom
EH16 4SA

Study participating centre
University of Nottingham
City Hospital and Queens Medical Centre
Nottingham
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NG7 2RD

Sponsor information

Organisation
University of Edinburgh

ROR
https://ror.org/01nrxwf90

Organisation
NHS Lothian

ROR
https://ror.org/03q82t418

Funder(s)

Funder type
Charity

Funder Name

Alzheimer's Society

Alternative Name(s)
alzheimerssoc

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Joanna Wardlaw (joanna.wardlaw@ed.ac.uk).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/05/2019	25/06/2019	Yes	No
Results article	safety data results	03/07/2019	25/07/2019	Yes	No
Results article		01/12/2021	17/08/2023	Yes	No
Protocol article	protocol and statistical analysis plan	01/07/2018		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes