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LACunar Intervention trial - Cognition 1

Submission date
17/01/2026

Recruitment status
Recruiting

Registration date
26/03/2026

Overall study status
Ongoing

Last Edited
09/06/2026

Condition category
Nervous System Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Memory and thinking problems (also called cognitive impairment) can be caused by damage to the small blood vessels in the brain – a condition known as small vessel disease (SVD). When these vessels don't function properly, they fail to deliver enough oxygen and nutrients to brain tissue. SVD may be responsible for up to 45% of all cases of dementia.
There are no effective treatments to improve the function of these small blood vessels or to address the memory and thinking problems caused by SVD. As a result, brain damage can continue to accumulate over time.
We have identified two drugs that may help protect the small vessels in the brain, potentially reducing the risk of stroke and memory or thinking problems caused by small vessel disease. One of the drugs, cilostazol, is commonly used in the UK to treat poor blood circulation in the legs. The other, isosorbide mononitrate, is widely used in the UK and worldwide to treat angina, a type of chest pain caused by reduced blood flow to the heart.

Who can participate?
We will recruit 60 participants aged 50 or over, with memory or thinking problems related to SVD. Our aim is to find out whether these medications, on their own or in combination, are well tolerated, and whether they might improve cognitive function.

What does the study involve?
Participants who are eligible and provide consent will be randomized to receive one, both, or neither of the trial drugs. They will be followed-up either in-person or by phone at 1, 3, 8, and 10 weeks, when we will collect information about their health, cognitive and physical function, quality of life, blood pressure, and (optional) brain and eye vessel function.
The results of the LACI-Cog1 study may inform future NHS care for people affected by SVD-related cognitive problems and may help prevent dementia before symptoms develop.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
The trial has been designed to minimise the participants' burden, and the trial materials allow them to contact the trial hospital, the research team, or an independent advisor at any time should they require advice.

The potential side effects of the study drugs are well known and recognized, and the hospital research team will explain the risks to the participants. Based on the results from the LACI1/2 trials, we know the study drugs are well-tolerated and safe.
Follow-ups are conducted at regular intervals during the 10-week study duration, and when possible, follow-ups will be delivered by phone. Participants will be asked about any new drug symptoms or health problems.
Whilst there are no definite direct benefits to participants from taking part in this study, participants will help us to study possible drugs to be used in the future to treat vascular cognitive impairment. Information about risks, burdens, and benefits is provided in the participant information sheet for participants considering taking part in the trial. Participants will receive advice on vascular risk factor management and on lifestyle to improve their blood vessel health which they may not have received otherwise.

Participants may find completing the questionnaires, and functional/cognitive/physical assessments inconvenient. However, the research teams will use follow-up visit to monitor the participants' health, including blood pressure checks.

Optional MRI and CVR and retinal imaging, including breathing 6% CO2 in air, procedures are safe and do not involve radiation. However, some participants may find the scan or CVR procedure uncomfortable, or may feel like it makes breathing a little harder. We keep the mask on for as little time as possible (12-15 min). Participants are also given a button to press whilst inside the scanner if they want the scan to stop at any time. Researchers will always be present during CVR to monitor breathing, pulse and oxygen levels to ensure the scan is very safe. Over 500 such examinations have now been done by the research group in Edinburgh- the examinations are well tolerated by patients with some returning for several such scans, and with no safety concerns. Participants can choose to decline the MRI or CVR without it affecting trial participation.

Where is the study run from?
The trial will be conducted at the Royal Infirmary of Edinburgh in Scotland, sponsored by the University of Edinburgh and NHS Lothian ACCORD Office.

When is the study starting and how long is it expected to run for?
February 2026 to August 2028

Who is funding the study?
Race Against Dementia (UK)

Who is the main contact?
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Additional identifiers

Integrated Research Application System (IRAS)
1012714

Central Portfolio Management System (CPMS)
71930

Sponsor's protocol code number
AC25417

Study information

Scientific Title
LACunar Intervention trial – Cognition 1 (LACI-Cog1): a feasibility study of cilostazol and isosorbide mononitrate in vascular cognitive impairment

Acronym
LACI-Cog1

Study objectives
The primary objective of the trial is to test the short-term feasibility of a trial testing cilostazol and ISMN in patients with vascular cognitive impairment.

Determine if cilostazol and ISMN, alone and combined, are safe, and collect intermediary mechanistic and clinical endpoints for efficacy.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 08/06/2026, East of Scotland Research Ethics Service (EoSRES) (Tayside Medical Science Centre Residency Block Level 3 George Pirie Way Ninewells Hospital and Medical School, Dundee, DD1 9SY, United Kingdom; -; tay.eosres@nhs.scot), ref: 26/ES/0010

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Factorial

Purpose
Treatment, Prophylaxis

Study type(s)
Efficacy, Safety, Treatment, Other

Health condition(s) or problem(s) studied
Vascular cognitive impairment in small vessel disease

Interventions
Eligible participants will be randomized into one of four trial arms: ISMN alone, Cilostazol alone, both ISMN and cilostazol, or neither drug. Randomization will be conducted using REDCap, which uses a secure web-based application programming interface (API) hosted within the University of Edinburgh to allocate treatment groups using minimization techniques. Treatment duration is 8 weeks, with follow-up to 10 weeks. ISMN will be administered orally once daily, starting at 25 mg daily and titrated to a target dose of 50 mg daily. Cilostazol will be administered orally twice daily, starting at 50 mg twice daily and titrated to a target dose of 100 mg twice daily. Participants randomized to both drugs will follow a staggered dose-escalation schedule to improve tolerability. At the end of the treatment period, participants will be provided with instructions to gradually reduce and stop the trial medication over one week. A follow-up telephone call at week 10 will confirm treatment discontinuation and collect safety information. All trial arms will follow the same schedule of assessments and follow-up procedures.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Cilostazol, Isotard 25XL Tablets [Isosorbide mononitrate]

Primary outcome(s)
1. Proportion of patients completing up-titration of target dose and maintain target dose by the end of study measured using Investigator-led clinical assessment based on participant report and review of study medication use at 8 weeks after randomization for each participant

2. Recruitment and retention of 60 participants measured using Number of participants recruited and retained in the trial at continuously throughout the recruitment period, until recruitment is complete

Key secondary outcome(s)
1. Treatment-related symptoms measured using Structured symptom questionnaire assessing headache, nausea, palpitations, loose stools, dizziness or unsteadiness, heartburn, bleeding, bruising and falls at Continuously throughout the study, and at 8 and 10 weeks

2. Safety and serious adverse events (SAEs) measured using Recording of SAEs, including systemic or intracranial bleeding, vascular events, death, or hospital admission judged by the investigator to be related to the study drug at Continuously throughout the study, and at 8 and 10 weeks

3. Blood pressure measured using Standardized seated blood pressure measurement at Baseline and 8 weeks

4. Global cognitive function measured using Montreal Cognitive Assessment (MoCA) at Baseline and 8 weeks

5. Attention and working memory measured using Spelling 'WORLD' backwards test at Baseline and 8 weeks

6. Functional outcome and disability measured using Modified Rankin Scale (mRS) at Baseline and 8 weeks

7. Health-related quality of life measured using Bristol Activities of Daily Living Scale (BADLS) at Baseline and 8 weeks

8. Upper limb motor function and dexterity measured using 9-hole Peg Test at Baseline and 8 weeks

9. Mobility and balance measured using Timed up and Go (TUG) test at Baseline and 8 weeks

10. Depression symptoms measured using Zung Self-Rating Depression Scale at Baseline and 8 weeks

Completion date
24/08/2028

Eligibility

Key inclusion criteria
1. Age ≥ 50 years.
2. Cognitive impairment* – mild cognitive impairment (abnormal cognitive testing in the view of the study investigator, but no functional impairment) or mild dementia (abnormal cognitive testing and functional impairment due to the cognitive problem). These diagnoses will be recorded in the medical notes.
3. A moderate to severe burden of cSVD on brain imaging (MRI or CT) within the last three years, defined as Fazekas score ≥2 in each of periventricular and deep regions (i.e., a total Fazekas score ≥4) or total Fazekas score ≥3 AND one or more lacunes. The brain imaging is performed as part of routine clinical care
4. The cSVD is considered to be a major contributor to the cognitive impairment in the opinion of the study investigator, documented in the medical record.**
5. Retained capacity to provide written consent themselves in the opinion of the study investigator.
6. Have a study partner*** who knows the participant sufficiently well to provide information about their functional abilities, in the view of the study investigator, and who is willing to join the study in this role.
7. Proficiency in written and spoken English to understand study materials and processes, in the view of the investigator, documented in the medical record.
*We will not use upper or lower bound cut-offs on cognitive testing to determine eligibility, but participants must be able to provide consent themselves. For the mild cognitive impairment stage (cognitive decline but no resulting functional impairment), cognitive impairment will be deemed present if the most recent cognitive testing performed during clinical care (usually an

Addenbrooke’s Cognitive Examination III) identifies lower than expected performance for that patient’s age and educational background.
**Participants will be eligible if they are thought to have mixed pathology (e.g. vascular and Alzheimer’s disease), providing the vascular changes are considered to be the major contributor. Patients with genetic SVD (e.g. CADASIL) will be eligible if presenting with cognitive impairment and meeting the other inclusion criteria.

Added 09/06/2026:
***A study partner is usually someone who lives with the participant (e.g., a spouse) or a close relative or friend who is in regular contact (at least weekly) and knows the participant well enough to comment on their day-to-day functioning. The study partner must have known the participant for a sufficient period and have regular contact to provide a meaningful assessment of cognitive change over time using the IQCODE. Suitability of the study partner will be determined by the Principal Investigator (or delegated qualified investigator) at screening. The study partner may, but is not required to be, the participant’s welfare guardian or Power of Attorney.

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
50 Years

Upper age limit
120 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current exclusion criteria as of 09/06/2026:
1. Unlikely to be able to manage medications without a dosette, based on information provided by the patient and family or carer. If a patient would be unable to manage their medications alone, but has sufficient family or carer support to take the trial medications in the view of the Principal Investigator, they can be included.
2. The cognitive impairment is thought to be mostly due to a cortical or large subcortical ischaemic or haemorrhagic stroke, rather than due to cSVD. This information will be contained within the medical record.
3. Significant active neurological illness, such as intractable epilepsy, multiple sclerosis, Parkinson’s disease, a neurodevelopmental disorder, or brain tumour. Wellcontrolled epilepsy (for example, seizurefree for more than 6 months) is not an exclusion criterion.
4. Hypotension, defined as sitting systolic blood pressure less than 100 mmHg.
5. Definite indication for (that is, already prescribed) either trial medication, or definite contraindication to both trial drugs as per SPCs. Lactose intolerance is a contraindication to ISMN preparations which contain lactose monohydrate. Having an indication for or

contraindication to one of the trial drugs still allows randomisation to the other trial drug.
6. Unable to swallow tablets, based on information provided by the patient and/or their family or carer.
7. Planned surgery during the trial period.
8. Other concurrent lifethreatening illness, with life expectancy expected to be less than 1 year in the view of the study investigator.
9. Unlikely to be available for followup (for example, moving outside of the area).
10. History of drug overdose, attempted suicide, or significant active mental illness documented in the medical notes.
11. Women of childbearing potential. Women of childbearing potential (WOCBP), defined in line with the Clinical Trials Coordination Group (CTCG; March 2024) guidance as fertile following menarche (and having not been free from menses for >1 year), and until becoming post-menopausal (no menses for 12 months without an alternative medical cause) unless permanently sterilised by hysterectomy, bilateral salpingectomy, and bilateral oophorectomy) will not be eligible for this single-centre short-term IMP administration pilot trial. Firstly, women of childbearing potential with VCI due to cSVD are extremely rare, and secondly, LACI-Cog-1 is a small, single-centre, short-term administration trial focused on the feasibility of recruitment and tolerance of IMP in a population that is more typical of patients attending memory clinics.
12. Prohibited medications to either trial drug. Prohibited medications to one of the trial drugs still allow randomisation to the other trial drug.
13. Renal impairment, defined as creatinine clearance less than 25 ml/min.
14. Moderate to severe hepatic impairment.
15. No renal or hepatic function tests within the last 12 months.
16. Previous participation in previous LACI trials (LACI1, LACI2, and LACI3).
17. Participation in another Clinical Trial of an Investigational Medicinal Product, up to and including at least five half-lives after the last dose of that Investigational Medicinal Product.
Cilostazol exclusion criteria (still allows randomisation to ISMN):
1. Definite indication for (that is, already prescribed) Cilostazol, or definite contraindication to cilostazol as per SPC section 4.3.
2. Prohibited medications to cilostazol (see appended SPCs and protocol section 6.7.3).
3. Active cardiac disease, including myocardial infarction within the last six months, uncontrolled atrial fibrillation, active angina, or symptomatic cardiac failure. Controlled atrial fibrillation alone is not an exclusion criterion; however, anticoagulant medication is an exclusion for cilostazol.
4. Bleeding tendency, for example, platelets less than 100, active peptic ulcer, previous intracranial haemorrhage (subdural haematoma, subarachnoid haemorrhage, intracerebral haemorrhage, but not asymptomatic haemorrhagic transformation from infarct or a few microbleeds on neuroimaging according to medical records), or prescribed anticoagulant medication. Participants on anticoagulant medication cannot receive cilostazol, but they can be randomised to ISMN versus no ISMN.
5. Prescribed dual antiplatelet therapy (aspirin and clopidogrel) or dual antiplatelets taken within the last week. Taking monotherapy antiplatelet treatment (aspirin or clopidogrel) is not a contraindication. Participants taking dual antiplatelets can be randomised to ISMN versus no ISMN.

ISMN exclusion criteria (still allows randomisation to Cilostazol)
1. Definite indication for (i.e., already prescribed) ISMN, or definite contraindication to ISMN as per SPCs section 4.3.
2. Prohibited medications to cilostazol (see appended SPCs and protocol section 6.7.3).
3. ISMN is contraindicated for patients with the rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency. The medical notes will be reviewed to apply this criterion.

For the MRI CVR imaging (tertiary endpoint 2), additional exclusion criteria are:
1. Unable to tolerate MRI or contraindication to MRI, such as claustrophobia, pacemaker, or cochlear implant.
2. Active respiratory illness, such as moderate to severe asthma or chronic obstructive pulmonary disease.
3. Unable to lie flat.

For the retinal/RVR imaging (tertiary endpoint 3), additional exclusion criteria are:
1. Active respiratory illness, such as moderate to severe asthma or chronic obstructive pulmonary disease.
2. History of photosensitive epilepsy.
3. Shallow anterior chambers, as assessed by torch test.
4. No view of the fundus in either eye.
MRI CVR and retinal imaging assessments are optional.

Previous exclusion criteria:
1. Unlikely to be able to manage medications without a dosette, based on information provided by the patient and family or carer. If a patient would be unable to manage their medications alone, but has sufficient family or carer support to take the trial medications in the view of the Principal Investigator, they can be included.
2. The cognitive impairment is thought to be mostly due to a cortical or large subcortical ischaemic or haemorrhagic stroke, rather than due to cSVD. This information will be contained within the medical record.
3. Significant active neurological illness, such as intractable epilepsy, multiple sclerosis, Parkinson's disease, a neurodevelopmental disorder, or brain tumour. Wellcontrolled epilepsy (for example, seizurefree for more than 6 months) is not an exclusion criterion.
4. Hypotension, defined as sitting systolic blood pressure less than 100 mmHg.
5. Definite indication for (that is, already prescribed) either trial medication, or definite contraindication to both trial drugs as per SPCs. Lactose intolerance is a contraindication to ISMN preparations which contain lactose monohydrate. Having an indication for or contraindication to one of the trial drugs still allows randomisation to the other trial drug.
6. Unable to swallow tablets, based on information provided by the patient and/or their family or carer.
7. Planned surgery during the trial period.
8. Other concurrent lifethreatening illness, with life expectancy expected to be less than 1 year in the view of the study investigator.
9. Unlikely to be available for followup (for example, moving outside of the area).
10. History of drug overdose, attempted suicide, or significant active mental illness documented in the medical notes.
11. Pregnancy or breastfeeding, or women of childbearing age not taking contraception. Acceptable contraception in women of childbearing age is a "highly effective" contraceptive measure as defined by the Clinical Trials Facilitation Group and includes combined (oestrogen and progesterone containing) or progesteroneonly contraception associated with inhibition of ovulation, intrauterine device, or bilateral tubal occlusion. Contraception must be continued for up to 30 days after the end of the IMP dosing schedule.
12. Prohibited medications to either trial drug. Prohibited medications to one of the trial drugs still allow randomisation to the other trial drug.
13. Renal impairment, defined as creatinine clearance less than 25 ml/min.
14. Moderate to severe hepatic impairment.
15. Previous participation in previous LACI trials (LACI1, LACI2, and LACI3).
16. Cilostazol exclusion criteria (still allows randomisation to ISMN):
17. Definite indication for (that is, already prescribed) Cilostazol, or definite contraindication to

Cilostazol as per SPC section 4.3.
18. Prohibited medications to Cilostazol (see appended SPCs and protocol section 6.7.3).
19. Active cardiac disease, including myocardial infarction within the last six months, uncontrolled atrial fibrillation, active angina, or symptomatic cardiac failure. Controlled atrial fibrillation alone is not an exclusion criterion; however, anticoagulant medication is an exclusion for cilostazol.
20. Bleeding tendency, for example platelets less than 100, active peptic ulcer, previous intracranial haemorrhage (subdural haematoma, subarachnoid haemorrhage, intracerebral haemorrhage, but not asymptomatic haemorrhagic transformation from infarct or a few microbleeds on neuroimaging according to medical records), or prescribed anticoagulant medication. Participants on anticoagulant medication cannot receive cilostazol, but they can be randomised to ISMN versus no ISMN.
21. Prescribed dual antiplatelet therapy (aspirin and clopidogrel) or dual antiplatelets taken within the last week. Taking monotherapy antiplatelet treatment (aspirin or clopidogrel) is not a contraindication. Participants taking dual antiplatelets can be randomised to ISMN versus no ISMN.

ISMN exclusion criteria (still allows randomisation to Cilostazol)
1. Definite indication for (i.e. already prescribed) ISMN, or definite contraindication to ISMN as per SPCs section 4.3.
2. Prohibited medications to Cilostazol (see appended SPCs and protocol section 6.7.3).

For the MRI CVR imaging (tertiary endpoint 2), additional exclusion criteria are:
1. Unable to tolerate MRI or contraindication to MRI, such as claustrophobia, pacemaker, or cochlear implant.
2. Active respiratory illness, such as moderate to severe asthma or chronic obstructive pulmonary disease.
3. Unable to lie flat.

For the retinal/RVR imaging (tertiary endpoint 3), additional exclusion criteria are:
1. Active respiratory illness, such as moderate to severe asthma or chronic obstructive pulmonary disease.
2. History of photosensitive epilepsy.
3. Shallow anterior chambers, as assessed by torch test.
4. No view of the fundus in either eye.
MRI CVR and retinal imaging assessments are optional.

Date of first enrolment
15/06/2026

Date of final enrolment
15/06/2028

Locations

Countries of recruitment
United Kingdom

Scotland

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Royal Infirmary of Edinburgh
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Sponsor information

Organisation
University of Edinburgh

ROR
https://ror.org/01nrxwf90

Organisation
NHS Lothian

ROR
https://ror.org/03q82t418

Funder(s)

Funder type

Funder Name
Race Against Dementia

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analyzed during the current study are/will be available upon reasonable request from other researchers aiming to conduct relevant analyses by contacting Joanna M. Wardlaw (Joanna.wardlaw@ed.ac.uk). An anonymized curated version with a DOI will be made available for open access use by other researchers via the University of Edinburgh DataShare system upon study completion and once the main trial papers have been published and for a minimum of 20 years. Explicit participant consent will be obtained to use anonymized data for future studies.

IPD sharing plan summary

Available on request