ISRCTN55927994 https://doi.org/10.1186/ISRCTN55927994

NOVEL: A Clinical Trial of the Oxygen-carrying Substance NanO2 to Protect the Brain after Stroke

Submission date 16/10/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 05/02/2025	**Overall study status** Ongoing	
Last Edited 16/05/2025	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
This is a National Institute for Health Research (NIHR) Efficacy and Mechanism Evaluation (EME) clinical trial aiming to investigate a possible new treatment to limit damage to the brain caused by a stroke. Strokes that are caused by a clot blocking an artery in the brain ('ischaemic' strokes) starve brain tissue of oxygen and nutrients. Over a short period of time without oxygen, this tissue becomes permanently damaged. We are investigating the effects of a drug that carries extra oxygen, called NanO2, on the amount of brain tissue damage. By carrying extra oxygen to brain tissue NanO2 may allow the tissue to survive for longer. It might be especially useful to prevent further damage happening while treatments to try and open the blocked blood vessel are given. Treatments may include 'clot-busting' drugs, or procedures to physically open a blocked artery. These treatments are very effective, but take time to successfully open the blockage. The study will involve treating people as early as possible after the stroke, and comparing brain scans before and after treatment.

Who can participate?
Patients diagnosed with a stroke that has occurred within the past 9 hours will be eligible to participate. The study will involve 8-15 hospitals across the UK.

What does the study involve?
Participation in the study will last approximately 90 days. The majority of the study assessments will be during the first 5 days during inpatient hospital stay. There will be a telephone follow-up at 30 days and 90 days post-discharge.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
As with all new medicines, there is limited experience of NanO2 and it is not currently approved for the treatment of any condition. NanO2 was first developed in the 1990s as a possible aid to ultrasound scanning and has since been given experimentally to over 2000 people. Possible side-

effects when used as an aid to ultrasound were mild to moderate in intensity and included feeling sick (nausea), vomiting, drowsiness, headache, high and low blood pressure and dizziness. Side-effects usually resolved quickly. Since these earlier studies were completed, changes have also been made on how NanO2 is given so as to minimise the risks of side effects occurring. In a small trial involving 24 people with stroke in the USA, patients were found to have high blood pressure and reported cough, headache and muscle pain but as yet no consistent side effects or safety concerns have been identified when used to treat stroke. Throughout the study we will record information about any possible symptoms related to involvement in the study. There are no identified risks linked with the placebo. This is a saline solution which contains no active form of medication.
Some people with claustrophobia find MRI scanning unpleasant, but it is possible for the participant to signal to scanning staff to let them know, and the scan can be stopped at any time. CT scans involve additional radiation. The screening CT scan will be performed as part of standard care and the result used to confirm eligibility. In current standard practice it is routine to perform CT Head examinations 24 hours after standard management of acute stroke patients who have undergone intravenous thrombolysis or medical thrombectomy interventions. For study specific purposes, a CT scan at 24 hours will only be performed if the participant cannot undergo MRI for clinical safety reasons and a CT scan has not been performed as part of standard care.

Where is the study run from?
University of Glasgow (UK)

When is the study starting and how long is it expected to run for?
October 2024 to July 2026

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
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Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1009637

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
GN21ST331

Study information

Scientific Title
NanO2 in Large VessEL Occlusion Stroke (NOVEL): a multicentre single-blind, randomised, placebo-controlled blinded biomarker end-point clinical trial of perfluorocarbon in acute ischaemic stroke due to large vessel occlusion

Acronym
NOVEL

Study objectives
The clinical trial will investigate whether an oxygen carrying perfluorocarbon, DDFPe (NanO2), increases the volume of ischaemic brain tissue that survives, is safe and well-tolerated, and improves neurological and functional outcomes after acute ischaemic stroke. The trial findings will inform the range of potential effect sizes and design of a future clinical efficacy trial.
The primary objective is to establish the effectiveness of NanO2 on the volume of ischaemic tissue salvaged at 24 hours.

The clinical outcome measures to be collected will inform future trial design. The clinical objectives are (i) to determine the effect of DDFPe on clinical outcome after LVO stroke, based on early neurological impairment and 3 month disability outcomes, and (ii) to confirm the safety and tolerability of NanO2 based on cumulative incidence of serious adverse events. The mechanistic objective is to determine the effects of DDFPe on brain tissue damage defined by imaging parameters.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 20/01/2025, Scotland A Research Ethics Committee (2nd Floor, Waverley Gate 2-4 Waterloo Place, Edinburgh, EH1 3EG, United Kingdom; +44 7814609032; Manx.Neill@nhslothian.scot.nhs.uk), ref: 24/SS/0084

Study design
Interventional single blind randomized parallel group placebo controlled trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Large vessel occlusion stroke

Interventions
Participants will be randomised (1:1) to either NanO2 or placebo. A web-based system will be used to allocate treatment group. Participants randomised to the intervention arm will receive intravenous NanO2 0.17ml/kg (three doses over 4.5 hours. Participants randomised to the control arm will receive placebo (equal volumes of sodium chloride 0.9%). Trial assessments will take place at 24 hours and 5 days (or discharge date, if earlier) post randomisation. Follow-up assessments will take place remotely at Day 30 and Day 90.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
NanO2 [Dodecafluoropentane emulsion (DDFPe)]

Primary outcome(s)
Volume of penumbral tissue salvaged based on follow-up imaging (diffusion weighted MRI, or non-contrast CT if MRI cannot be obtained) compared with pre-treatment penumbral tissue volume from CT Perfusion. Volume of penumbra – (24h infarct volume – core volume).

Key secondary outcome(s))
Clinical:
1. National Institutes of Health Stroke Scale (NIHSS) change from baseline to day 5.
2. NIHSS score change from baseline to 24h.
3. 24-hour NIHSS score.
4. Proportion achieving substantial early neurological improvement (NIHSS score reduced by ≥8 points or a score equal to 0 or 1) at 24 hours.
5. Distribution of modified Rankin Scale (mRS) scores at 30 and 90 days.
6. Proportion achieving independence (mRS score ≤2) at 90 days.
7. Proportion achieving excellent neurological outcome (mRS score 0-1) at 90 days.
8. Health-related Quality of Life using the EQ-5D score at 90 days.
9. Mortality.
10. Cumulative incidence of Serious Adverse Events at 24h, day 7, and day 90.

Mechanistic:
1. Volume of tissue infarction at 24h (volume of DWI lesion on MRI or hypoattenuated tissue on non-contrast CT if MRI cannot be obtained).

Completion date
31/07/2026

Eligibility

Key inclusion criteria
1. Male or non-pregnant female aged ≥18 years
2. Acute ischemic stroke fulfilling perfusion imaging criteria (ischemic core volume <70 mL, mismatch ratio >1.8 and mismatch volume >15 mL using RAPID or equivalent CE-marked software)
3. Eligible for thrombolysis or thrombectomy
4. Intracranial LVO on CTA (occlusion of the terminal ICA, MCA-M1, ≥1 proximal MCA-M2, or proximal posterior cerebral artery (PCA-P1))
5. ≤9 hours after last known well (if waking with symptoms, last known well time is calculated as the mid-point between going to sleep and waking)
6. Pre-stroke functional independence (estimated pre-stroke mRS ≤2)
7. NIHSS score ≥6 (or NIHSS ≥2 if PCA-P1 occlusion) at randomisation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. History of significantly impaired renal eGFR (30ml/min) or hepatic function (transaminases >3 times upper limit of normal or history of cirrhosis), unstable angina or heart failure (NYHA 3 or 4).
2. Pre-existing lung disease requiring supplemental chronic or intermittent oxygen therapy (NB oxygen therapy given post-stroke is not an exclusion)
3. Previous hypersensitivity reaction to NanO2 excipients and/or compounds similar to NanO2
4. Pregnancy (for women of child-bearing potential a negative pregnancy test will be required prior to randomisation) or breast feeding women. (Women of child-bearing potential is defined as experienced menarche; AND not undergone successful surgical sterilisation (hysterectomy, bilateral salpingectomy, or bilateral oophorectomy); AND not post-menopausal i.e. amenorrhea for ≥12 consecutive months (without another medical cause))
5. Participation in another CTIMP within preceding 90 days or 5 half-lives of the investigational product, ,whichever is longer or previous participation in NOVEL

Date of first enrolment
01/06/2025

Date of final enrolment
31/07/2026

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
NHS Greater Glasgow and Clyde
J B Russell House
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Study participating centre
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AB25 2ZN

Study participating centre
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Study participating centre
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Sponsor information

Organisation
University of Glasgow

ROR
https://ror.org/00vtgdb53

Organisation
NHS Greater Glasgow and Clyde

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	02/10/2024	03/02/2025	No	Yes