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Nimodipine for acute optic neuritis

Submission date 21/12/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 25/02/2025	**Overall study status** Ongoing	
Last Edited 23/01/2026	**Condition category** Nervous System Diseases	

Plain English summary of protocol

Background and study aims
The study drug, nimodipine, is being developed for the treatment of optic neuritis - an inflammatory disease of the eye that causes damage to the protective covering that surrounds fibres of the optic nerve and leads to vision loss. It is mainly associated with multiple sclerosis but can be associated with other diseases. As well as the inflammation caused by the disease, it is thought that tissue hypoxia (a lack of oxygen supply and blood flow to the brain) may drive damage to the optic nerve. Currently, optic neuritis can only be treated with steroids, which help to speed up the time taken for recovery, but do not provide any significant improvement in a patient's long-term health or quality of life. Their use is not without risk and they have negative side effects. Nimodipine is a cheap, widely used drug with very few side effects. It is used to treat symptoms resulting from a ruptured blood vessel in the brain (subarachnoid hemorrhage) by increasing blood flow to the brain. Therefore, it could be used to treat the tissue hypoxia caused by optic neuritis. This trial aims to investigate the efficacy of nimodipine in improving the visual function of patients who develop acute optic neuritis. The safety and tolerability of nimodipine will also be assessed.

Who can participate?
Participants who present acutely with optic neuritis and healthy participants for comparison and who will not receive nimodipine

What does the study involve?
All participants will undergo visual function assessments and participants with optic neuritis will receive a single oral 60 mg dose of nimodipine after baseline assessments have been conducted. Participants will remain at the hospital for approximately 3 hours to undergo visual function assessments and for any side effects to be recorded. Participants with optic neuritis will receive a follow-up phone call 24 hours later to ensure their ongoing wellbeing.

What are the possible benefits and risks of participating?
It is unknown whether taking part in the study will improve the participant's condition, however, the information we get from the study will help improve our knowledge of treating optic neuritis, which will benefit the treatment of people with optic neuritis in the future.

The main risks that may arise are from the administration of the trial drug (nimodipine) (to be administered to patient group only), however, such risks are relatively minimal given the single

dose that is to be given and the drug's well-established safety profile. The main risks may include side effects such as nausea or headaches which are relatively uncommon- all potential side effects are detailed in the Participant Information Sheet (PIS). In addition, complications such as an allergic reaction, thrombocytopenia, hypotension, tachycardia, ileus, bradycardia or transiently raised liver enzymes are potential risks, however, they are all relatively rare. Participants will be screened for risk of developing such complications early (i.e. identifying those with underlying comorbidities or abnormalities) using a thorough review of participants' medical history, clinical examination and review of medication. During the trial, participants in the patient group will be closely monitored before, during and after administration of the study drug (after, for at least 3 hours) as well as being followed up for any side effects the following day.

The trial population includes women of childbearing potential. The study drug might harm unborn children, so all participants in the patient group must follow the contraceptive restrictions as detailed in the PIS. Were a participant or a partner of a participant become pregnant during the trial, we would ask for their permission to follow the pregnancy.

Risks from study procedures:
- Taking blood samples (patient group only): Taking blood may cause temporary discomfort from the needle stick, bruising, fainting and very rarely infection at the puncture site but these problems usually clear up within a few days to a few weeks. Participants must lay down when blood samples are taken to mitigate against the risk of fainting.
- Neurological examination: A basic neurological exam should produce no discomfort.
- Electroretinogram: The risk associated with an ERG is a temporary scratch of the surface of the cornea due to the electrode. Otherwise, there are no risks associated with this procedure.
- Measuring blood pressure: The blood pressure cuff used to take a blood pressure reading may cause discomfort or bruising to the upper arm.
- Ophthalmic/Eye exam and OCT: The participant will be examined using Optical Coherence Tomography (OCT), a test using light to evaluate the retina. OCT is a non-invasive short test and does not typically carry any risks. The eye examination should not carry any significant risk or discomfort.

Given the importance of administrating nimodipine as quickly as possible after the start of clinical symptoms, as therapeutic effectiveness is likely greatest in this period, results for the serum AQP4-antibodies and MOG-antibodies will not be known yet when data is collected.
It takes up to a week for the results of these antibodies to be known. When testing positive for either AQP4 or MOG antibodies, the participant’s data will be retrospectively excluded from analysis and the participant will be considered withdrawn from the trial. This is likely to not occur for more than 1 out of 10 patients, given the low incidence of AQP4 and MOG seropositivity. Patients with AQP4-antibody or MOG-antibody seropositivity will still be followed up and analysed for safety outcomes. Patients will be informed of this possibility as part of the informed consent process.

Participants will receive payment for participating in the trial. There is always a risk that payment could represent coercion. However, payment will be based on travel and food expenses, not on risk. An Ethics Committee will review the payment to ensure that it is fair.

Where is the study run from?
University College London, UK

When is the study starting and how long is it expected to run for?
December 2024 to January 2027

Who is funding the study?
Fight for Sight, UK

Who is the main contact?
University College London, ctimps@ucl.ac.uk

Contact information

Type(s)
Public

Contact name
Ms Olivia Fox

Contact details
University College London
London
United Kingdom
NW1 2PG
-
Olivia.fox@ucl.ac.uk

Type(s)
Scientific, Principal investigator

Contact name
Dr Anand Trip

Contact details
Department of Neuroinflammation, National Hospital for Neurology and Neurosurgery, Queen Square
London
United Kingdom
WC1N 3BG
+44 (0)203 4567890
anand.trip@nhs.net

Additional identifiers

Integrated Research Application System (IRAS)
1007797

Protocol serial number
123776

Study information

Scientific Title

A proof-of-concept, open, single-site exploratory study investigating the safety and tolerability of oral nimodipine and the effect it has on visual function in acute optic neuritis

Study objectives
- To investigate the safety and tolerability of a single oral dose of 60 mg nimodipine in acute optic neuritis
- To describe changes in vision and the function of the visual pathway among individuals presenting with acute optic neuritis (<2-week onset) after a single dose of 60mg oral nimodipine
- To investigate the efficacy of a single oral dose of 60mg nimodipine in improving the oxygenation of the retina among individuals presenting with acute optic neuritis (< 2-week onset)

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 21/02/2025, HSC REC A (Business Services Organisation (BSO) Headquarters, 2 Franklin Street, Belfast, BT2 8DQ, United Kingdom; +44 28 9536 1400; RECA@hscni.net), ref: 25/NI/0009

Primary study design
Interventional

Study design
Proof-of-concept open-label single-site exploratory study

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Acute optic neuritis

Interventions
Treatment arm: A single oral 60 mg dose of Nimodipine tablets will be given on one occasion. Participants will receive ophthalmological and safety assessments over approximately 3 hours after dosing and will receive a follow-up phone call 24 hours after.
Control arm: No study drug given. Participants will receive ophthalmological and safety assessments over approximately 3 hours.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Nimodipine

Primary outcome(s)

Adverse events will be measured based on various ophthalmological and safety assessments, as well as verbal feedback from the participant, taken from screening until discharge from the study (24 hours after dosing)

Key secondary outcome(s)
1. Description of changes in (pattern) visual evoked potential (PVEP/VEPs) measurements taken at 60, 90, 150 and 180 minutes after dosing
2. Changes in (pattern) electroretinography (PERG/ERG) measurements taken at 180 minutes after dosing
3. Description of changes in visual acuity (high- and low-contrast with LogMAR and Sloan charts respectively) at 90 and 180 minutes after dosing
4. Description of changes in relative afferent pupillary deficits attenuated (RAPD) pupillary light responses in optic neuritis) using monocular pupillometry (NeurOptics) measured at 90 and 180 minutes after dosing
5. Description of changes in retinal oxygenation (using OCT) at 180 minutes after dosing

Completion date
01/01/2027

Eligibility

Key inclusion criteria
Treatment group:
1. Participants aged 18-60 years
2. A history of typical, demyelinating acute monocular (unilateral) optic neuritis
3. Symptom onset (pain and/or visual dysfunction) for less than 2 weeks before study inclusion
4. Baseline visually evoked potentials confirm optic nerve conduction delays, while baseline pattern on electroretinography is not suggestive of retinal disease as an alternative diagnosis
5. Participants must be willing and able to provide written informed consent
6. Female participants of childbearing potential must have a negative urinary pregnancy test on the date of inclusion and agree to use a highly effective method of contraception from the time consent is signed until 48 hours after treatment administration (due to a lack of safety data on the use of nimodipine in pregnant and breastfeeding women; and to allow for medication washout post treatment discontinuation).
Highly effective methods of contraception acceptable for this trial are barrier mechanisms and hormonal mechanisms with 100% compliance for the duration of treatment, these include:
6.1. Combined (estrogen and progestogen-containing) hormonal contraception associated with inhibition of ovulation
6.2. Oral
6.3. Intravaginal
6.4. Transdermal
6.5. Progesterone-only hormonal contraception associated with inhibition of ovulation
6.6. Oral
6.7. Injectable
6.8. Implantable
6.9 Intrauterine device
6.10. Intrauterine hormone-releasing system
6.11. Bilateral tubal occlusion
6.12. Vasectomised partner (when this is the sole partner of the WOCBP participant and the vasectomised partner has received a medical assessment of the surgical success)

6.13. Sexual abstinence (sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments, and the reliability of sexual abstinence is in line with the preferred and usual lifestyle of the subject)
NOTE: For the purpose of this document, a woman is considered of childbearing potential (WOCBP), i.e. fertile, following menarche and until becoming post-menopausal unless permanently sterile. Permanent sterilisation methods include hysterectomy, bilateral salpingectomy, and bilateral oophorectomy. A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high follicle-stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a post-menopausal state in women not using hormonal contraception or hormonal replacement therapy. However, in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient.

Control Group:
1. Age 18-60 years (inclusive).
2. No history of ophthalmological or neurological disease
3. Baseline visual evoked potentials confirm normal optic nerve conduction studies
4. Baseline pattern electroretinography does not suggest retinal disease as an alternative or concomitant diagnosis.
5. Willing and able to provide written informed consent.

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
Treatment Group:
1. Participants with a prior diagnosis of ophthalmic or retinal disease (i.e. diabetic retinopathy, macular degeneration, glaucoma, severe myopia (>5D)).
2. Participants with a history of significant cardiac disease (e.g., cardiac conduction block or ischaemic heart disease)
3. Participants who are pregnant at the time of study recruitment or currently breastfeeding
4. Participants with abnormal vital signs (pulse >120bpm or <50bpm; systolic BP >160mmHg or <100mmHg; diastolic BP >100mmHg or <50mmHg).

5. Participants with a known history of hepatic impairment (as dose reduction is normally advised as such for the IMP)
6. Participants with suspected raised intracranial pressure.
7. Participants with a known allergy to the IMP or its excipients
8. Participants who have concurrent involvement in other research studies, or the use of other experimental medication.
9. Participants who have had a significant head injury within 2 weeks of recruitment
10. Participants with a history of clinically significant medical or psychiatric illness, or laboratory abnormality that, in the opinion of the principal investigator, may affect the interpretation of the study results or participant safety.
11. Participants who are non-fluent English speakers
12. Participants with a history of photosensitive epilepsy.
13. Participants using concurrent medication as listed in Section 6.7
14. Recruited participants will be tested for serum MOG-antibodies or AQP4-antibodies as per usual clinical practice. Should the participant be found to have a positive antibody result (allowing 1-2 weeks for the results), they will be retrospectively excluded from the study.
NOTE: Patients with an established diagnosis of multiple sclerosis, including those taking disease-modifying treatments, who subsequently develop a first episode of optic neuritis episode are not excluded from the study.

Control Group:
1. Non-fluent English speakers
2. Concurrent involvement in other research or use of another experimental investigational medicinal product that is likely to confound ophthalmological investigation findings
3. Prior diagnosis of ophthalmic or retinal disease (i.e. diabetic retinopathy, macular degeneration, glaucoma, severe myopia (>5D))
4. History of photo-sensitive epilepsy

Date of first enrolment
09/02/2026

Date of final enrolment
01/01/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
National Hospital for Neurology & Neurosurgery - Queen Square
Queen Square
London
England
WC1N 3BG

Study participating centre
Moorfields Eye Hospital
162 City Rd
London
England
EC1V 2PD

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Charity

Funder Name
Fight for Sight UK

Alternative Name(s)
Fight for Sight, Fight for Sight (UK)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

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. Anonymised primary research data and aggregate group-level data may be shared with other professionals with adequate research experience on request.

IPD sharing plan summary

Available on request