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A nationwide clinical trial for patients with the eye condition vitreous haemorrhage due to proliferative diabetic retinopathy investigating whether early eye surgery and laser treatment is a safe and better option for improving visual outcomes than the current standard of care

Submission date
27/02/2025

Recruitment status
Recruiting

Registration date
10/06/2025

Overall study status
Ongoing

Last Edited
24/10/2025

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims

The most common cause of severe vision loss in people with diabetes is proliferative diabetic retinopathy (PDR). This condition affects about 3% of the UK population with diabetes, most being of working age. In PDR, the eye grows new blood vessels on the retina. The retina needs to be treated urgently by laser so that these blood vessels disappear or become inactive. If left untreated, these blood vessels can bleed into the vitreous region of the eye (termed vitreous haemorrhage [VH]) causing a sudden drop in vision and a delay to laser treatment. Nearly 50% of patients who develop PDR may still experience VH within 5 years despite good laser treatment. VH due to PDR is a global health problem that needs a new treatment strategy. The current Standard-of-Care (SoC) for patients involves:

1. A period of waiting for the bleeding to clear naturally, which usually lasts months.
2. Once the bleeding resolves, repeated laser treatments to prevent rebleeding.
3. If the blood does not clear sufficiently to apply laser treatment (about 20% of cases), the vitreous gel with blood is removed surgically (called vitrectomy) with laser treatment applied at the time of surgery. This procedure is typically offered after a long period of observation and several hospital appointments.

Clinical trials in the 1980s showed that patients with dense VH who underwent vitrectomy within 6 months had greater vision improvement, however, this approach was not recommended due to the risks of surgery. Since then, techniques and equipment for performing vitrectomy have advanced significantly reducing the risks of surgery.

This study aims to investigate whether for patients with VH due to PDR, early vitrectomy with laser treatment applied at the time of surgery is a safe and better option for improving visual outcomes, allowing faster visual rehabilitation, and reducing hospital appointments than the current SoC.

Who can participate?
Adults (aged 18 years and above) who have diabetes type 1 or 2 and vision impairment due to a diagnosis of VH due to PDR.

What does the study involve?
The study involves patients being randomly assigned to one of two treatment groups. One group will undergo SoC as described in the background. The other group will have surgery + laser treatment within 4 weeks of joining and a safety visit 2 weeks after their surgery + laser appointment. They will then follow a SoC pathway so if they require additional laser treatments or other interventions this will be provided. All patients on the trial will be followed up every 4 months over a 12-month period where they will undergo vision and optical function assessments, and take part in questionnaires to understand their quality of life and patient safety reviews. On entering and exiting the trial all patients will also undergo a blood test. Patients will be free to exit the trial at any point if they wish to do so.

What are the possible benefits and risks of participating?
This study will provide patients and the clinical community with information on the risk-to-benefit ratio of early vitrectomy for VH due to PDR. Participants assigned to the early surgery + laser treatment group and continuing for the full follow-up duration of 12 months would potentially benefit from faster visual recovery, improved visual outcomes, fewer complications, and reduced burden of outpatient visits and treatments compared to the current standard of care. However, the risks of participating are that, despite early surgery, patients may require postoperative intervention due to complications (e.g., detachment of the retina), infection, or limited response to the treatment. As with any surgery there will also be an intraoperative risk. Intra- and post-operative risks are now significantly reduced due to improved surgical techniques. For those in the standard-of-care arm, the benefits will be that, if the VH resolves spontaneously or early laser treatment is effective, then patients will not need to be exposed to the risks of surgery. As this is the current patient care pathway, the risks of being in this arm are the same as the current risks of care. The delay to surgery for those whose VH does not spontaneously resolve or does not respond well to early laser treatment may mean the surgery (>4 months) is less effective or results in further complications. This will be explored in this study.

Where is the study run from?
The study will be run across 25 NHS sites from across the UK and will be managed by Moorfields Eye Hospital NHS Foundation Trust in London (UK).

When is the study starting and how long is it expected to run for?
April 2025 to March 2028

Who is funding the study?
This study is being funded by the Medical Research Council (MRC) and National Institute of Health and Care Research (NIHR), with contributions from the CSO in Scotland, Health and Care Research Wales and the HSC R&D Division, Public Health Agency in Northern Ireland.

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Integrated Research Application System (IRAS)
357031

Central Portfolio Management System (CPMS)
61991

National Institute for Health and Care Research (NIHR)
167945

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Study information

Scientific Title
A multicentre randomised clinical trial comparing the clinical efficacy and safety of early vitrectomy plus endolaser versus standard of care for visual impairment due to vitreous haemorrhage secondary to proliferative diabetic retinopathy

Acronym
EVERLAST

Study objectives
In people with visual impairment due to vitreous haemorrhage (VH) due to proliferative diabetic retinopathy (PDR), does early vitrectomy (PPV) and endolaser as a primary intervention result in better visual outcome compared to standard of care (SoC) where PPV is done only for non-clearing VH following a period of observation waiting for the VH to clear whilst applying pan-retinal photocoagulation (PRP) laser over multiple visits as the blood clears spontaneously?

Ethics approval required
Ethics approval required

Ethics approval(s)
Not yet submitted, Ethics committee name not provided (Address not provided, City not provided, Zip/postal code not provided; Telephone number not provided; Email not provided), ref: Reference number not provided

Primary study design
Interventional

Study design
Phase II multicenter interventional outcome assessor masked randomized controlled trial

Study type(s)
Efficacy, Quality of life, Safety, Treatment

Health condition(s) or problem(s) studied
Adults with type 1 or type 2 diabetes presenting with visual impairment due to vitreous haemorrhage secondary to proliferative diabetic retinopathy

Interventions
Intervention:
Early pars plana vitrectomy (PPV) with endolaser performed within 4 weeks (+5 days) of clinical decision for intervention. This will be followed by a standard of care pathway.

Control (standard of care):
1. Observation for spontaneous resolution (clearing) of vitreous haemorrhage.
2. Panretinal photocoagulation laser applied to visible areas during outpatient visits over multiple sessions as the blood clears.
3. PPV reserved for non-clearing VH (≥4 months), as per NICE guidelines.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Best-corrected visual acuity (BCVA) is a key endpoint used to assess the effectiveness of treatments for visual impairments and eye diseases. For our patient population, this is measured using the Early Treatment of Diabetic Retinopathy Study (ETDRS) scale. BCVA will be assessed at 12 months.

Key secondary outcome(s)
1. Visual acuity changes over 12 months measured using ETDRS at baseline, 4 months, 8 months and 12 months and taking the area under the curve.
2. Patient-reported outcomes over 12 months measured using vision-related quality of life and satisfaction questionnaires taken at baseline and 12 months.
3. Rates of disease progression over 12 months measured using ophthalmic examinations (e.g., anterior and posterior eye segment examination and slit lamp) and imaging (e.g., colour fundus photographs and optical coherence tomography [OCT]) at baseline, 4 months, 8 months and 12 months.
4. Complications (e.g., recurrent VH, tractional retinal detachment, neovascular glaucoma) over 12 months measured using ophthalmic examinations (e.g., anterior and posterior eye segment examination and slit lamp) and imaging (e.g., colour fundus photographs and optical coherence tomography) at baseline, 4 months, 8 months and 12 months.
5. Hospital visit burden and additional treatments required (e.g., repeat PRP, intravitreal anti-VEGF injections, or further PPV) recorded from patient hospital visits over 12 months.
6. Macular ischaemia measured using OCT angiography at time 12 months.
7. Macular oedema and inner retinal thickness measured using OCT at time 12 months.

Completion date
31/03/2028

Eligibility

Key inclusion criteria
1. Adults (>18 years) with type 1 or 2 diabetes, with visual impairment (defined as Snellen 6/12 or worse/ETDRS 73 letters or fewer) and with a diagnosis of vitreous haemorrhage secondary to proliferative diabetic retinopathy, and requiring intervention.
2. Treatment naïve and previous laser-treated patients.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Previous surgery: history of PPV in the affected eye
2. Non-PDR VH caused by conditions unrelated to PDR
3. Other eye conditions: significant co-existing ocular pathology that might interfere with outcomes (e.g., advanced glaucoma, endophthalmitis)
4. Systemic conditions: any systemic condition preventing follow-up or compliance with the trial protocol

Date of first enrolment
02/01/2026

Date of final enrolment
31/03/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
NIHR Moorfields Biomedical Research Centre
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Sponsor information

Organisation
Moorfields Eye Hospital NHS Foundation Trust

ROR
https://ror.org/03zaddr67

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

Funder Name
Medical Research Council (MRC)

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 data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date