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Assessment of surgery and standard treatment to treat visual loss from diabetic eye disease

Submission date
15/12/2020

Recruitment status
No longer recruiting

Registration date
18/12/2020

Overall study status
Completed

Last Edited
09/08/2024

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims
Diabetic macular oedema (DMO) is swelling at the back of the eye in diabetic patients. This swelling damages the retina and affects patients' vision. The current NHS standard treatment for DMO is a course of injections of ranibizumab or aflibercept into the eye up to every month. These medications (ranibizumab and aflibercept) are collectively known as anti-VEGF injections. The average number of injections required by patients with DMO is around eight in the first year with some people requiring as many as 13 in the first year of treatment. The aim of treatment is to reduce the swelling of the retina and thereby improve the vision.
Performing an operation called a vitrectomy in patients with DMO can also reduce the swelling of the retina. Researchers want to investigate whether performing vitrectomy surgery earlier and in combination with anti-VEGF injections improves vision in the long term and or reduces the number of injections per year needed by patients with DMO.
It is not known whether performing a vitrectomy along with standard injections is better than performing standard injections alone. This study will help with the planning of a larger study to compare early vitrectomy surgery with the standard treatment of anti-VEGF injections. It would take a bigger study to provide proof. The researchers need to complete this smaller study first in order to plan the bigger definitive study.

Who can participate?
Patients with significant DMO which is affecting vision and otherwise good health.

What does the study involve?
All patients will receive the current standard treatment of monthly injections of a medicine called ranibizumab or aflibercept.
Initial treatment of ranibizumab starts with 3 injections, 1 month apart over a period of 8 weeks. Initial treatment with aflibercept starts with 5 injections 1 month apart over consecutive months. The average number of injections is between 7 and 9 in the first year and some people require as many as 13 in the first year of treatment.
If after 12 weeks patients still have significant DMO (swelling greater than 350 microns when measured on OCT scan) they will be asked again if they wish to take part in the study and will be asked to sign a consent form. They will be asked to complete a questionnaire and the researchers will perform a series of tests. These are routine tests with no recognised additional

risk that are performed on a regular basis for patients with DMO. Participants will then be allocated at random to one of two groups. There is an equal chance of being assigned to each group.
Group 1 will receive the current standard treatment of injections as often as is required.
Group 2 will undergo a vitrectomy as well as the standard care of injections as often as is required.
There are well-defined criteria for the number and timing of injections for patients with DMO, depending on the response to the previous injections. The same criteria will be used on everyone in the study.
The vitrectomy will be performed within 1 month, and patients will be asked to come back for a post-operative check within 2 weeks. Thereafter patients will be reviewed on a regular basis for assessment for injections, just like the group that hasn't had an operation. After 12 months the two groups will be compared to see if there is a difference between them.

What are the possible benefits and risks of participating?
Most studies show that vitrectomy gives a sustained improvement in the amount of DMO, which may be associated with an improvement in vision. It may be that the group undergoing vitrectomy require fewer injections than the group having injections alone and this is a potential benefit. The group undergoing vitrectomy may also have better vision than the other group at the end of the study, which is another potential benefit.
Participants' vision may be a little blurred for a week or two after the vitrectomy. It is unusual for there to be any deterioration of vision after that. A small number of patients (about 1 in 30) undergoing a vitrectomy may need a gas bubble in their eye to act as a splint if a hole or tear is found in the retina. This is absorbed by the body typically over 2 to 3 weeks. The vision is like looking through water until the gas absorbs.
Vitrectomy can speed up the onset of cataract, which is a very treatable cause of worsening vision. In previous studies very few patients with DMO undergoing vitrectomy developed a cataract that needed surgery. If participants develop a cataract that affects their vision after having the vitrectomy they will be offered treatment. A rise in eye pressure may occur after a vitrectomy. This is usually treatable with drops and usually resolves. There is about a 1:100 chance of needing long-term eye pressure treatment. Retinal detachment is a rare complication of surgery occurring in approximately 1 in 100 cases. This can usually be repaired with a single extra operation. The serious complication risk is about 1 in 1000 cases, where the eye becomes totally blind due to a bleed during surgery or an infection after surgery. Whilst this is a very real risk, the risk from an extra injection is not dissimilar.

Where is the study run from?
Guy's and St Thomas' NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
September 2018 to January 2022

Who is funding the study?
Fight for Sight (USA)

Who is the main contact?
Dr Matthew Maguire
Matthew.Maguire2@nhs.net

Contact information

Type(s)
Scientific

Contact name
Dr Matthew Maguire

ORCID ID
https://orcid.org/0000-0001-6746-0528

Contact details
Dept Academic Ophthalmology
St Thomas' Hospital
3rd Floor, D-block, South wing,
Westminster Bridge Road
London
United Kingdom
SE1 7EH
+44 (0)207 1887188 ext. 86753
Matthew.Maguire2@nhs.net

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
220073

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 220073

Study information

Scientific Title
A feasibility randomized controlled trial of vitrectomy plus standard care intravitreal ranibizumab or aflibercept injections versus standard care intravitreal ranibizumab or aflibercept injections alone in patients with centre involving diabetic macular oedema: the Vitrectomy in Diabetic Macular OEdema trial

Acronym
VIDEO

Study objectives
Diabetic macular edema (DME) is a prevalent cause of sight loss in working-age patients. The current standard NICE approved treatment involves intravitreal injections of anti-VEGF drugs, initially on a monthly basis. Whilst potentially restoring lost vision this therapy involves frequent protracted hospital visits and a considerable economic and capacity burden on health care

funders and providers. The effect of anti-VEGF therapy is also transient; depending on the drug and treatment regime patients need 3-13 injections in the first year (mean 7-9) and approximately 5 in the second year. Around 25% of patients do not respond to anti-VEGF therapy.
Most studies indicate that vitrectomy delivers sustained improvements in macular thickness. Evidence on whether acuity is improved is inconsistent. In the presence of traction vitrectomy is thought to be visually effective. In the absence of traction vitrectomy was usually performed as rescue therapy when repeated laser treatments had failed and visual improvement may not have been possible. Studies where vitrectomy was performed early in the disease showed visual benefit. All these data also predate the current gold standard anti-VEGF therapy for DME.

It is hypothesised that adding a vitrectomy and internal limiting membrane peel to standard care intravitreal Ranibizumab or Aflibercept injections in the management of centre involving diabetic macular edema will result in: improved or comparable visual outcomes, fewer anti-VEGF injections and reduced costs.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/09/2018, London Brent Research Ethics Committee (80 London Road, Skipton House, London, SE1 6LH, UK; +44 (0)207 104 8356; brent.rec@hra.nhs.uk), REC ref: 18/LO/0324

Study design
Pragmatic stratified single-masked randomized feasibility study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Diabetic macular oedema

Interventions
Eligible patients will only be enrolled after receiving three loading doses of Ranibizumab or Aflibercept, with subsequent (1:1) randomisation to the treatment or control group.
The treatment group will undergo vitrectomy within 4 weeks of enrolment.
Both groups will receive NHS standard, treat and extend ranibizumab injections or aflibercept.
Aflibercept injections will be given monthly for 5 months and thereafter on a treat and extend basis if the centre is practising this regimen as standard treatment.
Follow up will be for 52 weeks.

The treatment group: Vitrectomy, ILM peeling, ranibizumab or aflibercept ± PRP laser with ongoing NICE-mandated standard of care intravitreal injections of ranibizumab or aflibercept

The control group: Ongoing NICE mandated standard of care intravitreal injections of ranibizumab or aflibercept.

The recommended dose for ranibizumab is 0.5 mg given as a single intravitreal injection. Aflibercept is given as a single 2 mg intravitreal injection.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Distance best corrected visual acuity measured in the number of ETDRS letters at baseline and 12 months

Key secondary outcome(s))
1. Central macular thickness (CMT) measured on OCT scan over the central 1mm subfield at 12 months
2. Number of injections in 12 months measured documented in patient clinical research forms
3. Trial recruitment measured using number of randomised recruits entered into castor database from trial commencement to Jan 2021
4. Number completed follow up at 12 months measured using completed patient clinical research forms
5. Area under the curve of central macular thickness measured by statistical analysis at 12 months
6. Area under the curve of best corrected visual acuity measured using statistical analysis at 12 months
7. Need for rescue therapy measured using data entered in patient clinical research forms from recruitment to 12 months
8. Need for cataract surgery measured using documented cataract surgery on patient clinical research forms from recruitment to 12 months
9. Complications measured using documented events in patient clinical research forms and submitted serious adverse event forms

Completion date
31/01/2022

Eligibility

Key inclusion criteria
1. Patient over 18 years of age
2. Patient has the capacity to give informed consent
3. Patient has not previously been enrolled in this study in regards to their other eye
4. Symptomatic visual loss attributable to diabetic macular edema for less than one year
5. Patient has a formal diagnosis of diabetes mellitus
6. Patient has an HbA1c test (a blood test that looks at long term diabetic control) performed within the past 2 months
7. Ophthalmic criteria:
7.1. Symptomatic visual loss attributable to DME for less than one year
7.2. Best corrected visual acuity of better than 35 letters on formal testing
7.3. Central macular swelling greater than 350 microns

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
47

Key exclusion criteria
1. History of chronic renal failure requiring dialysis or transplantation
2. Patient suffered a major thromboembolic event within the past 6 months as (defined as TIA, stroke, or MI)
3. Patient has undergone major surgery within the past 6 months or has major surgery planned over the next 12 months defined as requiring GA or reduced mobilisation
4. Known adverse reaction to anti-VEGF medications
5. Blood pressure greater than 180 systolic or 100 diastolic
6. Use of pioglitazone (diabetic medication)
7. Any other condition that in the opinion of the investigator would preclude participation in the study (such as unstable medical status or severe disease that would make it difficult for the patient to be able to complete the study)
8. Very poor glycaemic control and has started intensive therapy within the previous 3 months.
9. The patient will use an investigational drug during the study
10. Previous macular laser within 750 microns of the foveal centre
11. Previous vitrectomy surgery in the study eye
12. Other than intravitreal ranibizumab or aflibercept therapy or cataract surgery: any other laser, surgical or injection therapy in the last 24 weeks
13. Cataract surgery within 3 months
14. Concomitant ophthalmic disease liable to affect central macular thickness or visual acuity
15. Centre involving vitreous haemorrhage
16. Proliferative diabetic retinopathy
17. Presence of visually significant cataract prior to enrolment

Date of first enrolment
25/06/2019

Date of final enrolment
31/01/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St Thomas' Hospital
Guy's and St Thomas' NHS Foundation Trust
Westminster Bridge Rd
London
United Kingdom
SE1 9RT

Sponsor information

Organisation
Guy's and St Thomas' NHS Foundation Trust

ROR
https://ror.org/00j161312

Funder(s)

Funder type
Charity

Funder Name
Fight for Sight

Alternative Name(s)
Fight for Sight, Inc., National Council to Combat Blindness, Fight for Sight (U.S.), FFS

Funding Body Type
Government organisation

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

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		08/08/2024	09/08/2024	Yes	No
HRA research summary			26/07/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes