ISRCTN92166560 https://doi.org/10.1186/ISRCTN92166560

A randomised controlled trial of alternative treatments to inhibit VEGF in age-related choroidal neovascularisation

Submission date
19/04/2007

Recruitment status
No longer recruiting

Registration date
19/04/2007

Overall study status
Completed

Last Edited
24/10/2022

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims
Wet or neovascular age-related macular degeneration (AMD) is a condition which causes severe sight loss in older people. This condition is due to new blood vessel growing into the central region of the retina of the eye, known as choroidal neovascularisation (CNV). These vessels are leaky and lead to the accumulation of fluid between and within the layers of the retina with serious adverse effects on central vision. Lucentis® is an 'anti-VEGF' drug which is injected monthly into the eye and causes these blood vessels to stop leaking and to shrink. With treatment, eyesight improves in a quarter of affected people and, in the majority (90% or more) eyesight does not deteriorate over two years. These results represent a major improvement over previous treatments. Another anti-VEGF drug, Avastin® (from which Lucentis was derived), may be equally good and is considerably less expensive, but its effectiveness and safety need to be confirmed. This study is a head-to-head comparison of the effectiveness and safety of Avastin® and Lucentis®. We are also studying whether the number of treatments needed can be reduced by comparing monthly anti-VEGF treatment for 2 years with monthly anti-VEGF treatment for 3 months only, with careful monthly review and re-starting treatment if any signs of disease recur.

Who can participate?
Adults aged 50 and over with CNV caused by AMD.

What does the study involve?
Patients are randomly allocated to various combinations of active treatment. Their eyesight is assessed at each visit and information is collected on their quality of life and the costs and burden of illness, which will be compared between the different groups after 1 and 2 years follow-up.

What are the possible benefits and risks of participating?
Although Lucentis has so far shown the best results of all the licensed anti-VEGF treatments in terms of maintained and improved eyesight, we believe that there will be benefits to patients if we can undertake fewer treatments without compromising eyesight. Patient support

organisations agree that this study is important and that it has considerable potential to benefit future patients.

Where is the study run from?
The Queen's University of Belfast (UK)

When is the study starting and how long is it expected to run for?
July 2007 to November 2012

Who is funding the study?
NIHR Health Technology Assessment Programme - HTA (UK)

Who is the main contact?
Prof Usha Chakravarthy
u.chakravarthy@qub.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Usha Chakravarthy

Contact details
The Queen's University of Belfast
Centre for Vision Sciences
Institute of Clinical Science
The Royal Hospitals
Grosvenor Rd
Belfast
United Kingdom
BT12 6BA
+44 (0)2890 632527
u.chakravarthy@qub.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 07/36/01; Sponsor ref: RGHT000449

Study information

Scientific Title

A randomised controlled trial of alternative treatments to inhibit VEGF in age-related choroidal neovascularisation

Acronym
IVAN

Study objectives
1. Avastin® (bevacizumab) is not inferior to Lucentis® (ranibizumub) with respect to the benefits of vascular endothelial growth factor (VEGF) inhibition in maintaining/improving visual acuity in eyes with chorodial neovascularisation (CNV).
2. Treatment with VEGF inhibition can be 'safely' withdrawn at 3 months with monthly review to detect CNV reactivation, i.e. criteria for re-starting treatment can be pre-specified to prevent any difference in average visual acuity compared with continuing monthly treatment.

More details can be found at http://www.nets.nihr.ac.uk/projects/hta/073601
Protocol can be found at http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0003/51780/PRO-07-36-01.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
Health and Personal Social Services 3 in Northern Ireland, ref: 07/NI R03/37

Study design
Multi-centre factorial randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Age-related macular degeneration (AMD)

Interventions
Participants, clinical staff and researchers will be masked to allocation of VEGF inhibition drug but not to stopping/continuing treatment at three months.

Factor 1: Intravitreal injection using either Avastin® or Lucentis® (VEGF inhibition drugs).
Factor 2: Intravitreal injection of VEGF inhibition drug, either monthly for 2 years or monthly for 3 months with subsequent monthly review to detect CNV reactivation.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Bevacizumab, ranibizumub

Primary outcome measure
The primary outcome is corrected 1 metre VAlogMAR, measured as the number of letters read on a standard ETDRS chart. The primary end point will be VAlogMAR after two years of follow-up.

Secondary outcome measures
Secondary outcomes will be analysed after one and two years of follow-up, unless otherwise stated.
1. Frequencies of adverse effects of treatment
2. Generic and vision-specific health-related quality of life (HRQoL)
3. Treatment satisfaction
4. Cumulative resource use/cost, and cost-effectiveness
5. Clinical measures of vision
6. CNV morphology (from masked grading of fundus fluorescein angiograms [FFA] and optical coherence tomography scans [OCTs]).
7. Distance VAlogMAR after all patients have been followed for 1 year after starting treatment.
8. Survival free from treatment failure (i.e. satisfying one or more of the criteria for re-treatment).

Overall study start date
01/07/2007

Completion date
30/11/2012

Eligibility

Key inclusion criteria
1. Adults age ≥50 of either sex
2. Newly referred for the treatment of CNV caused by Age-related Macular Degeneration (AMD) in the first or second eye
3. Corrected 1 metre logarithmic minimal angle resolution visual acuity (VAlogMAR) ≥25 letters read on a standard Early Treatment Diabetic Retinopathy Study (ETDRS) chart
4. CNV involving the centre of the fovea

If a fellow eye develops CNV from AMD, it will be treated with the optimal locally available treatment.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
600

Total final enrolment
610

Key exclusion criteria
1. Corrected 1 metre VAlogMAR <25 letters
2. Long standing CNV evidenced by the presence of fibrosis in excess of 50% of the total lesion
3. Presence of other active ocular disease causing concurrent vision loss, e.g. diabetic retinopathy
4. Previous treatment with PhotoDynamic Therapy (PDT) or a VEGF inhibitor in the eye being considered for inclusion

Date of first enrolment
01/07/2007

Date of final enrolment
30/11/2012

Locations

Countries of recruitment
Northern Ireland

United Kingdom

Study participating centre
The Queen's University of Belfast
Belfast
United Kingdom
BT12 6BA

Sponsor information

Organisation
Royal Group of Hospitals Trust (UK)

Sponsor details
Royal Research Office
First Floor Education Centre
The Royal Group of Hospitals Trust
Grosvenor Road
Belfast
Northern Ireland
United Kingdom
BT12 6BA
+44 (0)2890 632224
frances.burns@royalhospitals.n-i.nhs.uk

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/03rq50d77

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2012		Yes	No
Results article	results	01/07/2012		Yes	No
Results article	results	12/10/2013		Yes	No
Results article	results	01/12/2013		Yes	No
Results article	results	29/07/2014		Yes	No
Results article	results	01/10/2015		Yes	No
Results article	results	01/12/2016		Yes	No
Results article	results	01/02/2018		Yes	No
Results article	results	01/01/2019		Yes	No
Results article	7-year follow-up	01/08/2022	24/10/2022	Yes	No
Results article	Long-term visual outcomes	01/09/2020	24/10/2022	Yes	No