

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	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 19/04/2007	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 24/10/2022	Condition category Eye Diseases	<input type="checkbox"/> 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

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Contact information

Type(s)

Scientific

Contact name

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Contact details

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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® (ranibizumab) with respect to the benefits of vascular endothelial growth factor (VEGF) inhibition in maintaining/improving visual acuity in eyes with choroidal 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, ranibizumab

Primary outcome measure

The primary outcome is corrected 1 metre VAllogMAR, measured as the number of letters read on a standard ETDRS chart. The primary end point will be VAllogMAR 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 VAllogMAR 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 (VAllogMAR) ≥ 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 VAllogMAR <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

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BT12 6BA

Sponsor information

Organisation

Royal Group of Hospitals Trust (UK)

Sponsor details

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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