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Comparing different dosing regimens of Avastin® in the treatment of wet age-related macular degeneration

Submission date
29/06/2009

Recruitment status
No longer recruiting

Registration date
22/09/2009

Overall study status
Completed

Last Edited
28/05/2020

Condition category
Eye Diseases

[X] Prospectively registered
[X] 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 (nAMD) causes severe sight loss in older people. It develops when abnormal blood vessels form in the eye and damage its cells. Treatment with a drug known as Lucentis® (Ranibizumab) is now recommended best practice. This treatment prevents sight loss in over 90% of patients when given as injections into the eye with nAMD for periods of up to two years. Lucentis® is extremely expensive (approximately £750 per injection) and nAMD is common (about 25,000 newly affected people each year in the UK). Another drug called Avastin® (Bevacizumab) is licensed for colorectal cancer treatment and has similar properties. This drug has also been used to treat patients with nAMD and is also thought to confer similar benefits based on multiple studies. Avastin® is extremely cheap relative to Lucentis® because the dose for an eye injection is small, so the amount of drug needed for one colorectal cancer treatment can be made into very many doses for injection into the eye. There is an urgent need for more evidence about cost-effective ways to treat nAMD. Avastin® is widely used and some European countries have opted to provide Avastin® only. It is important to obtain more information to improve treatment with Avastin®, given that Avastin® appears to have similar effects on vision to Lucentis®. Different doses of Avastin® have not been tested and may be important for safety. There is also a pressing need to test different intervals for reviewing eyes that are being considered for re-treatment because monthly review is demanding for elderly patients, resource intensive and expensive. Therefore, the aims of this study are to compare the effectiveness of standard versus low doses of Avastin® and to compare monthly versus two-monthly review intervals. The study also assesses any side effects observed with different Avastin® doses and treatment schedules.

Who can participate?
Patients aged 50 and older starting treatment for nAMD

What does the study involve?
Participants are randomly allocated to be treated with a low dose or a high (conventional) dose of Avastin® and are also randomly allocated to return for reviews either monthly or two-monthly. Participants receive three injections of their allocated treatment on visits A, B and C

with 4-6 weeks between each visit. Following visit C and the third injection, the allocated treatment schedule is revealed, indicating how often patients should return for future review visits. Participants receive further injections (continuing the same dose) as required at review clinics until the affected eye(s) show reduced/reversed symptoms or until the participants withdraw from the study.

What are the possible benefits and risks of participating?
Possible harms to participants include the possibility of being allocated to an inferior treatment (a possible harm of participating in any study) and possible side effects of the treatments. Possible side effects of treatment include: complications of eye injection such as endophthalmitis (inflammation), traumatic cataract (clouding) and/or retinal detachment. An increased risk of thromboembolic (blood vessel blockage) side effects has been observed after use of doses required for cancer studies. The researchers will be extremely vigilant for such side events.

Where is the study run from?
Nottingham University Hospitals NHS Trust (UK)

When is the study starting and how long is it expected to run for?
January 2010 to March 2017

Who is funding the study?
East Midlands Primary Care Trust Consortium (UK)

Who is the main contact?
Rebecca Haydock

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2009-014280-38

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
09OY006

Study information

Scientific Title
A randomised controlled Trial of high and low dose Avastin® for Neovascular macular Degeneration in the East Midlands (TANDEM)

Acronym
TANDEM

Study objectives
It is hypothesised that Avastin® remains effective in treating neovascular age-related macular degeneration (nAMD) when administered in smaller doses and/or at less-frequent intervals than those typically used in clinical settings.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Leicestershire, Northamptonshire & Rutland Research Ethics Committee 1, 13/11/2009, REC ref: 09/H0406/86

Study design
Multi-centre four group (factorial design) 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
Neovascular (wet) age-related macular degeneration (nAMD)

Interventions
All patients will receive intraocular injections of Avastin® to treat nAMD. Patients will receive either a conventional dose (1.250 mg) or a low dose (0.625 mg) each month for three consecutive months. Following this, patients will receive further injections (continuing the same dose size) as required at review clinics. Patients will return for reviews either monthly or two-monthly.

As such there will be four different intervention groups:
L1: low dose Avastin®, one-monthly review
L2: low dose Avastin®, two-monthly review
H1: high (conventional) dose Avastin®, one-monthly review
H2: high (conventional) dose Avastin®, two-monthly review

Treatment will continue until the affected eye(s) demonstrate reduced/reversed symptoms or until patients are withdrawn.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Avastin®

Primary outcome measure
Time to an event, i.e. vision deterioration

Secondary outcome measures
1. Frequencies of adverse effects of treatment
2. Corrected distance visual acuity (VAlogMAR), measured as the number of letters read on a standard ETDRS chart at 1 metre

Measured 18 and 30 months after the start of recruitment and then annually

Overall study start date
01/01/2010

Completion date
31/03/2017

Eligibility

Key inclusion criteria
1. Adults of either sex aged 50 years and older
2. Newly referred for the treatment of nAMD
3. Corrected distance logarithm of the minimum angle of resolution visual acuity (VAlogMAR)

greater than or equal to 20 letters and less than 70 letters read on a standard ETDRS chart at 1 metre
4. Any component of the neovascular lesion (choroidal neovascularisation [CNV], blood, serous pigment epithelial detachment, elevated blocked fluorescence) involving the centre of the fovea

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
811

Total final enrolment
812

Key exclusion criteria
1. Aged less than 50 years
2. Corrected VAlogMAR less than 20 letters at 1 metre
3. Long standing CNV evidenced by the presence of fibrosis in excess of 50% of the total lesion
4. Greatest linear diameter greater than 6000 µm (equivalent to about 12 disc diameters)
5. Argon laser treatment to the proposed study eye within the last 6 months
6. Presence of thick blood involving the centre of the fovea
7. Presence of other active ocular disease causing concurrent vision loss, e.g. diabetic retinopathy
8. Previous treatment with photodynamic therapy (PDT) or a vascular endothelial growth factor (VEGF) inhibitor in either eye
9. Patients with 8 or more diopters of myopia
10. Pregnant and or lactating women
11. Women with child bearing potential (i.e. not sterilised or not post-menopausal) who are unwilling to use contraception
12. Men with a spouse or partner with child bearing potential unless the participant has agreed to use condoms
13. Patients with known hypersensitivity to recombinant human or humanised antibodies

Date of first enrolment
01/01/2010

Date of final enrolment
31/03/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Nottingham University Hospitals NHS Trust
Nottingham
United Kingdom
NG7 2UH

Sponsor information

Organisation
Nottingham University Hospitals NHS Trust (UK)

Sponsor details
Research and Development Department
E11 Curie Court
Derby Road
Nottingham
England
United Kingdom
NG7 2UH

Sponsor type
Hospital/treatment centre

Website
http://www.nuh.nhs.uk/

ROR
https://ror.org/05y3qh794

Funder(s)

Funder type
Government

Funder Name
East Midlands Primary Care Trust Consortium (UK)

Results and Publications

Publication and dissemination plan

Planned publication in a high-impact peer reviewed journal.

Intention to publish date
30/06/2020

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	10/03/2015		Yes	No
Basic results			28/05/2020	No	No
HRA research summary			28/06/2023	No	No