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A randomised, double-masked phase III study of the efficacy and safety of Avastin® (bevacizumab) intravitreal injections compared to best available therapy in subjects with choroidal neovascularisation secondary to age-related macular degeneration

Submission date 27/10/2006	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 29/11/2006	**Overall study status** Completed	
Last Edited 10/05/2012	**Condition category** Eye Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2006-001544-31

Protocol serial number

REC reference number 06/Q0504/46. EudraCT number 2006-001544-31

Study information

Scientific Title

Acronym
ABC

Study objectives
To determine the efficacy and safety of intravitreal Avastin® (bevacizumab) intravitreal injections compared to usual care (verteporfin photodynamic therapy, Macugen® or sham) in treating choroidal neovascularisation (CNV) due to age-related macular degeneration (AMD).

Please note that, as of 24/09/2008, the anticipated end date of this trial has been updated from 01/12/2007 to 05/12/2008.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Moorfields and Whittington Local Research Ethics Committee, date of approval 14 July 2006 (ref: 06/Q0504/46).

Added as of 06/10/2008: An additional approval has been granted from the Guy's Research Ethics Committee on the 5th April 2007 to allow recruitment at additional trial sites within the UK (ref: 07/Q0704/20).

Study design
Prospective, double masked, randomised, controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Choroidal neovascularisation (CNV) secondary to age-related macular degeneration (AMD)

Interventions
1. Intravitreal Avastin® (bevacizumab) with placebo PDT where necessary to maintain masking
2. Verteporfin PDT with sham intravitreal injection
3. Intravitreal Macugen® (pegaptanib sodium)
4. Sham intravitreal injection

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Avastin® (bevacizumab), verteporfin, Macugen® (pegaptanib sodium)

Primary outcome(s)
The proportion of subjects who gain 15 letters (3 lines) or more of best corrected visual acuity score at the 12 month timepoint compared with baseline, based on the ETDRS visual acuity chart and assessment at a starting distance of 4 m.

Key secondary outcome(s))
Secondary outcome measures amended as of 24/09/2008:
1. The proportion of subjects who lose fewer than 15 letters (approximately 3 lines), the proportion who have gained 5 letters or more (1 line), and the proportion who have gained 10 letters or more (2 lines) in the best corrected visual acuity score at 12 months compared with baseline, based on the ETDRS visual acuity chart and assessment at a starting distance of 4 m
2. The proportion of patients who meet these visual criteria at 6 months
3. To evaluate the safety and tolerability of intravitreal injections of Avastin® given every 6 weeks
4. Mean change in central OCT thickness
5. If the study is continued after the analysis of data at 12 month timepoint, after the second treatment year of the study, the same objectives will be analysed on unmasked data

Previous secondary outcome measures:
1. The proportion of subjects who lose fewer than 15 letters (approximately three lines) and the proportion who have gained five letters or more (one line) in the best corrected visual acuity score at 12 months compared with baseline, based on the ETDRS visual acuity chart and assessment at a starting distance of 4 m
2. The proportion of patients who meet these visual criteria at six months
3. To evaluate the safety and tolerability of intravitreal injections of Avastin® given every six weeks
4. Mean change in central OCT thickness
5. If study is continued after the analysis of data at 12 month time point then after the second treatment year of the study, the same objectives will be analysed on unmasked data

Completion date
05/12/2008

Eligibility

Key inclusion criteria
1. Aged over 50 years
2. Primary or subfoveal CNV lesions secondary to AMD in the study eye
3. An occult lesion must have presumed evidence of disease progression, defined as one or more of the following:
a. deterioration of best corrected vision by one Snellen line or five letters on Early Treatment Diabetic Retinopathy Study (ETDRS) chart within the past three months due to progression of CNV
b. presence of sub- or intra-retinal blood
c. growth of lesion size on the angiogram by more than 10% in the past three months

AND evidence of increased central macular thickness on Optical Coherence Tomography (OCT)
4. Area of sub-retinal blood less than 50% of total lesion area
5. Best corrected visual acuity, using ETDRS charts, of 20/40 (6/12) to 20/320 (6/96) Snellen equivalent in the study eye
6. Total lesion size less than 12 disc areas including all contiguous lesion components
7. Area of fibrosis less than 25% of the total lesion area

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
Ocular:
1. Sub-retinal haemorrhage in the study eye that involves the centre of the fovea, if the size of the haemorrhage is either more than 50% of the total lesion area or more than one disc areas in size
2. Subfoveal fibrosis or atrophy in the study eye
3. CNV in either eye due to causes other than AMD, such as ocular histoplasmosis, trauma, or pathologic myopia
4. Retinal pigment epithelial tear involving the macula in the study eye
5. Prior treatment with external-beam radiation therapy, Transpupillary Thermal Therapy (TTT), thermal laser, or Photo-Dynamic Therapy (PDT) in the study eye or history of submacular surgery or other surgical intervention for AMD in the study eye
6. PDT in the non-study eye less than seven days preceding day zero
7. Previous participation in a clinical trial (for either eye) involving anti-angiogenic drugs (Macugen®, Avastin®, anecortave acetate, protein kinase C inhibitors, etc.)
8. Previous intravitreal drug delivery (e.g., intravitreal corticosteroid injection or device implantation) in the study eye
9. Amblyopia, infective conjunctivitis or scleritis, glaucoma, corneal disease, inflammatory eye disease
10. Diabetic retinopathy more than mild nonproliferative in the fellow eye as defined by the ETDRS or any diabetic maculopathy
11. Intraocular surgery (including cataract surgery) in the study eye within two months preceding day zero
12. Aphakia or absence of the posterior capsule in the study eye
13. Previous violation of the posterior capsule in the study eye is also excluded unless it occurred as a result of Yttrium Aluminum Garnet (YAG) posterior capsulotomy in association with prior, posterior chamber intraocular lens implantation
14. Spherical equivalent of the refractive error in the study eye demonstrating more than -8 diopters of myopia or signs of pathologic myopia with a refraction of 4-8 diopters
15. For subjects who have undergone prior refractive or cataract surgery in the study eye, the preoperative refractive error in the study eye cannot exceed -8 diopters of myopia

Systemic:
1. Recent stroke (last six months), or cardiac event (last six months), uncontrolled angina or uncontrolled hypertension
2. Current treatment for active systemic infection
3. Unable to give informed consent
4. Anticoagulant treatment (anti-platelet drugs allowed)
5. Fluorescein or Indo-Cyanine Green (ICG) allergy
6. Pre-menopausal women not using adequate contraception; the following are considered effective means of contraception: surgical sterilisation, use of oral contraceptives, barrier contraception with either a condom or diaphragm in conjunction with spermicidal gel, an Intra-Uterine Device (IUD), or contraceptive hormone implant or patch

Date of first enrolment
11/08/2006

Date of final enrolment
05/12/2008

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Moorfields Eye Hospital NHS Foundation Trust
London
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Sponsor information

Organisation
Moorfields Eye Hospital NHS Foundation Trust (UK)

ROR
https://ror.org/03zaddr67

Funder(s)

Funder type
Government

Funder Name
The Special Trustees of Moorfields Eye Hospital NHS Foundation Trust (UK)

Results and Publications

Individual participant data (IPD) sharing plan

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	09/06/2010		Yes	No
Results article	results	11/05/2011		Yes	No
Results article	results	09/03/2012		Yes	No