ISRCTN42639823 https://doi.org/10.1186/ISRCTN42639823

Combination photodynamic treatment and intravitreal ranibizumab versus intravitreal ranibizumab alone in neovascular age-related macular degeneration

Submission date 03/12/2008	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 05/12/2008	**Overall study status** Completed	
Last Edited 04/12/2012	**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)
2006-005172-40

Protocol serial number
EudraCT:

Study information

Scientific Title
A randomised prospective exploratory study comparing combination photodynamic treatment and intravitreal ranibizumab versus intravitreal ranibizumab alone in the treatment of neovascular age-related macular degeneration

Study objectives
This study is designed to evaluate the safety and efficacy of intravitreal ranibizumab used in combination with verteporfin photodynamic therapy (Visudyne®) for the treatment of subfoveal choroidal neovascularisation secondary to age-related macular degeneration (AMD), compared to the use of intravitreal ranibizumab alone and to see whether combination treatment reduces retreatment rates.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North Somerset and South Bristol Research Ethics Committee gave approval on the 14th February 2007 (ref: 2389)

Primary study design
Interventional

Study design
Single-centre randomised controlled exploratory study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Neovascular age-related macular degeneration

Interventions
Intravitreal ranibizumab combined with photodynamic treatment versus intravitreal ranibizumab alone:
Ranibizumab 0.5 mg by intravitreal delivery. Given monthly for 3 months, then as required monthly depending on defined retreatment criteria. Total duration of treatment 1 year. For photodynamic treatment, this (or sham) is given only on the first treatment visit, and not again. Photodynamic treatment involves the intravenous administration of a drug called Visudyne®, dose depends on the body mass index of patient, followed by application of a laser to the affected eye.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Ranibizumab, verteporfin photodynamic therapy (Visudyne®)

Primary outcome(s)
The proportion of subjects who gain 15 or more letters of best corrected visual acuity at 12 months compared to baseline, based on the ETDRS visual acuity chart.

Key secondary outcome(s)
1. Mean change from baseline in best corrected visual acuity (BCVA) at months 6 and 12
2. Proportion of patients who gain greater than or equal to 5, greater than or equal to 10 letters of BCVA from baseline at months 6 and 12
3. Proportion of patients who lose less than 15 letters of BCVA from baseline at months 6 and 12
4. Mean change from baseline in total size of lesion and total size of CNV at 3, 6 and 12 months
5. Change in area of leakage at 3, 6 and 12 months
6. The number of treatments required with ranibizumab for each group

Completion date
20/01/2009

Eligibility

Key inclusion criteria
Patients (male and female aged 50 or over, no upper age limit) who at baseline:
1. Have a best-corrected logarithm of the minimum angle of resolution (logMAR) visual acuity in the study eye between 73 - 24 letters
2. Have a choroidal neovascularisation (CNV) lesion of any type in the study eye with the following characteristics as determined by fluorescein angiography:
2.1. Evidence that CNV extends under the geometric centre of the foveal avascular zone
2.2. The area of the CNV must occupy at least 50% of the total lesion
2.3. The lesion must be less than or equal to 5400 microns in greatest linear dimension (GLD)
2.4. No subfoveal atrophic change, no subfoveal fibrosis. Area of fibrosis less than or equal to 50% of total lesion area.
3. For occult with no classic CNV, the lesion must have presumed recent disease progression as assessed by the Investigator and defined as having at least one of the following criteria:
3.1. Blood associated with the lesion at baseline
3.2. Greater than or equal to 10% increase in the GLD as assessed by fluorescein angiography in the previous 3 months
3.3. Loss of VA in the previous 3 months defined as either:
3.3.1. Greater than or equal to 5 letters logMAR vision as determined by protocol refraction and protocol measurement, or
3.3.2. Two or more lines using a Snellen chart by standard examination

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria

1. Prior treatment with external-beam radiation therapy, transpupillary thermotherapy (TTT), thermal laser, or verteporfin therapy (PDT) in the study eye
2. Treatment with verteporfin in the non-study eye less than 7 days preceding Day 0
3. Previous participation in a clinical trial (for either eye) involving anti-angiogenic drugs (Macugen®, Avastin®, anecortave acetate, protein kinase C inhibitors, etc.)
4. Previous intravitreal drug delivery (e.g., intravitreal corticosteroid injection or device implantation) in the study eye
5. History of vitrectomy surgery in the study eye
6. History of greater than mild non-proliferative diabetic retinopathy or any diabetic maculopathy
7. History of retinal vascular occlusions
8. History of glaucoma filtering surgery in the study eye
9. History of corneal transplant in the study eye
10. History of submacular surgery or other surgical intervention for AMD in the study eye
11. Previous participation in any studies of investigational drugs within 1 month preceding Day 0 (excluding vitamins and minerals)
12. Subretinal haemorrhage in the study eye that involves the centre of the fovea, if the size of the haemorrhage is either greater than 50% of the total lesion area or greater than 1 disc area in size
13. Subfoveal fibrosis or atrophy in the study eye. Area of fibrosis greater than 50% of total lesion area.
14. CNV in either eye due to causes other than AMD, such as ocular histoplasmosis, trauma, or pathologic myopia
15. Retinal pigment epithelial tear involving the macula in the study eye
16. Any concurrent intraocular condition in the study eye (e.g., cataract or diabetic retinopathy) that, in the opinion of the investigator, could either require medical or surgical intervention during the 12-month study period to prevent or treat visual loss that might result from that condition, or if allowed to progress untreated, could likely contribute to loss of at least two Snellen equivalent lines of best corrected visual acuity over the 12-month study period
17. Active intraocular inflammation (grade trace or above) in the study eye
18. Current vitreous haemorrhage in the study eye
19. History of rhegmatogenous retinal detachment or macular hole (Stage 3 or 4) in the study eye
20. History of idiopathic or autoimmune-associated uveitis in either eye
21. Infectious conjunctivitis, keratitis, scleritis, or endophthalmitis in either eye
22. Aphakia or absence of the posterior capsule in the study eye
23. Previous violation of the posterior capsule in the study eye is also excluded unless it occurred as a result of YAG posterior capsulotomy in association with prior, posterior chamber intraocular lens implantation
24. 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
25. For subjects who have undergone prior refractive or cataract surgery in the study eye, the pre-operative refractive error in the study eye cannot exceed -8 diopters of myopia
26. Intraocular surgery (including cataract surgery) in the study eye within 2 months preceding Day 0
27. Uncontrolled glaucoma in the study eye (defined as intraocular pressure greater than 30 mmHg despite treatment with anti-glaucoma medication)
28. Concurrent systemic conditions
29. Premenopausal women not using adequate contraception. The following are considered effective means of contraception:

29.1. Surgical sterilisation
29.2. Use of oral contraceptives
29.3. Barrier contraception with either a condom or diaphragm in conjunction with spermicidal gel
29.4. An intrauterine device (IUD)
29.5. Contraceptive hormone implant or patch
30. History of other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use an investigational drug or that might affect interpretation of the results of the study or render the subject at high risk for treatment complications
31. Current treatment for active systemic infection
32. Recent stroke, or cardiac event, uncontrolled angina or hypertension
33. History of allergy to fluorescein
34. Inability to obtain fundus photographs or fluorescein angiograms of sufficient quality to be analysed
35. Inability to comply with study or follow-up procedures

Date of first enrolment
07/07/2007

Date of final enrolment
20/01/2009

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Bristol Eye Hospital
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Sponsor information

Organisation
University Hospitals Bristol NHS Foundation Trust (UK)

ROR
https://ror.org/04nm1cv11

Funder(s)

Funder type
Industry

Funder Name
Novartis Pharmaceuticals (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	01/10/2010		Yes	No