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Diabetic Macular Oedema: a prospective randomised trial of management with intravitreal bevacizumab (Avastin®) versus conventional laser therapy in diabetic macula oedema

Submission date 31/05/2007	**Recruitment status** No longer recruiting
Registration date 16/07/2007	**Overall study status** Completed
Last Edited 08/02/2012	**Condition category** Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
BELS1001

Study information

Scientific Title

Acronym
BOLT (Bevacizumab Or Laser Treatment)

Study objectives
Intravitreal injections of Avastin® are better at improving and stabilising vision than laser therapy in clinically significant macula oedema secondary to diabetes mellitus.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved by the Moorfields and Whittington Ethics Committee on the 11th May 2007 (ref: 07 /Q0504/28).

Primary study design
Interventional

Study design
Randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Diabetes mellitus

Interventions
Intervention group: 40 patients for intravitreal avastin every six weeks
Control group: 40 patients for focal laser as ETDRS criteria

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome(s)
Visual acuity.

Key secondary outcome(s)
OCT thickness.

Completion date
31/12/2008

Eligibility

Key inclusion criteria
1. Patients of either sex aged 18 years or over
2. Diagnosis of diabetes mellitus (type one or type two). Any one of the following will be considered to be sufficient evidence that diabetes is present:
2.1. Current regular use of insulin for the treatment of diabetes
2.2. Current regular use of oral anti-hyperglycaemic agents for the treatment of diabetes
2.3. Documented diabetes by American Diabetes Association (ADA) and/or World Health Organisation (WHO) criteria
3. Best corrected visual acuity in the study eye between 35 and 69 Early Treatment Diabetic Retinopathy Study (ETDRS) letters at 4 metres (Snellen equivalent of 6/60 or better and less than 6/12) within 14 days of randomisation
4. On clinical examimation, definite retinal thickening due to diabetic macular oedema involving the centre of the macula: Optical Coherence Tomography (OCT) central subfield greater than or equal to 270 microns within 14 days of randomisation
5. Media clarity, pupillary dilation, and subject cooperation sufficient for adequate fundus photographs
6. At least one prior macular laser therapy
7. Intraocular pressure less than 30 mmHg
8. Written informed consent
9. Ability to return for study visits
10. Vision in fellow eye of 3/60 or better
11. Fellow eye has no anti-Vascular Endothelial Growth Factor (anti-VEGF) treatment within the past three months and no expectation of such treatment in next three months

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
The following exclusions apply to the study eye only (i.e., they may be present for the non-study eye):
1. Macular ischaemia (Foveal Avascular Zone [FAZ] greater than 1000 um in diameter or severe perifoveal intercapillary loss in Intravenous Fluorescein Angiography [IVFA])
2. Macular oedema is considered to be due to a cause other than diabetic macular oedema. An eye should not be considered eligible if:
2.1. The macular oedema is considered to be related to cataract extraction, or
2.2. Clinical examination and/or OCT suggest that vitreoretinal interface abnormalities disease

(e.g., a taut posterior hyaloid or epiretinal membrane) is the primary cause of the macular oedema
3. Co-existent ocular disease:
3.1. An ocular condition is present such that, in the opinion of the investigator, visual acuity would not improve from resolution of macular oedema (e.g., foveal atrophy, pigmentary changes, dense subfoveal hard exudates, non-retinal conditions, such as amblyopia)
3.2. An ocular condition is present (other than diabetes) that, in the opinion of the investigator, might affect macular oedema or alter visual acuity during the course of the study (e.g., vein occlusion, uveitis or other ocular inflammatory disease, neovascular glaucoma, Irvine-Gass Syndrome, etc.)
3.3. A substantial cataract that, in the opinion of the investigator, is likely to be decreasing visual acuity by three lines or more (i.e., cataract would be reducing acuity to 20/40 or worse if eye was otherwise normal)
4. History of treatment for Diabetic Macula Oedema (DMO) at any time in the past three months (such as focal/grid macular photocoagulation, intravitreal or peribulbar corticosteroids, anti-VEGF drugs, or any other treatment)
5. History of Panretinal scatter Photocoagulation (PRP) within three months prior to randomisation
6. Anticipated need for PRP in the six months following randomisation
7. Proliferative diabetic retinopathy in the study eye except for tufts of new vessels less than one disc in area with no vitreous haemorrhage
8. A condition that, in the opinion of the investigator, would preclude participation in the study:
8.1. HbA1c greater than 11.0 mmol
8.2. A past medical history of significant renal disease, defined as a history of chronic renal failure requiring dialysis or kidney transplant
8.3. Blood pressure greater than 170/100 mmHg (i.e. systolic above 170 mmHg OR diastolic above 110 mmHg). If blood pressure is brought below 170/100 mmHg by anti-hypertensive treatment, subject can become eligible
8.4. Myocardial infarction, other cardiac event requiring hospitalisation, stroke, transient ischaemic attack, or treatment for acute congestive heart failure within six months prior to randomisation
8.5. Major surgery within 28 days prior to randomisation or major surgery planned during the next 12 months. Major surgery is defined as a surgical procedure that is more extensive than fine needle biopsy/aspiration, placement of a central venous access device, removal/biopsy of a skin lesion, or placement of a peripheral venous catheter
9. Participation in an investigational trial within 30 days of randomisation that involved treatment with any drug that has not received regulatory approval at the time of study entry. Note: subjects cannot receive another investigational drug while participating in the study
10. Systemic anti-VEGF or pro-VEGF treatment within three months prior to randomisation
11. Pregnant or lactating women or women intending to become pregnant within the study period including three months after study cessation
12. History of major ocular surgery (including cataract extraction, scleral buckle, any intraocular surgery, etc.) within prior three months or anticipated within the next six months following randomisation
13. Aphakia
14. Uncontrolled glaucoma (in investigators judgment)
15. Exam evidence of external ocular infection, including conjunctivitis, chalazion, or severe blepharitis. If treated these patients can be included
16. Known allergy to fluorescein dye or to any component of the study drug

Date of first enrolment

31/05/2007

Date of final enrolment
31/12/2008

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
162 City Road
London
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EC1V 2PD

Sponsor information

Organisation
Moorfields Eye Hospital NHS Foundation Trust (UK)

ROR
https://ror.org/03zaddr67

Funder(s)

Funder type
Charity

Funder Name
Moorfield Eye Hospital Special Trustees (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	01/06/2010		Yes	No