Comparing the effectiveness and costs of bevacizumab to ranibizumab in patients with diabetic macular edema

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The goal of the trial is to compare the efficacy and costs of bevacizumab 1.25 mg and ranibizumab 0.5mg given as monthly intravitreal injections over 6 months for the treatment of diabetic macular edema.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Retina, choroid and vitreous haemorrhages and vascular disorders
Study type	Interventional

Summary

ID

NL-OMON47349

Source
ToetsingOnline

Brief title
BRDME

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders

Synonym
diabetic macular edema

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: bevacizumab, diabetic macular edema, randomized clinical trial, ranibizumab

Outcome measures

Primary outcome

The primary study parameter is the mean change in best corrected visual acuity

after 6 months compared to baseline.

Secondary outcome

Amongst others:

The proportion of patients with a decrease of the best corrected visual acuity

less than 15 letters on the EDTRS chart at 6 months compared to baseline.

The proportion of patients with a decrease of the best corrected visual acuity

of 15 letters or more on the EDTRS chart at 6 months compared to baseline.

For the full listings we refer to the protocol chapter 7.1 study endpoints

Study description

Background summary

Ranibizumab (Lucentis), a VEGF inhibitor, is registered for the use of intravitreal treatment of age-related macular degeneration (AMD) and meant a breakthrough for the treatment of these patients. Recently, it will also be registered for the intravitreal treatment of macular edema secondary to retinal vein occlusions (RVO). The therapy has also shown good results for this condition.
The comparable product bevacuzimab (Avastin) is registered for the systemic treatment of patients with metastasized colorectal carcinoma but has been used in an off-label setting in ophthalmology for the intravitreal treatment of AMD and macular edema secondary to a retinal vein occlusion.

The treatment with bevacizumab is much cheaper than the treatment with ranibizumab. The efficacy and safety of bevacizumab has been studied in case-series and internet based patient registries only, but a directly comparative study for this indication has not yet been published. The general impression is that both products are equally effective.

Study objective

The goal of the trial is to compare the efficacy and costs of bevacizumab 1.25 mg and ranibizumab 0.5mg given as monthly intravitreal injections over 6 months for the treatment of diabetic macular edema.

Study design

It is a comparative, randomised, double masked study.

Intervention

Bevacizumab 1.25 mg and ranibizumab 0.5mg are administered as monthly intravitreal injections for 6 months to patients with diabetic macular edema. During the study visual acuity will be measured, safety assessments, optical coherence tomography and fluorescein angiography will be performed and a questionnaire concerning the costs should be filled in.

Study burden and risks

In this trial patients will receive in total 6 intravitreal injections according to a fixed schedule. In the regular treatment in the first 6 months 3-6 injections are administered in a variable schedule depending on the evolution of the disease. Hence in some cases, study patients will receive more injections than in the regular treatment. This is done in order to compare the maximal effect of both products after 6 months. For each intravitreal injection there is a risk of around 0.05% to develop an endophtalmitis; because of the higher increase in number of injections, this risk is slightly higer for study patients than for the regular treament.
Besides there are possibly unkown risks for the ophthalmological treatment with bevacizumab which is not registered for the treatment of macula edema secondary to retinal vein occlusion.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Male or female patients > 18 years of age who have signed an Informed Consent.
* Patients with Type 1 or Type 2 diabetes mellitus (according to American Diabetes Association or World Health Organization (WHO) guidelines) with glycosylated haemoglobin (HbA1c) less than 12.0% at screening (Visit 1). Patients should be on a dietary, exercise and/or pharmacological program for diabetes. Treatment for diabetes must have been stable for at least 2 months
* Patients with visual impairment due to DME (within the EDTRS criteria of clinically significant macular edema) in at least one eye, with a central area thickness >325 micron, who are eligible for anti-VEGF treatment according to the investigator. If both eyes are eligible, the one with the worse visual acuity, as assessed at Visit 1, will be selected by the investigator as the study eye.
* BCVA equal or more than 24 and less or equal to 78 letters in the study eye and, inclusively, using ETDRS- like visual acuity testing charts at a testing distance of 4 meter (approximate Snellen equivalent of 20/32 to 20/320) at screening.
* Concomitant conditions in the study eye which, in the opinion of the investigator, do not prevent improvement of visual acuity on study treatment

Exclusion criteria

see also protocol 4.4

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-06-2012
Enrollment:	126
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Avastin
Generic name:	bevacizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Lucentis
Generic name:	ranibizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	09-12-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-01-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-05-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-01-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-09-2014

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2011-000806-23-NL
CCMO	NL35860.018.11