A 12-month, randomized, double-masked, sham-controlled, multicenter study to evaluate the efficacy and safety of 0.5 mg ranibizumab intravitreal injections in patients with visual impairment due to vascular endothelial growth factor (VEGF) driven macular edema (ME) (CRFB002G2302)

Published: 13-08-2013
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Primary: To demonstrate that intravitreal injection of 0.5 mg ranibizumab administered based on individual patient needs has superior efficacy compared to sham treatment in adult patients with visual impairment due to VEGF-driven ME. Secondary: Best...

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

Summary

ID

NL-OMON40497

Source
ToetsingOnline

Brief title
CRFB002G2302 (PROMETHEUS)

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders

Synonym
macular edema

Research involving
Human

Sponsors and support

Primary sponsor: Novartis Pharma BV
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: edema, macular, ranibizumab, VEGF

Outcome measures

Primary outcome

BCVA change from baseline to month 2.

Secondary outcome

Time course of BCVA and OCT parameters, active ME leakage, rescue treatment

month 1, ranibizumab requirements over time. Adverse events.

Study description

Background summary

Vascular leakage leading to macular edema (ME) can result in irreversible structural damage and permanent loss of vision. The pathogenesis of ME is complex. The chronic tissue hypoxia and other metabolic causal risk factors initiate a cascade of biochemical and physiopathological changes, such as abnormal increased vascular endothelial growth factor (VEGF) levels in the inner layers of the retina, generating the disruption of the blood-retinal barrier followed by the increased accumulation of fluid within the intraretinal layers of the macula, i.e. macular edema.
The VEGF-driven ME conditions other than diabetic macular edema (DME) and ME associated with retinal vein occlusion (RVO) are considered to be less frequent, the overall incidence and prevalence varies across countries or regions worldwide. Some ocular conditions that cause ME in adults < 50 years of age can also occur among adolescents between 12 and 18 years of age with VEGF

playing a major role in the pathogenesis.
Currently, there is no established standard of care therapy for persistent ME due to these various etiologies. Treatments include topical NSAIDs, topical steroids, intravitreal steroids, laser photocoagulation, etc. While the efficacy of anti-VEGF medications in the treatment of DME and RVO has been proven, published reports have shown in addition that intravitreal anti-VEGF treatment could
also be beneficial in the management of ME due to various other underlying conditions.
Ranibizumab (Lucentis) has been registered for the treatment of age-related macular degeneration and visual impairment due to DME and ME associated with RVO.
The purpose of this study is to determine whether intravitreal injections of 0.5 mg ranibizumab administered based on individual patient needs improve visual acuity and reduce disease activity compared to sham treatment in adult patients with visual impairment due to VEGF-driven ME conditions other than diabetic macular edema DME and RVO.

Study objective

Primary: To demonstrate that intravitreal injection of 0.5 mg ranibizumab administered based on individual patient needs has superior efficacy compared to sham treatment in adult patients with visual impairment due to VEGF-driven ME.
Secondary: Best-corrected visual acuity (BCVA) change from baseline by visit, change in optical coherence tomography (OCT) parameters from baseline over time, presence of active ME leakage assessed by fluorescein angiography (FA), requirement for rescue treatment at Month 1, whether treatment with ranibizumab was given by visit, number of ranibizumab treatments and re-treatments by Month 2, Month 6 and Month 12. Adverse events.

Study design

Multicenter randomized double-masked sham-controlled phase III parallel-group study.
Randomisation (1:1) to one of the treatment regimens:
* 0.5 mg intravitreal injections of ranibizumab.
* Sham treatment. At Month 2, all adult patients assigned to the sham group will switch to the ranibizumab treatment group.
NB: There is an open-label ranibizumab group of minors (12-18 years). However no minors will not be included in NL.
Treatment of one eye. If both eyes are affected: the *study eye* will be chosen by the investigator. The treatment of the other eye will be selected by the investigator.
Study duration 12 months.
Approx. 187 patients.

Intervention

Treatment withranibizumab or ni intervention till month 2. Thereafter everybody monthly ranibizumab.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: Study duration approx. 1 year. Screening, baseline, day 8, month 1, thereafter monthly visits and end of study visit.
Intravitreal injection ranibizumab or sham on day 1. Retreatment with monthly injections based on individual needs.
Blood tests (approx. 10 ml/occasion) at screening, month 2, 6, 9, 12.
All visits: ophthalmic examinations, incl. OCT.
Fluorescence angiography at screening, months 2, 6, 12.
Electroretinography (not in all centers) at screening, months 2, 6, 12.
Questionnaire, ophthalmic symptoms and signs, at screening, months 2, 6, 12.

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 at least 12 (in NL: 18) years of age.
* Naïve active ME secondary to any causes (for adult patients: except DME and RVO). See protocol page 25 for details.
* Visual impairment predominantly only due to the presence of any eligible types of ME, see protocol page 25 for details.
* BCVA score at Screening and Baseline * 24 and * 83 letters (see protocol page 25 for details).

Exclusion criteria

* Pregnant or nursing (lactating) women. Women of child-bearing potential, not practicing adequate contraception.
* Stroke less than 6 months prior to Screening.
* Systolic BP >160 mm Hg or diastolic BP >100 mm Hg at Screening or Baseline.
* Any active systemic inflammation or infection related directly to the underlying causal disease of ME at screening.
* Active diabetic retinopathy, active ocular/periocular infectious disease or active intraocular inflammation at screening.
* Intraocular pressure * 25 mmHg.
* Neovascularization of the iris or neovascular glaucoma.
* Exclusion criteria study eye and prior or current medications: see protocol page 27-28.

Study design

Design

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

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-04-2014
Enrollment:	20
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	13-08-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-12-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-02-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-06-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-07-2014

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-03-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
Other	clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2012-005418-20-NL
CCMO	NL45422.091.13