A 24-month, phase IIIb, open-label, randomized, active-controlled, 3-arm, multicenter study assessing the efficacy and safety of an individualized, stabilization-criteria-driven pro re nata (PRN) dosing regimen with 0.5-mg ranibizumab intravitreal injections applied as monotherapy or with adjunctive laser photocoagulation in comparison to laser photocoagulation in patients with visual impairment due to macular edema secondary to branch retinal vein occlusion (BRVO)

Published: 16-12-2011
Last updated: 01-05-2024

Primary objective:To demonstrate that an individualized stabilization-criteria-driven PRN dosingregimen (PRN) with 0.5-mg ranibizumab administered with or without adjunctive lasertreatment has superior efficacy as compared to the current standard of...

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

Summary

ID

NL-OMON37792

Source
ToetsingOnline

Brief title
BRIGHTER

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders

Synonym
visual impairment

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: branch retinal vein occlusion, laser photocoagulation, macular edema, visual impairment

Outcome measures

Primary outcome

The primary variable is the mean BCVA change at Month 6 compared to Baseline in

patients with visual impairment due to ME secondary to BRVO.

Secondary outcome

Key secondary

variables include the mean average BCVA change from Month 1 to Month 24

compared to Baseline and the number of ranibizumab treatments.

Study description

Background summary

The present study will generate comparative data for 0.5-mg ranibizumab using PRN dosing administered with or without adjunctive laser treatment versus laser photocoagulation (the current standard of care) up to Month 6 and will provide efficacy and safety data for 0.5-mg ranibizumab using PRN dosing, administered with or without adjunctive laser treatment, over 24 months in patients with visual impairment due to macular edema (ME) secondary to BRVO. Spectral domain high-definition optical coherence tomography (OCT) images will be explored to gain insights into predictive factors for disease progression and the possibility of reduced monitoring will be assessed in Year 2. The results of this study will provide long-term safety and efficacy data to further guide recommendations on the use of ranibizumab in this indication.

Study objective

Primary objective:
To demonstrate that an individualized stabilization-criteria-driven PRN dosing regimen (PRN) with 0.5-mg ranibizumab administered with or without adjunctive laser treatment has superior efficacy as compared to the current standard of care, laser photocoagulation, in patients with visual impairment due to ME secondary to BRVO.
The primary objective will be assessed by the mean best-corrected visual acuity (BCVA) change at Month 6 compared to Baseline.
Key secondary objective:
To demonstrate in a first step that treatment with ranibizumab with adjunctive laser is non-inferior to treatment with ranibizumab monotherapy as assessed by the mean average BCVA change from Month 1 through Month 24 compared to Baseline. To demonstrate in a second step (after demonstrating non-inferiority) that ranibizumab with adjunctive laser reduces the number of ranibizumab retreatments as compared to ranibizumab monotherapy by assessing the number of ranibizumab treatments

applied up to Month 23.

Study design

This is a phase IIIb, randomized, open-label, active-controlled, 3-arm, multicenter study. Patients will be randomized in a 2:2:1 ratio to 1 of the 3 treatment
arms. Ranibizumab will be administered using a stabilization-criteria-driven PRN dosing regimen. In addition to Screening and Baseline, there will be a visit on Day 8
followed by monthly visits from Month 1 to Month 12. In Year 2, 12 monthly visits may
occur, but the possibility to skip visits may reduce this number.

Intervention

The investigational treatment in this study is
0.5-mg ranibizumab administered PRN by intravitreal injections, with or without adjunctive laser treatment. The control treatment is laser photocoagulation applied as
monotherapy. Patients will be assigned to one of the following 3 treatment arms in a
ratio of 2:2:1.
• Arm 1: ranibizumab monotherapy
• Arm 2: ranibizumab with adjunctive laser
• Arm 3: laser monotherapy (option for ranibizumab as of Month 6)

Study burden and risks

27x: vital signs, ETDRS BCVA (visual sharpness), Ophthalmic examination, tonometry en OCT scan
25x: Color fundus photography, Fluorescein angiography
24x: laser treatment
6x: NEI-VFQ-25 (questionnaire)

Ranibizumab can have the following side-effects:
Very common (10 or more in every 100 patients): bloodshot eye, eye pain, small particles or spots in your vision, bleeding in the back of the eye, increased eye pressure, displacement of the jelly-like portion inside the eye, troubling of (a part of) the lens, inflammation of the eye, eye irritation, a feeling of having something in the eye, visual disturbance, inflammation or infection of the eyelid margins, formation of fibrous tissue under the retina, redness of the eye, itching of the eye, dry eye, inflammation of the jelly-like portion inside the eye, headache, runny nose and sore throat, back pain, pains in the joints, elevated blood pressure, and decreasing number of red blood cells and nausea.

Common (between 1 and 10 in every 100 patients): discomfort of the eye, deposits in the back of the eye, bleeding at the site of the injection into the eye, infection of the surface of the eye, infection of the eyeball, changes in the part of the retina responsible for central vision, degeneration of the retina, detachment of or rip in the retina or a layer of the retina causing flashes of light with floaters and shadows progressing to a loss of sight, blurred or decreased sharpness of vision, inflammation of the colored part of the eye, the radial body (corpus ciliare) or an internal part of the eye, little spots on the surface of the eye, bleeding of the eye, scratch or inflammation of the cornea, increasing production of tears, discharge of the eye with itching, redness and swelling, swelling of the eyelid, eyelid pain, and sensitivity to light, infection of the lower part of the airways, flu, urinary tract infection, stroke, anxiety, cough, and allergic reactions.
Uncommon (less than 1 in every 100 patients): changes in or thickening or thinning of the central part of the surface of the eye, disorder in the back of the eye or the jelly-like portion inside the eye, a specific type of glaucoma, blindness, inflammatory deposits in the front part of the eye, pain or irritation at the site of injection, abnormal sensation in the eye, irritation of the eyelid, and accumulation of blood in the front part of the eye, wheezing, increased secretion of the upper airways, changes in heart rhythm, and inflammatory disease of the skin.
Finally, there are risks related to the procedures performed for study purposes; the injection procedures and/or additional research procedures.

Contacts

Public
Novartis

Lichtstrasse 35
Basel 4002
NL
Scientific
Novartis

Lichtstrasse 35
Basel 4002
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Male or female patients >=18 years of age
2. Diagnosis of visual impairment exclusively due to ME secondary to BRVO
3. BCVA score at Screening and Baseline between 73 and 19 letters Early Treatment Diabetic Retinopathy Study (ETDRS), inclusively (approximate Snellen chart equivalent of 20/40 and 20/400)

Exclusion criteria

1. Stroke or myocardial infarction less than 3 months before Screening
2. Uncontrolled blood pressure defined as systolic value of >160 mm Hg or diastolic value of >100 mm Hg at Screening or Baseline. Antihypertensive treatment can be initiated and must be taken for at least 30 days after which the patient can be assessed for study eligibility a second time
3. Any active periocular or ocular infection or inflammation (eg, blepharitis, conjunctivitis, keratitis, scleritis, uveitis, endophthalmitis) at Screening or Baseline in either eye
4. Uncontrolled glaucoma (intraocular pressure [IOP] >=30 mm Hg while on medication or according to investigator*s judgment) at Screening or Baseline or diagnosed within 6 months before Baseline in either eye
5. Neovascularization of the iris or neovascular glaucoma in the study eye
6. Use of any systemic antivascular endothelial growth factor (anti-VEGF) drugs within 6 months before Baseline (eg, sorafenib [Nexavar®], sunitinib [Sutent®], bevacizumab [Avastin®])
7. Treatment (or anticipated treatment in the fellow eye for non-RVO indications during the study) with any anti-angiogenic drugs (including any anti-VEGF agents) within 3 months before Baseline in either eye (eg, pegaptanib [Macugen®], ranibizumab [Lucentis®], bevacizumab [Avastin®])
8. Panretinal laser photocoagulation within 3 months before Baseline or anticipated or scheduled within the next 3 months following Baseline in the study eye
9. Focal or grid laser photocoagulation within 4 months before Baseline in the study eye

10. Use of intra- or periocular corticosteroids (including sub-Tenon) within 3 months before Screening in the study eye

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-08-2012
Enrollment:	21
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	16-12-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Approved WMO Date:	18-04-2012
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	02-05-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	28-06-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	17-07-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	26-07-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	07-09-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	19-09-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	16-05-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	04-05-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO	

Date:	07-05-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2011-002859-34-NL
ClinicalTrials.gov	NCT01599650
CCMO	NL38016.058.11