A 24-month, phase IIIb, open-label, single arm, multicenter study assessing the efficacy and safety of an individualized, stabilization criteria-driven pro re rata (PRN) dosing regimen with 0.5-mg ranibizumab intravitreal injections applied as monotherapy in patients with visual impairment due to macular edema secondary to central retinal vein occlusion (CRVO).

Published: 16-12-2011
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The primary objective is to evaluate the efficacy of an individualized stabilization criteriadrivenPRN dosing regimen with 0.5 mg ranibizumab as assessed by the mean best-corrected visualacuity (BCVA) change at Month 12 compared to Baseline.

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

Summary

ID

NL-OMON37905

Source
ToetsingOnline

Brief title
CRYSTAL

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: central retinal vein occlusion (CRVO), macular edema, visual impairment

Outcome measures

Primary outcome

The primary efficacy variable is the mean change in BCVA at Month 12 compared to Baseline.

Secondary outcome

Secondary efficacy endpoints related to the mean change from Baseline will be assessed as per the primary efficacy endpoint. For more information about the secondary study parameters/outcomes please refer to protocol (v00 26May2011) page 42.

Study description

Background summary

The present study will provide additional efficacy and safety data for 0.5-mg ranibizumab using PRN dosing over 24 months in patients with visual impairment due to macular edema secondary to CRVO. Spectral domain high-definition optical coherence tomography (OCT) images will be analyzed 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 open-label study will provide long-term safety and efficacy data to further guide recommendations on the use of ranibizumab in this indication.

Study objective

The primary objective is to evaluate the efficacy of an individualized stabilization criteriadriven
PRN dosing regimen with 0.5 mg ranibizumab as assessed by the mean best-corrected visual
acuity (BCVA) change at Month 12 compared to Baseline.

Study design

Phase IIIb, open-label, single arm, multicenter study. 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 is 0.5 mg ranibizumab administered PRN by intravitreal injections.

Study burden and risks

Assuming a patient with maximal study treatment during the whole study (2 years):
27 times vital functions, ETDRS BCVA (visus sharpness), Ophthalmic examination, tonometry, OCT scan
25 times Color fundus photography, Fluorescein angiography
6 times 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
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Scientific
Novartis

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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 must be at least 18 years of age
2. Diagnosis of visual impairment exclusively due to ME secondary to central retinal vein occlusion (CRVO)
3. BCVA-sore at Screening and Baseline must be 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 prior to 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 has to
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 on medication or according to
investigator*s judgment) at Screening or Baseline or diagnosed within 6 months prior to Baseline in either eye
5. Neovascularization of the iris or neovascular glaucoma in either eye
6. Use of any systemic anti-vascular endothelial growth factor (VEGF) drugs within 6 months prior to Baseline (eg, sorafenib [Nexavar®], sunitinib [Sutent®], bevacizumab [Avastin®])
7. Prior treatment with any anti-angiogenic drugs (including any anti-VEGF agents) within 3 months prior to Baseline in either eye (eg, pegaptanib [Macugen®], ranibizumab [Lucentis®],

bevacizumab [Avastin®])
8. Panretinal laser photocoagulation within 3 months prior to 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 prior to Baseline in the study eye
10. Use of intra- or periocular corticosteroids (including sub-Tenon) within 3 months prior to Screening in the study eye
11. Any use of intraocular corticosteroid implants (eg, dexamethasone [Ozurdex®], fluocinolone
acetonide [Iluvien®]) in the study eye

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-07-2012
Enrollment:	25
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:	17-04-2012
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	EUCTR2011-002350-31-NL
ClinicalTrials.gov	NCT01535261
CCMO	NL38012.058.11