An Eighteen-Month, Two-Arm, Randomized, Double-Masked, Multicenter, Phase III Study assessing the Efficacy and Safety of Brolucizumab versus Aflibercept in Adult Patients with Visual Impairment due to Macular Edema secondary to Central Retinal Vein Occlusion (RAVEN)

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To evaluate the efficacy and safety of brolucizumab in the treatment of patients with macular edema (ME) secondary to central retinal vein occlusion (CRVO) and its potential to reduce the treatment burden for patients.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Vision disorders
Study type	Interventional

Summary

ID

NL-OMON55506

Source
ToetsingOnline

Brief title
CRTH258C2302 (RAVEN)

Condition

- Vision disorders

Synonym
Central Retinal Vein Occlusion, CRVO

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: Aflibercept, Brolucizumab, CRVO, Macular Edema

Outcome measures

Primary outcome

To demonstrate that brolucizumab is non-inferior to aflibercept with respect to

the change in best-corrected visual acuity (BCVA) from baseline up to Month 6.

Secondary outcome

- To assess the effect of brolucizumab as compared to aflibercept on BCVA

- To evaluate the anatomical outcome with brolucizumab relative to aflibercept

- To evaluate the treatment frequency with brolucizumab during the

individualized flexible treatment (IFT) period relative to aflibercept

- To assess the safety and tolerability of brolucizumab relative to aflibercept

- To evaluate the effect of brolucizumab relative to aflibercept on

patient-reported vision-related quality of life

- To assess the immunogenicity of brolucizumab.

Study description

Background summary

Retinal vein occlusion (RVO) is the second most common retinal vascular permeability disorder after diabetic retinopathy and is a significant cause of visual impairment. Macular edema (ME) is the most common cause of vision loss in patients with branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO).

Anti-VEGF therapies have revolutionized the treatment of ME secondary to RVO and are currently the standard of care in this indication as VEGF is a major mediator for ME in RVO. The most commonly used VEGF inhibitors, i.e. bevacizumab (Avastin®), aflibercept (Eylea®) and ranibizumab (Lucentis®) have demonstrated compelling evidence for resolution of ME and improvement of VA subsequent to the treatment with an anti-VEGF.

Ranibizumab, aflibercept and brolucizumab all inhibit the activity of VEGF-A with all three having proven efficacy in the treatment of nAMD while both ranibizumab and aflibercept have also previously demonstrated efficacy in the treatment of patients with ME secondary to BRVO and CRVO. These findings support the evaluation of brolucizumab in RVO patients. Furthermore, the efficacy profile of brolucizumab in nAMD patients indicates a potential of brolucizumab to differentiate versus existing anti-VEGFs on duration of action and anatomical efficacy in CRVO patients.

Study objective

To evaluate the efficacy and safety of brolucizumab in the treatment of patients with macular edema (ME) secondary to central retinal vein occlusion (CRVO) and its potential to reduce the treatment burden for patients.

Study design

The study is an eighteen-month randomized, double-masked, multicenter, activecontrolled, non-inferiority, 2-arm study in subjects with visual impairment due to ME secondary to CRVO.

Subjects will be randomized in a 1:1 ratio to 1 of 2 treatment arms:
- Brolucizumab 6 mg: 6 x every 4 weeks (q4w) followed by 48 weeks of individualized flexible treatment (IFT) from Week 24 onwards
- Aflibercept 2 mg: 6 x q4w followed by 48 weeks of IFT from Week 24 onwards.

Intervention

- Brolucizumab 6 mg/0.05 mL
- Aflibercept 2 mg/0.05 mL

Study burden and risks

Visits will be 21 times in 18 months. The visits usually last from 1 to 1,5 hours. The screening visit takes about 2,5 hours. All study procedures that are applied are standard medical procedures, with the exception of questionnaires. No complications caused by study procedures or treatments are expected. The intended benefit for the patient is that it improves vision and that fewer injections will be needed. In this study, the comparator is also an anti-VEGF treatment, so there is no risk of sub-optimal treatment.

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

- Signed informed consent must be obtained prior to participation in the study - Male or female patients to be 18 years of age or over at screening - Patients with visual impairment due to ME secondary to CRVO diagnosed less than 6 months prior to screening; hemiretinal vein occlusion will be classified as CRVO (study eye) - BCVA score between 78 and 23 letters, inclusive, using ETDRS visual acuity testing charts (approximate Snellen equivalent of 20/32 to 20/320) at both screening and baseline (study eye)

Exclusion criteria

- Concomitant conditions or ocular disorders in the study eye at screening or baseline which could, in the opinion of the investigator, prevent response to study treatment or may confound interpretation of study results, compromise visual acuity or require medical or surgical intervention during the first 12-month study period (e.g. structural damage of the fovea, vitreous hemorrhage, retinal vascular occlusion other than BRVO, retinal detachment, macular hole, or choroidal neovascularization of any cause, diabetic retinopathy (except mild nonproliferative) and diabetic macular edema). Hemiretinal vein occlusion should be excluded. - Any active intraocular or periocular infection or active intraocular inflammation (e.g. infectious conjunctivitis, keratitis, scleritis, endophthalmitis, infectious blepharitis, uveitis) in study eye at screening or baseline - Uncontrolled glaucoma in the study eye defined as intraocular pressure (IOP) > 25 mmHg on medication, or according to investigator's judgment, at screening or baseline - Presence of amblyopia, amaurosis or ocular disorders in the fellow eye with BCVA < 20/200 at screening (except when due to conditions whose surgery may improve VA, e.g. cataract) - Previous treatment with any anti-VEGF therapy or investigational drugs in the study eye at any time prior to baseline - Previous use of intraocular or periocular steroids in study eye at any time prior to baseline - Macular laser photocoagulation (focal/grid) in the study eye at any time prior to baseline and peripheral laser photocoagulation in the study eye within 3 months prior to the baseline - Intraocular surgery in the study eye during the 3-month period prior to baseline - Vitreoretinal surgery in the study eye at any time prior to baseline - Aphakia with the absence of posterior capsule in the study eye

Study design

Design

Study phase: 3

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-11-2019
Enrollment:	13
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Beovu
Generic name:	Brolucizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Eylea
Generic name:	Aflibercept
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	15-04-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-09-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	04-10-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-10-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-10-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-12-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-01-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-01-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-01-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-03-2020

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-04-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-08-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-08-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-09-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-03-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-03-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-06-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2018-001788-21-NL
ClinicalTrials.gov	NCT03810313
CCMO	NL68931.100.19