A 64-week, two-arm, randomized, double-masked, multicenter, phase IIIb study assessing the efficacy and safety of brolucizumab 6 mg compared to aflibercept 2 mg in a treat-to-control regimen in patients with neovascular agerelated macular degeneration (TALON)

Published: 05-07-2019
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To evaluate the efficacy and safety of brolucizumab used in a Treat-to-Control (TtC) regimen for the treatment of patients with neovascular age-related macular degeneration (nAMD) with the objective to evaluate the potential to reduce treatment...

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

Summary

ID

NL-OMON49739

Source
ToetsingOnline

Brief title
CRTH258A2303 (TALON)

Condition

- Vision disorders

Synonym
nAMD, wet age-related macular degeneration

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, Macular Degeneration, nAMD

Outcome measures

Primary outcome

To demonstrate that brolucizumab is superior to aflibercept with respect to the

duration of treatment intervals at Week 32

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

average change in best corrected visual acuity (BCVA) from baseline at Weeks 28

and 32

Secondary outcome

1. To evaluate the durability of brolucizumab relative to aflibercept

2. To evaluate the functional outcomes with brolucizumab relative to aflibercept

3. To evaluate the anatomical outcomes with brolucizumab relative to aflibercept

4. To evaluate the effect of brolucizumab relative to aflibercept on

Patient-Reported Outcomes (PRO)

5. To assess the safety and tolerability of brolucizumab relative to

aflibercept

Study description

Background summary

Age-related macular degeneration (AMD) is a major cause of severe loss of vision in humans.
Age-related macular degeneration causes damage to the macula. There is a dry and a wet form of macular degeneration. This study is performed in patients with the wet form (nAMD). In the case of wet AMD, new blood vessels are formed in the retina. However, these are of poor quality. Blood or fluid leaks through the wall to the surrounding tissue. This leads to damage to, among other things, the rods and cones of the retina, which play an important role in sharp vision. As a result, sharp vision deteriorates further and further, especially in the central part of the field of vision.
There is no treatment that addresses the cause of macular degeneration. The main goal is to prevent the formation of new (bad) blood vessels and leakage from the vessel wall. Anti-VEGF-therapies have revolutionized the treatment of nAMD. The most commonly used VEGF inhibitors, i.e. bevacizumab (Avastin®), aflibercept (Eylea®) and ranibizumab (Lucentis®) have shown convincing evidence for the treatment of nAMD. Brolucizumab also belongs to this group of medicines (anti-VEGF treatment).
The efficacy profile of brolucizumab in nAMD patients further indicates a potential for brolucizumab to be associated with longer treatment intervals, and thus fewer visits, than aflibercept, with similar visual results, based on the recent results of previous studies (Hawk/Harrier).

Study objective

To evaluate the efficacy and safety of brolucizumab used in a Treat-to-Control (TtC) regimen for the treatment of patients with neovascular age-related macular degeneration (nAMD) with the objective to evaluate the potential to reduce treatment frequencies

Study design

The study is a 64-week, randomized, double-masked, multi-center, active controlled, two-arm study in patients with nAMD.

Patients will be randomized in a 1:1 ratio to one of the two treatment arms:
- Brolucizumab 6 mg : 3 x 4-week injections and one 8-week injection, followed by Treat-to-Control treatment from Week 16 up to Week 60/62.
- Aflibercept 2 mg: 3 x 4-week injections and one 8-week injection, followed by Treat-to-Control treatment from Week 16 up to Week 60/62.

Intervention

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

Study burden and risks

Visits will take place 9-18 times in 15 months. Visits usually last 2-3 hours. The screening visit lasts about 3.5 hours. All study procedures, with the exception of questionnaires, are standard medical procedures. No complications caused by study procedures or treatments are expected. The intended benefit for the patient is improved vision and 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.
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 * 50 years of age at screening who are treatment naive
- Active choroidal neovascularization (CNV) secondary to AMD that affects the central subfield, including retinal angiomatous proliferation (RAP) with a CNV component, confirmed by presence of active leakage from CNV seen by fluorescein angiography and sequellae of CNV, e.g. pigment epithelial detachment (PED), subretinal or sub-retinal pigment epithelium (sub-RPE) hemorrhage, blocked fluorescence, macular edema (study eye)
- Presence of intraretinal fluid (IRF) or subretinal fluid (SRF) that affects the central subfield, as seen by Spectral Domain Optical Coherence Tomography (SD-OCT) (study eye)
- Best-corrected visual acuity (BCVA) score between 83 and 38 letters, inclusive, using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts (approximate Snellen equivalent of 20/25 to 20/200) at both screening and baseline visit (study eye)

Exclusion criteria

- Ocular conditions/disorders 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 planned medical or surgical intervention during the first 12-month study period, structural damage of the fovea, atrophy or fibrosis at the center of the fovea (study eye)
- Any active intraocular or periocular infection or active intraocular inflammation, at screening or baseline (study eye)
- Uncontrolled glaucoma defined as intraocular pressure (IOP) > 25 mmHg on medication, or according to investigator*s judgment, at screening or baseline (study eye)
- Presence of amblyopia, amaurosis or ocular disorders in the fellow eye with BCVA < 20/200 at screening (except when due to conditions which can lead to improved VA after surgery eg cataract)
- Ocular treatments: previous treatment with any anti-vascular endothelial growth factor (VEGF) drugs or investigational drugs, intraocular or periocular steroids, macular laser photocoagulation, photodynamic therapy, vitreoretinal surgery, intraocular surgery (study eye)
- Stroke or myocardial infarction during the 6-month period prior to baseline
- Systemic anti-VEGF therapy at any time.

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):	31-10-2019
Enrollment:	14
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:	05-07-2019
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-07-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-08-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-09-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-01-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-02-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-04-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	17-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2019-000716-28-NL
ClinicalTrials.gov	NCT04005352
CCMO	NL70015.056.19