A 56-week phase IIIb/IV, open-label, one-arm extension study to assess the efficacy and safety of brolucizumab 6mg in a Treat-to-Control regimen with maximum treatment intervals up to 20 weeks for the treatment of patients with neovascular Age-related Macular Degeneration who have completed the CRTH258A2303 (TALON) study

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

Summary

ID

NL-OMON55258

Source
ToetsingOnline

Brief title
CRTH258A2303E1

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

Duration of the last interval with no Disease Activity (DA) up to Week 56

Change in BCVA from baseline at Week 52 and Week 56

Secondary outcome

In all patients and per randomized arm in the TALON study:

Change in CSFT from baseline to Week 52 and Week 56

Number of visits with presence of IRF and/or SRF, and sub-RPE fluid in the

central subfield, as assessed by SD-OCT at Week 52 and Week 56

Duration of the last interval with no DA up to Week 56

Duration of the maximal intervals with no DA up to Week 56

Change of the duration of last interval with no DA between baseline and Week 56

Change in BCVA from baseline to Week 52 and Week 56

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 brolucizumab to be associated with longer treatment intervals, and thus fewer visits, than aflibercept, with similar visual results and comparable safety, based on the results of previous studies (Hawk/Harrier).
Since the first marketing authorization approval in October 2019 for the treatment of nAMD, adverse events of retinal vasculitis and/or retinal vascular occlusion, that may result in severe vision loss and typically in the presence of intraocular inflammation, have been reported from post-marketing experience with brolucizumab (Beovu®). Considering these events, the overall risk/benefit assessment remains positive.
The ongoing core study CRTH258A2303 (TALON) intends to complement the current clinical dataset on brolucizumab by generating new evidence based on the T&E concept prevalent in the current management of patients with nAMD. It will be comparing the efficacy and safety of brolucizumab and aflibercept administered in an identical 4-week-adjustment Treat-to-Control regimen with treatment intervals from 4 to 16 weeks.
This study, CRTH258A2303E1, is an extension study of the CRTH258A2303 (TALON) study, aiming at gathering additional long-term efficacy and safety evidence

about brolucizumab in a TtC treatment regimen with treatment intervals further extended up to 20 weeks in nAMD. It intends to contribute to the growing clinical dataset of brolucizumab by generating supplementary evidence on treatment safety, efficacy, and durability in nAMD.

Study objective

The purpose of this study is to evaluate the efficacy and safety of brolucizumab used in a Treat- to-Control (TtC) regimen with maximum treatment intervals up to 20 weeks for the treatment of patients with neovascular age-related macular degeneration (nAMD) who have completed the CRTH258A2303 study (TALON). In addition, switch data from aflibercept to brolucizumab is collected.

Primary Objectives:
To evaluate the extended durability of brolucizumab in a Treat-to-Control regimen assessed as duration of the last interval with no disease activity up to Week 56.
To evaluate the functional outcomes of brolucizumab in a Treat-to-Control regimen assessed as average change of best corrected visual acuity from baseline at week 52 and week 56

Study design

This is a 56-week, one-arm, open-label, multi-center extension study where all patients are to be treated with brolucizumab up to week 52 in a Treat-to-Control regimen with treatment intervals up to maximum 20 weeks

Intervention

Brolucizumab 6 mg/0.05 mL

Study burden and risks

Visits will take place 4-14 times in 56 weeks. Visits usually last 2-3 hours.
All study procedures 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.

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

1. Signed informed consent must be obtained prior to participation in the study
2. The participant has successfully completed the TALON core study at the week 64 visit (End of Study)

Exclusion criteria

1. Participant has a medical condition or personal circumstance which precludes study participation or compliance with study procedures, as assessed by the Investigator
2. Participant has discontinued study treatment in the core study
3. Anti-VEGF treatment is futile in the study eye, in the investigator's opinion
4. Pregnant or nursing (lactating) women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive human chorionic gonadotropin (hCG) pregnancy test

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-01-2021
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Beovu
Generic name:	brolucizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	10-09-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-11-2020
Application type:	First submission
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)
Approved WMO Date:	24-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-01-2022
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	EUCTR2020-002349-40-NL
CCMO	NL74590.056.20