A Phase 3, Multicentre, Double-masked, Randomised Study to Evaluate the Efficacy and Safety of Intravitreal OPT-302 in Combination with Aflibercept, Compared with Aflibercept Alone, in Participants with Neovascular Age-related Macular Degeneration (nAMD) (COAST)

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This study has been transitioned to CTIS with ID 2024-512880-30-00 check the CTIS register for the current data. To determine the efficacy of intravitreal 2.0 mg OPT-302 when administered in combination with intravitreal 2.0 mg aflibercept, in…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Anterior eye structural change, deposit and degeneration
Study type	Interventional

Summary

ID

NL-OMON54023

Source
ToetsingOnline

Brief title
OPT-302-1005 (COAST)

Condition

- Anterior eye structural change, deposit and degeneration

Synonym
age-related macular degeneration, macular degeneration

Research involving
Human

Sponsors and support

Primary sponsor: Opthea Limited
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: aflibercept, intravitreal injection, neovascular age-related macular degeneration (AMD), OPT-302

Outcome measures

Primary outcome

Mean change in Early Treatment Retinopathy Study (ETDRS) best corrected visual

acuity (BCVA) letters [Time Frame: Baseline to Week 52]

Secondary outcome

Efficacy

• Proportion of participants gaining 15 or more ETDRS BCVA letters from

Baseline to Week 52.

• Proportion of participants gaining 10 or more ETDRS BCVA letters from

Baseline to Week 52.

• Change in choroidal neovascularisation (CNV) area by fluorescein angiography

(FA) from Baseline to Week 52.

• Proportion of participants with absence of both sub-retinal fluid (SRF)

and intra-retinal (IR) cysts by spectral domain optical coherence tomography

(SD-OCT) at Week 52.

Safety:

• Incidence of ocular and non-ocular Treatment-Emergent Adverse Events (TEAEs).

• Proportion of participants losing 15 or more ETDRS BCVA letters from Baseline

to Week 52.

• Participant incidence of anti-OPT-302 antibody (ADA) formation.

Pharmacokinetic:

• OPT-302 pharmacokinetic parameters.

Study description

Background summary

Age-related macular degeneration (AMD) is a chronic degenerative eye disease of the central retina, that causes a progressive, irreversible, severe loss of central vision. In many countries, AMD leads to as many blind registrations than all other eye diseases combined. There are two main types of AMD: dry-AMD and neovascular AMD (nAMD). Although nAMD is less common, affecting only 10% of AMD patients, it is more likely to lead to significant vision loss and blindness. Visual deterioration associated with nAMD can be rapid, generally severe, and significantly deteriorates patients* quality of life.
There is a high unmet medical need for more effective treatments in patients with sub-optimal responses to current treatments for nAMD (primarily intravitreally administered vascular endothelial growth factor A [VEGF-A] inhibitors). The investigational product, 2.0 mg OPT-302, is a therapeutic candidate for the treatment of nAMD, and when co-administered with a VEGF-A inhibitor, it is expected to provide improved responses compared to treatment with an anti-VEGF-A therapy alone.
Based on the positive Phase 2b study results from study OPT-302-1002, Opthea is conducting a prospective Phase 3 programme in treatment-naïve participants with nAMD, which comprises of two Phase 3 studies: (i) intravitreal of 2.0 mg OPT-302 in combination with 0.5 mg ranibizumab (OPT-302-1004) and of (ii) intravitreal 2.0 mg OPT-302 in combination with 2.0 mg aflibercept (OPT-302-1005), compared with 0.5 mg ranibizumab or 2.0 mg aflibercept, with sham control in each trial respectively.

Study objective

This study has been transitioned to CTIS with ID 2024-512880-30-00 check the CTIS register for the current data.

To determine the efficacy of intravitreal 2.0 mg OPT-302 when administered in combination with intravitreal 2.0 mg aflibercept, in participants with neovascular AMD.

Study design

Phase 3, multicentre, randomised, parallel-group, sham-controlled, double-masked, superiority study

Intervention

Three study arms, randomised in a 1:1:1 ratio:
• Standard Dosing 2.0 mg OPT-302 (50 µl) intravitreal injection at 4-weekly intervals (q4w), with 2.0 mg aflibercept (50 µl) intravitreal injection (3 doses at 4-weekly intervals, and then 8-weekly [q4w x 3 then q8w]).
• Extended Dosing 2.0 mg OPT-302 (50 µl) intravitreal injection (q4w x 3 then q8w) with sham injection at visits when OPT-302 is not administered, with 2.0 mg aflibercept (50 µl) intravitreal injection (q4w x 3 then q8w).
• Control Sham intravitreal injection 4-weekly, with 2.0 mg aflibercept (50 µl) intravitreal injection (q4w x 3 then q8w).

Study burden and risks

Burden: Subject*s participation will last a total of approximately about 23 months and 2 weeks and is divided into 3 periods: screening period, treatment period, and a final study visit. After the screening period, there will be a Baseline visit (Visit 2) within 2 weeks of the first visit (screening visit).
The treatment period will have 25 planned visits to the study centre. Prior to each injection, the subject will be given numbing drops. Aside from the intervention, participation in the study involves eye exams, physical exam, vital signs measurements, blood draws and urine collection. Participants will be subjected to a diary and questionnaires for completion, as well as to the review of their medical history. Risks: A total of 399 participants have received eye injections with the study drug, OPT-302, to date. The study drug alone or in combination with aflibercept was reported to be well tolerated. The very common side effects of the study drug (OPT-302) (seen in more than 1 in 10 participants) in participants who received the study drug in combination with aflibercept were conjunctival haemorrhage (blood spots in the white of the eye), increased intraocular pressure (increase in eye pressure in the eyes), These side effects were reported in the study eye. The common side effects (seen in up to 1 in 10 participants) in participants who received the study drug in combination with aflibercept were eye pain, vitreous floaters (black grey spots or strings in vision that drift across the eyes), eye irritation,

punctate keratitis (condition that causes red watery eyes, light sensitivity, and decreased vision), increased lacrimation (watering eyes), ocular hyperaemia (redness of the eye), anterior chamber cell - this is a sign there is inflammation in the eye, blurred vision. These side effects were reported in the study eye. There may be other unforeseen risks that can occur. Risk-benefit analyses: There is a high unmet medical need for more effective treatments in patients with sub-optimal responses to current treatments for nAMD (primarily intravitreally administered vascular endothelial growth factor A [VEGF-A] inhibitors). The investigational product, 2.0 mg OPT-302, is a therapeutic candidate for the treatment of nAMD, and when co-administered with a VEGF-A inhibitor, it is expected to provide improved responses compared to treatment with an anti-VEGF-A therapy alone. Almost 400 participants have received >1,800 intravitreal injections of OPT-302 (any dose) during the clinical programme to date, of which 282 participants have received 1,515 intravitreal injections in combination with 0.5 mg ranibizumab, and 104 participants have received 288 intravitreal injections in combination with 2.0 mg aflibercept. Based on the studies conducted, there appears to be no significant additional safety risks associated with the addition of OPT-302 to ranibizumab or aflibercept intravitreal therapy over and above those identified after intravitreal injection of anti-VEGF-A therapies. The risk profile in relation to the high unmet medical need supports a favorable benefit/risk ratio for this study of OPT-302.

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

* Male or female participants at least 50 years of age.
• Active subfoveal CNV lesion or juxtafoveal CNV lesion with foveal involvement that is secondary to AMD in the Study Eye.
• An ETDRS BCVA score between 60 and 25 (inclusive) letters in the Study Eye

Exclusion criteria

Study Eye
• Any previous treatment for neovascular AMD.
• Clinically significant ocular disorders (other than neovascular AMD), which may interfere with assessment of BCVA, assessment of safety, or fundus imaging.
General
• Any current (or history of a) social, psychological, or medical condition that precludes enrolment into the study.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-01-2022
Enrollment:	22
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Eylea 40mg/ml solution for injection in pre-filled syringe
Generic name:	Aflibercept
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	NA
Generic name:	OPT-302

Ethics review

Approved WMO Date:	22-06-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-09-2021
Application type:	First submission
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:	24-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-06-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-03-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-05-2024
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
EU-CTR	CTIS2024-512880-30-00
EudraCT	EUCTR2020-004694-46-NL
ClinicalTrials.gov	NCT04757636
CCMO	NL77391.056.21