A Multicenter, Double-Masked, Randomized, Dose-Ranging Trial to Evaluate the Efficacy and Safety of Conbercept Intravitreal Injection in Subjects with Neovascular Age related Macular Degeneration

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

Summary

ID

NL-OMON48627

Source
ToetsingOnline

Brief title
KHB-1801 Conbercept in Subjects with *wet* AMD

Condition

- Eye disorders

Synonym
Neovascular Age Related Macular Degeneration, wet AMD

Research involving

Human

Sponsors and support

Primary sponsor: Chengdu Kanghong Biotechnology Co., Ltd.
Source(s) of monetary or material Support: Industry

Intervention

Keyword: AMD, Conbercept, intravitreal injection

Outcome measures

Primary outcome

The primary objective is to determine if 0.5 mg or 1.0 mg conbercept is non-inferior to aflibercept 2.0 mg as measured by the change from baseline in best corrected visual acuity (BCVA) by Early Treatment of Diabetic Retinopathy Study (ETDRS) method at the Week 36 visit.

The primary endpoint is the mean change from baseline in ETDRS BCVA letter score at Week 36 in the study eye.

Secondary outcome

The secondary objectives of this study are:

1. To evaluate the difference in efficacy between conbercept doses and aflibercept, with respect to the following:

* Proportion of subjects maintaining vision (i.e., losing <15 ETDRS BCVA letters) from baseline to Week 36;

* Proportion of subjects gaining *15 ETDRS BCVA letters from baseline to Week 36;

* Mean change from baseline in central retinal thickness (μm) by SD-OCT at Week

36;

* Proportion of subjects maintaining vision (i.e. losing <15 ETDRS BCVA

letters) from baseline to Week 48;

* Mean change from baseline in ETDRS BCVA letter score at Week 96

2. To compare the safety and tolerability of conbercept doses and aflibercept,

and to evaluate the pharmacokinetics and immunogenicity of conbercept doses,

when feasible

Study description

Background summary

AMD is the leading cause of severe and irreversible vision loss in people over the age of 65. Available therapies are not singularly effective. The main feature of wet AMD is an increased blood vessel growth that leads to macular bleeding and accumulation of fluid in the retina (retinal edema), as well as damage to the retinal tissue, and can finally lead to scarring and loss of vision. An important factor in this increased blood vessel formation is the protein called vascular endothelial growth factor (VEGF). An anti-VEGF study medication (such as Eylea® and the study drug) works by stopping this protein from being made in the eye.

Study objective

The purpose of this study is to investigate how safe and effective the new drug conbercept given as intravitreal injections (*study drug*) is when compared with Eylea® injections in patients with neovascular *wet* age-related macular degeneration (AMD) who have not received treatment before.
The study drug is *Investigational*, which means that it has not been approved by the European Union (EU) authorities or U.S. FDA. The study drug has obtained approval for the use in patients with wet AMD in China.

Eylea® is currently one of the standard care treatment options for wet AMD and will be provided to assigned study subjects to be injected into the study eye for study purposes as the active comparator (or control).

Study design

Multicenter, Multinational, Double-masked, Parallel-group, Dose ranging, Active-controlled, Randomized trial

Duration:
A screening period of less than or equal to 14 days, followed by a treatment period of 92 weeks (last assessment at 96 weeks) with primary efficacy analysis at 36 weeks

Intervention

The study will randomize approximately 1140 subjects in a ratio of 1:1:1 to receive IVT injections of 0.5 mg conbercept, 1.0 mg conbercept, or 2.0 mg aflibercept.
Subjects randomized to the conbercept treatment arms will receive an IVT injection of either 0.5 mg or 1.0 mg conbercept at 4-week intervals on Day 1, Week 4 and Week 8 (loading phase).
Subjects in the conbercept treatment 0.5 mg arm will begin dosing every 8 weeks (q8w) after the first three injections.
Subjects in the conbercept treatment 1.0 mg arm will begin dosing every 12 weeks (q12w) after the first three injections.
Aflibercept will be dosed as an IVT injection on Day 1, Week 4 and Week 8 and every 8 weeks (q8w) thereafter.
All subjects will receive sham procedure at visit intervals between each scheduled IVT injection to mask any differences in dosing frequency.

Control:
Aflibercept 2.0 mg/eye monthly IVT (at 4-week intervals) for the first 12 weeks (loading phase) followed by dosing every 8 weeks (q8w) to Week 96

Study burden and risks

Clinical data and use in patients in China show efficacy of the study drug and a well described safety profile in humans. The burden/inconvenience of the use of the study drug compared to current treatment standards are considered equal.

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. Men and women * 50 years of age at the Screening visit;, 2. Females must be at least 1 year postmenopausal, or surgically sterilized, or, if of childbearing potential, must have a negative pregnancy test at the Screening visit;, o Women of childbearing potential must agree to use a highly effective method of contraception throughout the study (See complete list in the Study Procedures Manual);, 3. Have received no previous treatment for neovascular AMD, including laser photocoagulation and/or photodynamic therapy (PDT) and/or IVT VEGF antagonists (treatment naïve) and;, 4. Have active subfoveal CNV lesions secondary to AMD (including polypoidal choroidal vasculopathy (PCV)) evidenced by subfoveal FA leakage, or definite subfoveal fluid by SD-OCT in the study eye at Screening;, 5. Have CNV that is at least 50% of total lesion size in the study eye at Screening;, 6. Have a ETDRS BCVA letter score of 78 to 25 (approximately 20/32 to 20/320 equivalent) in the study eye at Screening;, 7. Have ocular media (lens, cornea, vitreous) of adequate clarity to permit high quality fundus imaging;, 8. Are willing and able to sign the study written informed consent form (ICF).

Exclusion criteria

1. Have had any prior ocular or systemic treatment (investigational or approved) or surgery for the treatment of neovascular AMD in the study eye except dietary supplements or vitamins;
2. Have participated as a subject in any interventional clinical trial within one month (30 days) prior to Baseline visit;
3. Have a total lesion size greater than twelve disc areas (30.5 mm2), including blood, fibrosis and neovascularization, as assessed by FA in the study eye at Screening;
4. Have a subretinal hemorrhage that is either 50% or more of the total lesion area, or blood is under the fovea and is one or more disc areas in size (greater than 2.5 mm2) in the study eye at Screening;
5. Have scarring or fibrosis making up greater than 50% of total lesion in the study eye at Screening; and/or scarring, fibrosis or atrophy involving the center of the fovea in the study eye at Screening;
6. Have any retinal pigment epithelial tears or rips in the study eye at Screening or upon examination at Baseline;
7. Have any vitreous hemorrhage in the study eye upon examination at Baseline or history of vitreous hemorrhage within eight weeks prior to Screening;
8. Have any other cause of CNV, including pathologic myopia (defined per protocol as spherical equivalent of -8 diopters or more), ocular histoplasmosis syndrome, angioid streaks, inherited macular dystrophies, choroidal rupture, uveitis, punctate inner choroidopathy, or multifocal choroiditis in the study eye at Screening;
9. Have a history of or clinical evidence of significant diabetic retinopathy that could impact assessment of vision or affect central vision, diabetic macular edema, or any other vascular disease other than AMD including history or clinical evidence of retinal vein occlusion affecting the study eye at Screening;
10. Have had prior pars plana vitrectomy in the study eye;
11. Have presence of a full thickness macular hole at Screening or upon examination at Baseline or a history of a full thickness macular hole in the study eye;
12. Have a history of intraocular or periocular surgery within three months of Baseline in the study eye, except in the case of lid surgery, which may not have taken place within one month of Baseline as long as it is unlikely to interfere with IVT injection;
13. Have prior trabeculectomy or other filtration surgery in the study eye;
14. Have uncontrolled glaucoma (defined as intraocular pressure (IOP) greater than or equal to 22 mmHg at Baseline despite treatment with more than two anti-glaucoma medications) in the study eye;
15. Have active intraocular inflammation in either eye at Screening or upon examination at Baseline or a history of uveitis in either eye;
16. Have active ocular or periocular infection in either eye, or a history of any ocular or periocular infection within the two weeks prior to Screening in

either eye;
17. Have presence or history of scleromalacia in either eye;
18. Have aphakia or pseudophakia with absence of posterior capsule (unless it occurred as a result of yttrium aluminum garnet (YAG) posterior capsulotomy) in the study eye;
19. Have had previous therapeutic radiation in the region of the study eye;
20. Have history of corneal transplant or presence of a corneal dystrophy that interferes with IOP measurements or imaging in the study eye;
21. Significant media opacities, including cataract, in the study eye that, in the opinion of the Investigator, could require either medical or surgical intervention during the study period;
22. Have any concurrent ocular condition in the study eye that, in the opinion of the Investigator, could either increase the risk to the subject beyond what is to be expected from standard procedures of intraocular injection, or that otherwise may interfere with the injection procedure or with evaluation of efficacy or safety during the study;
23. Have any evidence by medical history, physical examination or clinical laboratory testing at Screening or Baseline that shows reasonable suspicion of a disease or condition that contraindicates the use of study medication (conbercept or aflibercept) or that might affect interpretation of the results of the study or render the subject at high risk for treatment complications;
24. Have any use of long acting intraocular steroids, including implants, within six months prior to Day 1, Baseline;
25. Have any known allergy to povidone iodine or known serious allergy to the fluorescein sodium for injection in angiography;
26. Any history of known contraindications indicated in the Food and Drug Administration (FDA)-approved label for the active control;
27. If female, be pregnant (positive urine pregnancy test at Screening) or breastfeeding

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:	Recruitment stopped
Start date (anticipated):	11-02-2019
Enrollment:	28
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Eylea®
Generic name:	Aflibercept
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Lumitin
Generic name:	Conbercept

Ethics review

Approved WMO Date:	04-07-2018
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-12-2018
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-01-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-04-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO	

Date:	08-05-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-06-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-01-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-01-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	16-07-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-08-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	EUCTR2017-004825-34-NL
CCMO	NL66004.028.18
Other	pending/ nog niet bekend