Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Jun 2026

A Phase III, multicenter, randomized, two-armed, double-blind, parallel, active-controlled, non-inferiority clinical trial to compare efficacy and safety of test-Aflibercept (CinnaGen Co, Iran) to the reference Aflibercept product (Eylea®, Regeneron, USA) in patients with Neovascular age-related macular degeneration.

Protocol summary

Study aim

The aim of this study is to assess non-inferiority of Aflibercept (CinnaGen co.) to Eylea® (Regeneron, USA) in terms of achieving maintaining vision in patients with neovascular age-related macular degeneration.

Design

This is a phase III, randomize, parallel, double-blind and active-control with the sample size of 168 patients.

Settings and conduct

This is a multicenter, phase 3 clinical trial

Participants/Inclusion and exclusion criteria

Patients aged 55-80 years with primary active CNV subfoveal lesion secondary to AMD (according to the physician's decision based on the results of ocular examination, or OCT) and the ETDRS-best-corrected visual acuity index with the score of 20/40 to 20/320 with include to the study. This study has 34 exclusion criteria which include any prior ocular or systemic anti-VEGF therapy during the past 3 months, presence of scar, fibrosis, or atrophy in the central part of the fovea in the study eye, active intraocular inflammation in either eye and histories such as the history or evidence of diabetic retinopathy, diabetic macular edema and the history of uveitis in either eye.

Intervention groups

Intervention group 1: Aflibercept (CinnaGen Co, Iran) 2 mg by intravitreal injection every 4 weeks for the first 3 injections, followed by 2 mg every 8 weeks until week 48 of study. Intervention group 2: Eylea (Regeneron, USA) 2 mg (0.05 mL) by intravitreal injection every 4 weeks (Monthly) for the first 3 injections, followed by 2 mg every 8 weeks (every two months) Until week 48 of study.

Main outcome variables

Assessing the main outcome is based on evaluating visual acuity with Tumbling-E ETDRS chart

General information

Reason for update

- The secondary endpoint number 2 is revised to “The percentage of patients who have increase of ≥15 score on ETDRS chart at week 52 visit compared to baseline”. - The timepoints for the assessment of laboratory parameters is changed to the screening visit, week 24, and week 52. - “visit 0” is changed to visit 1 (baseline visit (week 0)). - Inactive study centers are removed and new centers/investigators are added to increase patient recruitment rate.

Acronym

IRCT registration information

IRCT registration number: **IRCT20150303021315N14**
Registration date: **2019-06-30, 1398/04/09**
Registration timing: **prospective**

Last update: **2020-11-24, 1399/09/04**
Update count: **1**

Registration date

2019-06-30, 1398/04/09

Registrant information

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Name of organization / entity

Orchid Pharmed

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2019-07-23, 1398/05/01

Expected recruitment end date

2020-03-19, 1398/12/29

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

A Phase III, multicenter, randomized, two-armed, double-blind, parallel, active-controlled, non-inferiority clinical trial to compare efficacy and safety of test-Aflibercept (CinnaGen Co, Iran) to the reference Aflibercept product (Eylea®, Regeneron, USA) in patients with Neovascular age-related macular degeneration.

Public title

The Effect of Aflibercept on Treatment of Age-related macular Degeneration

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

male or female aged 55-80 years at the time of signing the informed consent form. Patients with Primary active CNV subfoveal lesion secondary to AMD (with definite diagnosis of AMD according to physician’s decision based on the results of ocular examination, or OCT) the ETDRS-best-corrected visual acuity index with the score of 20/40 to 20/320 (or BCVA letter score of 73 to 25 in the study eye) Willing, committed, and able to return for clinic visits and complete all study-related procedures Patients with the ability to read, understand and willing to sign the informed consent form for participation in the study

Exclusion criteria:

Any prior ocular (in the study eye) or systemic anti-VEGF therapy, during the past 3 months, Photodynamic Therapy (PDT) or surgery for neovascular AMD. The need for receiving ocular anti-VEGF simultaneously in both eyes in the loading phase for the treatment of neovascular AMD Scar, fibrosis, or extensive subretinal hemorrhage of more than 50% of the total lesion area in the study eye, according to the physician's opinion based on clinical presentation or according to fundus photography. The presence of scar, fibrosis, or atrophy in the central part of the fovea in the study eye The presence of retinal pigment epithelial tears or rips involving the macular part of the study eye at the time of entering the study The history of any vitreous hemorrhage within 4 weeks prior to the first visit of the study in the study eye Presence of other causes of CNV in the study eye Clinical or paraclinical diagnosis of PCV by physician’s diagnosis The history or clinical evidence of diabetic retinopathy, diabetic macular edema, or any other vascular disease affecting the retina, other than AMD in either eyes Prior vitrectomy in the study eye History of retinal detachment or treatment or surgery for retinal detachment in the study eye Any history of a macular hole of stage 2 or above in the study eye Any intraocular or periocular surgery within three months of the screening visit on the study eye except lid surgery, which may not have taken place within one month of screening visit Prior trabeculectomy or any other filtration surgery in the study eye Uncontrolled glaucoma (defined as intraocular pressure ≥ 25 mmHg despite treatment with anti-glaucoma medication) in the study eye Active intraocular inflammation in either eye Active ocular or periocular infection in either eye or any ocular or periocular infection within the last two weeks prior to screening visit in either eye Any history of uveitis in either eye Presence or history of scleromalacia in either eye Aphakia or pseudophakia with the absence of posterior capsule (unless it occurred as a result of a yttrium aluminum garnet [YAG] posterior capsulotomy) in the study eye Previous therapeutic radiation in the region of the study eye History of corneal transplant or corneal dystrophy in the study eye Any significant media opacities, including cataract, in the study eye that might interfere with visual acuity, assessment of drug safety, or fundus photography Patients with amblyopia. Patients with blindness in the fellow eye Any concurrent intraocular condition in the study eye that, in the opinion of the investigator, could require either medical or surgical intervention during the study period Any concurrent ocular condition in the study eye which, in the opinion of the investigator, could either increase the risk to the patient beyond what is to be expected from standard procedures of intraocular injection, or which otherwise may interfere with the injection procedure or with evaluation of efficacy or safety History of other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or that might affect the interpretation of the results of the study or render the patient at high risk for treatment complications Participation as a patient in any clinical study within the 12 weeks prior to the screening visit The use of long-acting steroids, either systemically or intraocularly, in the six months prior to screening visit Any history of allergy to povidone iodine Females who are pregnant, breastfeeding, planning to become pregnant during the study period, unwilling to practice adequate contraception throughout the study and for at least 60 days following the last dose of study medication History of stroke, myocardial infarction or uncontrolled hypertension (blood pressure >160/100 despite receiving medical treatment) for less than three months from the date of the Screening visit Evidence of significant uncontrolled concomitant diseases such as cardiovascular disease, nervous system, pulmonary, renal, hepatic, endocrine, or gastrointestinal disorders

Age

From **55 years** old to **80 years** old

Gender

Both

Phase
3
Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

Sample size
Target sample size: **168**
Randomization (investigator's opinion)
Randomized
Randomization description
The randomization plan of the patients will be carried out centrally using an R-CRAN software version 3.2.3. Blocks (with the size 2 or 4) will be made using permuted block randomization for a total of 168 patients (1:1 allocation ratio). After the randomization procedure, a code will be allocated to each patient that will be used as a patient identifier throughout the study. The assigned code will be denoted by 4 initials (corresponding to the first two letters of the first name, first two letters of surname) and 3 numbers (center code). Moreover, the described code is followed by study unique identification code consisting of first three letters of the generic name of the investigational product (AFL), and three numbers (corresponding to the randomization number), e.g. ABCD001AFL-001. The randomization number will be assigned in a consecutive way.
Blinding (investigator's opinion)
Double blinded
Blinding description
Both Aflibercept products used in the study will be entirely indistinguishable for patients and health care providers since they are identical in shape, size, label, and color. The container of the drugs will be labeled using identical Labels so they will be impossible to differentiation. Patients groups and their drugs will not be disclosed to investigators. After that, the patient signed Informed consent and considered to be eligible base on the inclusion and exclusion criteria; he or she will be allocated to one of each group. The investigator will not be informed of randomization, and all the drug codes will be placed in an opaque pocket inside each sites trial Master file. Data analyzers will not be informed of the patients' grouping.
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
The Ethics Committee of Tehran University of Medical Sciences
Street address
Qods St., Keshavarz Blvd
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Province
Tehran
Postal code
1417653761
Approval date
2019-05-07, 1398/02/17
Ethics committee reference number
IR.TUMS.VCR.REC.1398.116

Health conditions studied

1

Description of health condition studied
Neovascular age-related macular Degeneration
ICD-10 code
H35.32
ICD-10 code description
Exudative age-related macular degeneration

Primary outcomes

1

Description
The proportion of patients achieving maintaining vision (losing<15 letter on ETDRS chart) at week 52, in comparison to visit 0.
Timepoint
baseline visit, 52 weeks after first intervention
Method of measurement
Tumbling-E ETDRS chart

Secondary outcomes

1

Description
Mean changes in the Best-Corrected Visual Acuity Index measured with ETDRS chart from visit baseline to week 52
Timepoint
baseline visit and 52 weeks after first intervention
Method of measurement
Tumbling E ETDRS chart

2

Description
The percentage of patients who have increase of ≥15 score in ETDRS at week 52
Timepoint
baseline visit and 52 weeks after first intervention
Method of measurement
Tumbling E ETDRS chart

3

Description
The mean change in National Eye Institute Visual Function Questionnaire (NEI VFQ-25) at week 52 compared to the visit baseline.
Timepoint
Baseline Visit and 52 weeks after first intervention
Method of measurement
NEI VFQ-25

4

Description
Mean changes in central retinal thickness based on structural OCT at week 52 compared to the screening visit
Timepoint
screening visit and 52 weeks after first intervention
Method of measurement
Optical Coherence Tumography (OCT)

5

Description
The percentage of patients without intra-retinal fluid and subretinal fluid based on structural OCT at week 52
Timepoint
52 weeks after first intervention
Method of measurement
Optical Coherence tumography

6

Description
Systemic and Ophthalmic Adverse events (AEs) and adverse drug reactions (ADR) – at screening, visit 1 and all the follow-up visits until week 52
Timepoint
All of the study visits
Method of measurement
Physical examination

7

Description
Comparing immunogenicity of two products and evaluating antibody formation- at screening visit, week 24 and week 52.
Timepoint
screening visit, 24 weeks, and 52 weeks after first intervention
Method of measurement
ELISA Assay

8

Description
Evaluation of blood pressure- at screening visit and week 52
Timepoint
Screening Visit, 52 weeks after first intervention
Method of measurement
blood pressure meter

9

Description
Clinical laboratory testing for systemic safety, including liver and kidney functions, complete blood count and clinical bio-chemistries- at regular intervals
Timepoint
screening visit, 24 weeks and 52 weeks after first intervention
Method of measurement
Lab test

10

Description
Changes in physical examination findings- at screening visit and week 52
Timepoint
Screening Visit, and 52 weeks after first intervention
Method of measurement
Physical examination

Intervention groups

1

Description
Aflibercept (CinnaGen Co, Iran) 2 mg (0.05 mL) by intravitreal injection every 4 weeks (Monthly) for the first 3 injections, followed by 2 mg every 8 weeks (every two months) Until week 48 of study
Category
Treatment - Drugs

2

Description
Eylea (Regeneron, USA) 2 mg (0.05 mL) by intravitreal injection every 4 weeks (Monthly) for the first 3 injections, followed by 2 mg every 8 weeks (every two months) Until week 48 of study.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Farabi Hospital
Full name of responsible person
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Recruitment center
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3

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4

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5

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6

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
CinnaGen company
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Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
Yes

Title of funding source
CinnaGen company

Proportion provided by this source
100

Public or private sector
Private

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
Industry

Person responsible for general inquiries

Contact

Name of organization / entity
Orchid Pharmed Co.
Full name of responsible person
Dr. Nasim Anjidani
Position
medical department manager
Latest degree
Medical doctor
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Person responsible for scientific inquiries

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Person responsible for updating data

Contact

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Latest degree

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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Undecided - It is not yet known if there will be a plan to make this available

Study Protocol

Undecided - It is not yet known if there will be a plan to make this available

Statistical Analysis Plan

Not applicable

Informed Consent Form

Undecided - It is not yet known if there will be a plan to make this available

Clinical Study Report

Undecided - It is not yet known if there will be a plan to make this available

Analytic Code

Undecided - It is not yet known if there will be a plan to make this available

Data Dictionary

Undecided - It is not yet known if there will be a plan to make this available