ISRCTN42621450 https://doi.org/10.1186/ISRCTN42621450

Study to assess safety and efficacy of ADVM-022 in patients having already received anti-VEGF treatment for neovascular (wet) age-related macular degeneration (nAMD) [LUNA]

Submission date
23/09/2022

Recruitment status
No longer recruiting

Registration date
21/10/2022

Overall study status
Completed

Last Edited
01/11/2022

Condition category
Eye Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
This clinical study will evaluate the safety, tolerability, and effect of a single intravitreal (IVT) injection of either a low or high dose of an investigational medicinal product, ADVM-022, in patients with neovascular (wet) age-related macular degeneration (nAMD).

Who can participate?
Patients aged 50 years old and over with nAMD

What does the study involve?
The goal of this clinical study is to determine the appropriate dose of a one-time IVT injection of ADV-022 and the appropriate corticosteroid dosing regimen that together, will allow for the optimum risk benefit profile for the sustained treatment of wet AMD in patients who have been previously treated with anti-VEGF injections. During the study period, study participants will be assessed for the need of supplemental aflibercept treatment. The total study duration will be approximately 1 year.

What are the possible benefits and risks of participating?
There is no guarantee that you will benefit from taking part in this study. It is possible the study drug may decrease the need for regular anti-VEGF injections. There may also be an improvement in your visual acuity or a slowing of progression of your visual loss from wet AMD.

It is possible that the results may not help you individually but the information we get from this study will help us improve treatment for patients with the same disease as yours in the future.

Risks related to ADVM-022:
ADVM-022 is being evaluated in humans. There is a small possibility of an allergic reaction with the study drug. If it is the case, the immune response developed could prevent the participant from participating in future gene therapy studies which use the same or a similar adeno-

associated virus as part of the product.
In a study of ADVM-022 in wet AMD patients, the study drug was well tolerated. Mild eye inflammation was common, consistent with the inflammation seen in animal studies. Mild eye inflammation in wet AMD patients improved following treatment using steroid eye drops.
Data from the study in wet AMD patients showed that eye inflammation may occur and may continue over time. Inflammation may be treated with additional steroid eye drops. Changes to the colour or structure of the iris may occur.
Aflibercept that is produced after treatment with the study drug, ADVM-022, is similar to Eylea®, another drug commonly used to treat wet AMD and it is possible to experience similar side effects as described for Eylea®. Because the effect of the study drug may be long-lasting, there are potential risks for side effects that appear only after a long period of time that are currently unknown.

Risks related to the study procedures:
Intravitreal injection:
Possible complications of intravitreal injection to the study eye include but are not limited to eye-related side effects such as retinal detachment, a serious infection (endophthalmitis), swelling within the eye (inflammation), cataract formation (clouding of the lens of the eye), glaucoma (increased pressure in the eye), damage to the retina or cornea (structures of the eye), and bleeding. Eye drops or other medicine may be used to reduce the possibility of this occurring. Any of these rare complications may lead to severe, permanent loss of vision. The most common side effects are increased subconjunctival haemorrhage (bleeding in the whites of your eye) eye pain, cataract, vitreous detachment (separation of the gel in the back of your eye from the retina), small specks in vision (floaters), increased eye pressure, and the feeling that something is in the eye.
Patients receiving an intravitreal injection to the eye may experience side effects related to the pre-injection preparation procedure (injury resulting from the instrument to hold the eyelid, anaesthetic drops, dilating drops, antibiotic drops, povidone-iodine drops and the injection of the anaesthetic to the surface of the eye). These side effects may include eye pain, subconjunctival haemorrhage (bleeding in the whites of your eyes), vitreous (gel part of the back of your eye) floaters, irregularity or swelling of the cornea (the clear part of the front of your eye), inflammation of the eye, and changes in your vision.
With the blood sampling on study, there is a risk of slight bruising and risk of infection.

Where is the study run from?
The John Radcliffe Hospital (UK)

When is the study starting and how long is it expected to run for?
September 2022 to February 2024

Who is funding the study?
Adverum Biotechnologies Inc (USA)

Who is the main contact?
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05536973

Clinical Trials Information System (CTIS)
2022-002261-15

Integrated Research Application System (IRAS)
1006271

Central Portfolio Management System (CPMS)
53941

Protocol serial number
ADVM-022-11

Study information

Scientific Title

A multi-center, randomized, double-masked phase II study to assess safety and efficacy of ADVM-022 (AAV.7m8-aflibercept) in anti-VEGF treatment-experienced patients with neovascular (wet) age-related macular degeneration (nAMD) [LUNA]

Acronym
LUNA

Study objectives
Primary objective:
To assess the safety, tolerability, and efficacy of a single intravitreal (IVT) injection of ADVM-022 in anti-VEGF treatment-experienced patients with neovascular (wet) age-related macular degeneration (nAMD)

Secondary objectives:
1. To evaluate the effect of ADVM-022 on best corrected visual acuity (BCVA) using an an early treatment diabetic retinopathy study (ETDRS) visual acuity chart
2. To assess the durability of a single IVT injection of ADVM-022
3. To evaluate the effect of ADVM 022 on Central Subfield Thickness (CST)
4. To assess the effectiveness of prophylactic corticosteroid treatment regimens on minimizing post-prophylactic inflammation events

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, ref: 22/SC/0390

Primary study design
Interventional

Study design
Randomized multi-center double-Masked parallel group study with two doses of ADVM-022 and four prophylaxis corticosteroid regimens

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Neovascular (wet) age-related macular degeneration

Interventions
For experimental arm dose 1, a single intravitreal injection of ADVM-022 2E11 vg/eye. The treatment is a single IVT injection of 2E11 vg/eye ADVM-022 dose in combination with one (1) of four (4) corticosteroid treatment regimens.

For experimental arm dose 2, a single intravitreal injection of ADVM-022 6E10 vg/eye. The treatment is a single IVT injection of 6E10 vg/eye ADVM-022 dose in combination with one (1) of four (4) corticosteroid treatment regimens.

Intervention Type

Genetic

Primary outcome(s)
1. Incidence and severity of ocular and non-ocular adverse events from baseline through Week 50
2. Mean change in BCVA from the Screening Visit (Baseline) using an ETDRS visual acuity chart at Week 50/ End of Study (EOS)

Key secondary outcome(s)
1. Percentage of participants who lose/gain at least 5, 10 or 15 letters in BCVA using an ETDRS visual acuity chart compared with Baseline through Week 50.
2. Mean change in BCVA using an ETDRS visual acuity chart from baseline to Week 26.
3. Percentage of participants who are supplemental aflibercept injection-free through Week 50.
4. Percentage reduction in mean rate of anti-VEGF injections over one year relative to number of anti-VEGF injections received in the year prior to Baseline.
5. Mean change in Central Subfield Thickness (CST) as measured on SD-OCT from Baseline through Week 26 and Week 50.
6. Percentage of participants without CST fluctuations > 50 µm as measured on SD-OCT through Week 50.

Completion date
26/02/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 27/10/2022:

1. Male or female participants, age ≥ 50 years of age
2. Willing and able to provide written, signed informed consent for this study
3. Demonstrated a meaningful response to anti-VEGF therapy.
4. Current evidence of active primary or recurrent sub-foveal choroidal neovascularization (CNV) assessed by Spectral Domain Optical Coherence Tomography (SD-OCT)e 7
5. Subjects must be under active anti-VEGF treatment for wet AMD and received a minimum of 2 injections within 4 months prior to screening
6. BCVA ETDRS Snellen equivalent between ≤20/32 and ≥20/320

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Previous inclusion criteria:

1. Ability and willingness to provide informed consent to participate in the study requirements and visits prior to any study procedure
2. Male or female participants, aged 50 years old and over
3. Have CST of at least 275 µm in the study eye at the Screening Visit (Baseline) as assessed by SD-OCT, confirmed by the CRC, and agreed upon by the Investigator
4. The study eye at the Screening Visit (Baseline) must have current evidence of active primary or recurrent subfoveal CNV or CNV with subfoveal involvement with fluid as assessed by SD-OCT, confirmed by the CRC, and agreed upon by the Investigator
5. Received a minimum of 2 anti-VEGF injections in the 4 months prior to the Screening Visit (Baseline), will have received anti-VEGF injections for no more than 3 calendar years (36 months) prior to the Screening Visit, and no anti-VEGF injection in the 28 days prior to receiving

aflibercept at Baseline
6. Vision of the study eye at Baseline: BCVA in the range of 25 – 78 ETDRS letters, inclusive (approximate Snellen equivalent visual acuity range of 20/32 – 20/320)
7. Vision of the non-study eye at Baseline: BCVA ≥ 50 ETDRS letters (approximate Snellen equivalent of 20/100 or better)
8. Demonstrate a meaningful anatomic response 7 to 14 days after IVT aflibercept injection administered at the Screening Visit (Baseline) as confirmed by the CRC and agreed upon by the Investigator and defined as:
8.1. Reduction from the Screening Visit (Baseline) in CST by ≥ 20% as assessed using SD-OCT, or
8.2. Reduction of 30% in thickest paracentral subfield within ETDRS 3 mm grid, or
8.3. No anatomical evidence of SRF or IRF if fluid is present at Baseline by clinical examination or SD-OCT

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Key exclusion criteria
Current exclusion criteria as of 27/10/2022:

1. Any condition that could affect the interpretation of results or render the participant at high risk of treatment complications in the opinion of the Investigator
2. Ocular or periocular infection or intraocular inflammation in either eye within 1 month prior to or at the Randomization Visit (Day -7)
3. Uncontrolled diabetes or HbA1c ≥ 7.0 %
4. History or evidence of significant uncontrolled concomitant disease within 6 months of the Screening visit
5. History within the 12 months prior to Screening or evidence of renal or hepatic dysfunction at Screening
6. Any history of ongoing bleeding disorders or INR >3.0
7. History or evidence of macular or retinal disease other than nAMD
8. Active or history of retinal detachment or retinal pigment epithelium rip/tear
9. Uncontrolled ocular hypertension or glaucoma
10. Prior treatment with photodynamic therapy or retinal laser for the treatment of nAMD
11. Any history of vitrectomy or any other vitreoretinal surgery within 3 months prior to the Randomization Visit (Day -7)
12. Prior treatment with gene therapy

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Previous exclusion criteria:

1. Serum anti-AAV.7m8 neutralizing antibody titer levels of 1:125 or higher determined from blood drawn during the Screening Period (Day -21 to Day -14)
2. History of other disease, metabolic dysfunction, physical examination finding, or clinical laboratory findings giving reasonable suspicion of a condition that contraindicates the use of ADVM-022, contraindicates the use of systemic prednisone or prednisolone for 10 weeks, compromises the participant's ability to comply with the planned study activities, or that might affect the interpretation of the results of the study or render the participant at high risk for treatment complications in the opinion of the Investigator
3. Ocular or periocular infection (e.g., conjunctivitis, chalazion, significant blepharitis) or intraocular inflammation (grade trace or above by standardization of uveitis nomenclature (SUN) criteria) in either eye within 1 month prior to or at the Randomization Visit (Day -7) (mild anticipated post-operative inflammation subsequent to the aflibercept injection administered at the Screening Visit that resolved is acceptable)
4. Received any prior gene therapy at any time or any investigational treatment or medical device within 3 months of the Screening Visit or 5 half-lives of the investigational medicinal product (IMP) (whichever is longer) (observational studies involving over the counter (OTC) vitamins, supplements, or diets are not exclusionary)
5. Evidence of poorly controlled diabetes or HbA1c ≥ 7.0 % within the Screening period
6. History or evidence of significant uncontrolled concomitant disease within 6 months of the Screening Visit such as cardiovascular disease, hypertension (defined as blood pressure systolic over 180 mmHg or diastolic over 100 mmHg), or nervous system, pulmonary, renal, hepatic, endocrine, or gastrointestinal disorders
7. History of allergy to aflibercept, corticosteroid, or fluorescein dye or sodium fluorescein used in angiography (mild allergy amenable to treatment is allowable)
8. Any history of ongoing bleeding disorders or INR >3.0 (the use of aspirin or other anticoagulants [e.g., Factor Xa inhibitors] is not an exclusion)
9. Use of systemic steroids or immunosuppressive treatments, or any systemic anti-VEGF therapy within 3 months prior to the Randomization Visit (Day -7)
10. Any febrile illness within 1 week prior to the Randomization Visit (Day -7)
11. History of malignancy within the last 5 years except for the following adequately treated:
11.1 Local basal cell carcinoma of the skin
11.1 Carcinoma in situ of the cervix or breast
11.3 Papillary, noninvasive bladder cancer
11.4 Prostate cancer Stage 1 and 2 for which observation is clinically indicated with stable prostate-specific antigen for 6 months
11.5 Any other cancer that has been in complete remission for at least 2 years or considered surgically cured
12. History within the 12 months prior to the Screening Visit or evidence of renal dysfunction (i.e., creatinine clearance ≤ 50 mL/min) or hepatic dysfunction (i.e., AST or ALT ≥ 2.5X ULN) at Screening
13. Positive for human immunodeficiency virus (HIV) infection or hepatitis B or C at Screening (unless having received a documented cure for hepatitis C) or history or documented evidence of the following systemic or ocular bacterial or viral infections: SARS-CoV-2 2019 (COVID-19) , syphilis, or known to be positive (in either eye) for ocular herpes simplex virus (HSV), varicella-zoster virus (VZV), cytomegalovirus (CMV) infection including viral uveitis, retinitis or keratitis
14. Women who are currently pregnant or lactating (or intend to become pregnant or breastfeed during the study) and women of childbearing potential (defined as all women physiologically capable of becoming pregnant), unless they are using an appropriate form of contraception during investigational medicinal product administration and for at least 12 weeks after administration. Appropriate forms of contraception include:
14.1. Complete abstinence (periodic abstinence and withdrawal are not acceptable methods of contraception)

14.2. Bilateral tubal ligation, surgical male sterilization of the participant's sole partner
14.3. Oral, implantable or injectable hormonal contraceptives that inhibit ovulation, including hormone-releasing intrauterine devices (IUD) and copper IUD and other forms of hormonal contraception with a failure rate of < 1 % (contraception methods that do not result in a failure rate of < 1 % per year such as use of a male or female condom with or without spermicide, cervical cap, diaphragm or contraceptive sponge with spermicide are not acceptable)
14.4. Note that sexually active male participants will agree to use an acceptable contraceptive method during investigational medicinal product administration and for at least 12 weeks after administration to ensure that pregnancy is avoided in their female partners that are of childbearing potential
See protocol for Ocular Exclusion Criteria (Study Eye)

Date of first enrolment
23/08/2022

Date of final enrolment
13/03/2023

Locations

Countries of recruitment
United Kingdom

France

United States of America

Study participating centre
Oxford Eye Hospital
John Radcliffe Hospital
Headley Way
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Study participating centre
Moorfields Eye Hospital
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Sponsor information

Organisation
Adverum Biotechnologies Inc

Funder(s)

Funder type
Industry

Funder Name
Adverum Biotechnologies Inc

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Data sharing statement to be made available at a later date