ForPatients
by Roche

Neovascular Age-related Macular DegenerationWet Age-Related Macular Degeneration

A clinical trial to evaluate maintenance of vision after switching to treatment with an eye implant containing ranibizumab in participants with neovascular age-related macular degeneration

A Study Assessing Corneal Endothelial Cells in Participants With Neovascular Age-related Macular Degeneration (nAMD) Treated With the Port Delivery System With Ranibizumab (PDS)

Trial Status	Trial Runs In	Trial Identifier
Recruiting	1 Country	NCT04853251 ML43000

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Phase IV, Multicenter, Open-label Study to Assess Corneal Endothelial Cells in Patients With Neovascular Age-related Macular Degeneration Treated With the Port Delivery System With Ranibizumab (PDS)

Trial Summary:

This study will assess corneal endothelial cells in participants with nAMD treated with PDS refilled every 24 weeks (Q24W).

Genentech, Inc. Sponsor	**Phase 4** Phase

NCT04853251 ML43000
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#50 Years	No

1. Why is the Belvedere clinical trial needed?

Age-related macular degeneration (AMD) is a condition that causes blurred or reduced central vision in one or both eyes. There are two forms of AMD depending on how the back of the eye (known as the macula) is damaged, ‘dry AMD’ and ‘neovascular

AMD' (also called wet AMD). In wet AMD, a chemical produced by the body called vascular endothelial growth factor (VEGF) causes abnormal blood vessels to be formed in the eye that can leak fluid onto the back of the eye and affect vision.

Wet AMD can be treated by injecting a type of drug called anti-VEGF (e.g. ranibizumab), into the eye (also known as an intravitreal injection). However, many people find anti-VEGF intravitreal injections burdensome, as they are given as often as every 1#2 months. To reduce this burden, a refillable eye implant was designed that continuously releases ranibizumab over time, with refills of ranibizumab approximately every 6 months. This is called the port delivery system with ranibizumab. After testing in previous trials, the port delivery system with ranibizumab is now approved for the treatment of wet AMD.

In this trial, researchers will assess how well vision is maintained in people who switch from a previous anti-VEGF treatment (other than ranibizumab) to the eye implant that contains ranibizumab.

2. How does the Belvedere clinical trial work?

This clinical trial is recruiting people who have a health condition called wet AMD. People can take part if they have previously received treatment with at least three anti-VEGF intravitreal injections other than ranibizumab, within 9 months prior to Day 1 of the clinical trial.

One eye will be chosen as the 'study eye', and all participants in this trial will receive the eye implant pre-filled with ranibizumab, in the study eye using a surgical procedure. The eye implant will be refilled with ranibizumab during clinic visits on Weeks 24 and 48. Participants will have approximately 11 in-person clinic visits, and these may last 2#4 hours. These visits are to see how the participant is responding to the treatment and any side effects they may be having. Participants will also have approximately five clinical trial assessments by telephone or video call. Participants' total time in the clinical trial will be roughly 1 year. Participants are free to stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the Belvedere clinical trial?

The main clinical trial endpoint (the main results that are measured in the trial) is to evaluate the maintenance of vision after treatment in the study eye at Week 40, which is measured using an eye chart at a starting distance of 4 metres.

The other clinical trial endpoints include an assessment of the maintenance of vision in the study eye at Week 40 according to previous intravitreal treatments received, measurement of visual maintenance up to Week 52, and the number and seriousness of any side effects experienced by the participant during the trial.

4. Who can take part in this clinical trial?

People can take part in this trial if they are at least 50 years old, have been diagnosed with wet AMD within the past 6#18 months, and have previously been treated with at least three anti-VEGF intravitreal injections other than ranibizumab.

People may not be able to take part in this trial if they have had previous eye surgery (except for cataract surgery if done more than 6 months ago), or received certain treatments, have a history of certain other medical conditions, are pregnant or are planning to soon become pregnant, or are breastfeeding.

5. What treatment will participants be given in this clinical trial?

This is an open-label trial, which means everyone involved, including the participants and the doctors, know which clinical trial treatment is being used. Everyone who joins this clinical trial will receive the eye implant (pre-filled with the clinical trial drug, ranibizumab) in the study eye. This procedure takes around 30 minutes. The eye implant will then be refilled with ranibizumab at Week 24 and Week 48, during a procedure in the clinical trial doctor’s clinic that takes typically less than 15 minutes.

If the treatment is not having the desired effect, participants may receive an extra intravitreal injection of ranibizumab at the clinical trial specified visits (Week 16 and Week 40 or possibly at Week 20 and Week 44).

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the clinical trial treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant, although it may not be greater than the risks related to routine medical care or the natural progression of the health condition. Potential participants will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests, or assessments they will be asked to undergo. These will all be described in an informed consent document (a document that provides people with the information they need to make a decision to volunteer for a clinical trial). A potential participant should also discuss these with members of the research team and with their usual healthcare provider. Anyone interested in taking part in a clinical trial should know as much as possible about the trial and feel comfortable asking the research team any questions about the trial.

Risks associated with the clinical trial drug (1) and device (2)

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drug or device used in this clinical trial. Side effects can be mild to severe and even life-threatening, and can vary from person to person.

Ranibizumab given via an eye implant

- Participants will be told about the known side effects of the clinical trial drug, ranibizumab, when given with an eye implant device.
- Potential participants will be told about the known side effects of the procedures involved in inserting, filling, refilling and removing (if needed) the eye implant device, and where relevant, also potential side effects based on human and laboratory studies or knowledge of similar devices.

Potential benefits associated with the Belvedere clinical trial

Participants' health may or may not continue to improve from participation in the clinical trial, but the information that is collected may help other people who have a similar medical condition in the future.

For more information about this clinical trial see the **For Expert** tab on the specific ForPatients page or follow this link to ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT04853251

Inclusion Criteria:

Ocular Inclusion Criteria:

- Diagnosis of nAMD prior to screening as determined by the investigator
- Difference of <10% in ECD at screening between the 2 eyes as measured by specular microscopy and determined by the independent reading center
- Availability of historical visual acuity (VA) data and spectral-domain optical coherence tomography (SD-OCT). Additionally, fluorescein angiography or color fundus photography can both be used to support participant eligibility per protocol at investigator discretion
- Availability of comprehensive historical anti-vascular endothelial growth factor (VEGF) injection data, including agent administered and date of administration from the time of diagnosis, or for at least 2 years prior to screening if diagnosis was made more than 2 years before screening
- Response to at least two prior anti-VEGF IVT injections as determined by the investigator based on the following:
- Overall decrease in nAMD disease activity detected on historical or screening OCT
- Stable or improved best-corrected visual acuity (BCVA)
- BCVA of 34 letters (approximate 20/200 Snellen equivalent) or better, using Early Treatment of Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters at screening and enrollment
- All subtypes of nAMD lesions are permissible
- nAMD lesions at the time of diagnosis must involve the macula
- Sufficiently clear ocular media and adequate pupillary dilation to allow for clinical examination and analysis and grading by the central reading center of SD-OCT images

Exclusion Criteria:

Prior Ocular Treatment

Study Eye:

- Prior treatment with external-beam radiation therapy or transpupillary thermotherapy
- Previous treatment with verteporfin injection (PDT) or corticosteroid IVT injection within 2 years of screening
- Previous laser (except PDT as stated above) used for age related macular degeneration (AMD) treatment
- History of corneal transplant
- History of conjunctival surgery in the superotemporal quadrant
- History of intraocular inflammation following anti-VEGF injection

Either Eye:

- Previous PDS implantation
- Previous intraocular surgery (including cataract surgery) within 6 months of study enrollment
- Prior vitrectomy surgery, submacular surgery, or other surgical intervention for age-related macular degeneration (AMD)
- Prior pars plana vitrectomy surgery
- Previous intraocular device implantation, excluding intraocular lenses
- History of glaucoma-filtering surgery, tube shunts, or microinvasive glaucoma surgery
- Prior participation in a clinical trial involving any intravitreal agents that are not approved at time of screening
- Intraocular laser therapy, including selective laser trabeculoplasty, yttrium-aluminum garnet (YAG), prophylactic peripheral iridotomy within 1 year of screening, or YAG capsulotomy within 3 months of screening
- Contact lens wear in either eye within 2 months of screening
- Any prior penetrating ocular trauma
- Any prior ocular blunt trauma affecting corneal or retinal health in the opinion of the investigator, or any ocular blunt trauma within 6 months of screening
- History of corneal transplantation, including partial-thickness corneal grafts
- Prior treatment with brolucizumab
- Prior treatment with external-beam radiation therapy or brachytherapy
- History of hypersensitivity to ranibizumab or any excipients of Susvimo

Macular Neovascularization Lesion (MNV) Characteristics

Study Eye:

- Subretinal hemorrhage that involves the center of the fovea, if the hemorrhage is greater than 0.5-disc area [1.27 square millimeters (mm^2)] in size
- Subfoveal fibrosis or subfoveal atrophy

Either Eye:

- MNV due to other causes, such as ocular histoplasmosis, trauma, or pathologic myopia
- MNV masquerading lesions (e.g., cone dystrophy, adult vitelliform dystrophy, pattern dystrophy)

Current or Historical Ocular Conditions

Study Eye:

- Retinal pigment epithelial tear
- Retinal tears or peripheral retinal breaks on depressed fundus exam that are untreated, or treated within the 3 months prior to study enrollment
- Current vitreous hemorrhage
- Current or history of retinal detachment
- Previous violation of the posterior capsule is also an exclusion criterion unless it occurred as a result of YAG laser posterior capsulotomy in association with prior, posterior chamber intraocular lens implantation
- Spherical equivalent of the refractive error demonstrating more than 8 diopters of myopia or evidence of pathologic myopia on depressed fundus examination
- Preoperative refractive error that exceeds 8 diopters of myopia, for participants who have undergone prior refractive or cataract surgery
- Spherical equivalent of the refractive error demonstrating more than 5 diopters of hyperopia
- Preoperative refractive error that exceeds 5 diopters of hyperopia, for participants who have undergone prior refractive or cataract surgery
- Uncontrolled ocular hypertension or glaucoma and any such condition the investigator determines may require a glaucoma-filtering surgery during a patient's participation in the study
- Scleral pathology in the superotemporal quadrant (e.g., scleral thinning or calcification)
- Conjunctival pathologies in the superotemporal quadrant
- History or presence of severe posterior blepharitis, recurrent chalazia or hordeolum, severe dry eye syndrome, or severe allergic conjunctivitis
- Ectropion, entropion or other impairment of the upper or lower eyelid impacting lid functionality needed to protect the ocular surface from exposure
- Trichiasis
- Corneal neuropathy
- Lagophthalmos or incomplete blink
- Active or history of facial nerve palsy/paresis

Fellow (Non-Study) Eye:

• Concurrent or history of PDS implantation

Either Eye:

- Aphakia or absence of the posterior capsule
- Any concurrent intraocular condition that would either require surgical intervention during the study to prevent or treat visual loss that might result from that condition or affect interpretation of study results
- Corneal ECD #1500 cells/mm2 in either eye at screening as determined by the independent reading center
- Fuchs endothelial corneal dystrophy Grade # 2
- Previous corneal endothelial cell damage, including from blunt or surgical trauma
- Any ocular condition that precludes obtaining an analyzable specular microscopy image
- Active or history of corneal edema
- Active or history of corneal dystrophies
- Active or history of iridocorneal endothelial syndrome
- Active or history of pseudoexfoliation syndrome
- Active or history of herpetic keratitis or kerato-uveitis
- Any active or history of uveitis
- Active intraocular inflammation
- Active or history of keratitis, scleritis, or endophthalmitis
- Active ocular or periocular infection
- Active or history of Sjogren's syndrome or keratoconjunctivitis sicca

- Active or history of floppy eyelid syndrome
- Active or history of chronic eye rubbing
- Active thyroid eye disease

Concurrent Systemic Conditions:

- History of uncontrolled blood pressure
- Active or history of autoimmune diseases such as rheumatoid arthritis, lupus, granulomatosis with polyangiitis (Wegener's)
- History of stroke within the last 3 months prior to screening
- Uncontrolled atrial fibrillation within 3 months of screening
- History of myocardial infarction within the last 3 months prior to screening
- History of other disease, metabolic dysfunction, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of ranibizumab or placement of the implant and that might affect interpretation of the results of the study or renders the patient at high risk of treatment complications, in the opinion of the investigator
- Current active systemic infection
- Use of any systemic anti-VEGF agents
- Chronic use of oral corticosteroids
- Active cancer within 12 months of enrollment except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, and prostate cancer with a Gleason score of # 6 and a stable prostate-specific antigen for > 12 months
- Previous participation in any non-ocular (systemic) disease studies of investigational drugs within 1 month prior to screening (excluding vitamins and minerals)
- Use of antimitotic or antimetabolite therapy within 30 days or 5 elimination half-lives of the screening visit
- Requirement for continuous use of any medications or treatments indicated as prohibited therapy
- Pregnant or breastfeeding, or intention to become pregnant during the study
- Women of childbearing potential must have a negative urine pregnancy test result within 28 days prior to initiation of study treatment. If the urine pregnancy test is positive, it must be confirmed by a serum pregnancy test