ForPatients
by Roche

Age-Related Macular DegenerationNeovascular Age-related Macular Degeneration

A clinical trial in people with wet age-related macular degeneration (wet AMD) which compares (a) ranibizumab delivered by a permanent eye implant with (b) aflibercept delivered by injections into the eye

A Study Of The Effectiveness And Safety Of A 36-Week Refill Regimen For The Port Delivery System With Ranibizumab Vs Aflibercept Treat & Extend In Subjects With Neovascular Age-Related Macular Degeneration

Trial Status	Trial Runs In	Trial Identifier
Withdrawn	7 Countries	NCT05126966 2021-003226-71 MR42410

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 IIIb, Multicenter, Randomized, Visual Assessor-Masked Study Of The Effectiveness And Safety Of A 36-Week Refill Regimen For The Port Delivery System With Ranibizumab Vs Aflibercept Treat & Extend In Subjects With Neovascular Age-Related Macular Degeneration

Trial Summary:

This study will evaluate the effectiveness and safety of a 36-week refill regimen for the Port Delivery System with ranibizumab 100 mg/mL (PDS Q36W) compared with intravitreal injections of aflibercept (2 mg) administered per treat-and-extend (aflibercept T&E) in subjects with neovascular (wet) age-related macular degeneration (nAMD).

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT05126966 2021-003226-71 MR42410
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#50 Years	No

How does the DIAGRID clinical trial work?

This clinical trial is recruiting people who have a disease called wet age-related macular degeneration (wet AMD).

Wet AMD is currently treated with anti-vascular endothelial growth factor (anti-VEGF) therapies such as ranibizumab or aflibercept. Anti-VEGF therapy consists of ongoing injections into the affected eye. For example, aflibercept is typically injected once every two months – this can be a burden for patients.

Currently, many doctors use an approach called “treat-and-extend” to give anti-VEGF injections less often while protecting vision at the same time. If the patient’s wet AMD is under control at an injection visit, then the doctor may increase (“extend”) the amount of time to the next injection. If the patient’s wet AMD has worsened, then the doctor may reduce the time to the next injection instead.

The Port Delivery System (PDS) is a new and alternative way to reduce the number of anti-VEGF injections needed. The PDS is a tiny implant that is permanently placed into your eye through the sclera, the white part of your eye. The PDS contains a supply of ranibizumab, which is slowly released into the eye. Every few months, the PDS is refilled with ranibizumab through an outside port. Different refill intervals are being studied.

The purpose of this clinical trial is to compare the effects, good or bad, of PDS with ranibizumab versus afilbercept injections given via treat-and-extend regimen. In this clincal trial, you will get either PDS with ranibizumab or afilbercept injections given via treat-and-extend regimen.

How do I take part in this clinical trial?

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor. If your doctor thinks that you might be able to take part in this clinical trial, he/she may refer you to the closest clinical trial doctor. They will give you all the information you need to make your decision about taking part in the clinical trial. You can also find the clinical trial locations on this page.

To be able to take part in this clinical trial, you must:

- be at least 50 years old
- have been diagnosed with wet AMD within the last 9 months
- have received at least three injections into the eye of a standard anti-VEGF treatment for your condition within the last 6 months
- have had your wet AMD improve since starting the anti-VEGF injections (in other words, your vision did not worsen and examination of your retina showed the wet AMD had been controlled since starting the injections)

You must not:

- have any allergy to either ranibizumab or aflibercept
- have certain conditions or previous surgeries to one or both of your eyes
- have certain serious health problems unrelated to your eyes (though other eye conditions, surgeries, or health problems are allowed)
- have taken certain medications

Your doctor will consider your medical history and medications list to see if you can participate in this clinical trial.

You will have further tests to make sure you will be able to take the treatments given in this clinical trial. Some of these tests or procedures may be part of your regular medical care. They may be done even if you do not take part in the clinical trial. If you have had some of the tests recently, they may not need to be done again.

Before starting the clinical trial, you will be told about any risks and benefits of taking part in the trial. You will also be told what other treatments are available so that you may decide if you still want to take part.

While taking part in this clinical trial, women (if they are not currently pregnant but can become pregnant) will need to either not have heterosexual intercourse or take contraceptive medication for safety reasons.

What treatment will I be given if I join this clinical trial?

Once your clinical trial doctor confirms you are eligible to take part in this trial, you may have one dose of ranibizumab injected into the eye (depending on your treatment history) before you are put into a treatment group. Everyone who joins this clinical trial will be put into one of two groups randomly (like flipping a coin) and have either:

- A PDS with ranibizumab device permanently implanted on Day 1 and then refilled at Week 36 and Week 72. There is a small chance that you will need one or two additional injections of ranibizumab into the eye before the refills planned at Week 36 and Week 72
- OR aflibercept given as an injection into the eye on Day 1, then again at Week 4. After Week 4, your doctor will use treat-and-extend to decide when your next aflibercept injection will be. The maximum time between injections will be 12 weeks and the minimum time between injections will be 4 weeks

You will receive these treatments until Week 80 (roughly one and a half years after starting the clinical trial). You will have an equal chance of being placed in either group.

How often will I be seen in follow-up appointments and for how long?

You will be given the clinical trial treatment PDS with ranibizumab OR aflibercept injections following the treat-and-extend regimen for around a year and a half. You are free to stop this treatment at any time. After starting treatment, you will still be seen regularly by the clinical trial doctor.

If you receive PDS with ranibizumab, you will be seen on Day 1, Day 2, Day 7, Week 4, then every 4 to 8 weeks until your first refill at Week 36. After your first refill, you will be seen every 4 to 12 weeks depending on what your clinical trial doctor feels is most suitable.

If you receive aflibercept injections you will be seen every 4 to 12 weeks depending on what your clinical trial doctor feels is most suitable, according to the treat-and-extend regimen.

Whichever treatment you receive, these clinic visits will include checks to see how you are responding to the treatment and any side effects that you may be having. These checks may include:

- Questionnaires on how well your eyes are working
- Eye tests and examinations
- Photographs of your eyes

You will also occasionally receive follow-up calls to check on how you are doing. If you experience any side effects or injury during the trial, your clinical trial doctor will explain your options and discuss a plan for further treatment with you.

What happens if I am unable to take part in this clinical trial?

If this clinical trial is not suitable for you, you will not be able to take part. Your doctor will suggest other clinical trials that you may be able to take part in or other treatments that you can be given. You will not lose access to any of your regular care.

For more information about this clinical trial see the **For Expert** tab on the specific ForPatient page or follow this link to ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT05126966

Trial-identifier: NCT05126966

Inclusion Criteria:

- Signed Informed Consent Form
- Age # 50 years, at time of signing Informed Consent Form
- Ability and willingness to undertake all scheduled visits and assessments
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures

Ocular Inclusion Criteria:

- Initial diagnosis of nAMD within 9 months prior to the screening visit
- Previous treatment with at least three anti-VEGF intravitreal injections for nAMD per standard of care within 6 months prior to the screening visit
- Demonstrated response to prior anti-VEGF intravitreal treatment since diagnosis
- Availability of historical visual acuity data obtained at or after nAMD diagnosis and prior to the first anti-VEGF treatment for nAMD
- Availability of historical SD-OCT image data obtained at or after nAMD diagnosis and prior to the first anti-VEGF treatment for nAMD
- BCVA of 34 letters or better (20/200 or better approximate Snellen equivalent), using ETDRS chart at a starting distance of 4 meters (see the BCVA manual for additional details) at screening and randomization visits
- With any subtype of nAMD lesions (i.e., type I, type II, type III, or mixed forms per OCT classification, including polypoidal choroidal vasculopathy and retinal angiomatous proliferation)
- Sufficiently clear ocular media and adequate pupillary dilation to allow for clinical examination and analysis and grading by the central reading center of fundus photography (FP), FA, fundus autofluorescence (FAF) image, and SD-OCT images

Exclusion Criteria:

Prior Ocular Treatment - Study Eye

- History of vitrectomy surgery, submacular surgery, or other surgical intervention for AMD
- Prior pars plana vitrectomy surgery
- Prior treatment with Visudyne® (verteporfin for injection), external-beam radiation therapy, or transpupillary thermotherapy
- Previous treatment with corticosteroid intravitreal injection
- Previous intraocular device implantation (not including intraocular lens implants)
- Previous intraocular surgery (including cataract surgery) within 3 months of randomization
- Previous laser (any type) used for AMD or diabetic retinopathy treatment
- History of vitreous hemorrhage
- History of rhegmatogenous retinal detachment
- Concurrent conjunctival, Tenon's capsule, and/or scleral condition in the supero temporal quadrant of the eye (e.g., scarring, thinning, mass) that may affect the implantation, subsequent tissue coverage, and refill-exchange procedure of the PDS implant
- History of glaucoma-filtering surgery, tube shunts, or microinvasive glaucoma surgery
- History of corneal transplant
- History of conjunctival surgery in the superotemporal quadrant (including pterygium surgery)

Prior Ocular Treatment Either Eye:

- History of a severe allergic reaction or anaphylactic reaction to a biologic agent or known hypersensitivity to any component of the ranibizumab or aflibercept injections, study-related procedure preparations (including fluorescein), dilating drops, or any of the anesthetic and antimicrobial preparations used by a subject during the study
- Any contraindication to aflibercept as per local label
- Prior participation in a clinical trial involving any anti-VEGF drugs within 6 months prior to the randomization visit
- Prior treatment with brolucizumab (at any time prior to the screening visit)
- Prior treatment with external-beam radiation therapy or brachytherapy

MNV (CNV) Lesion Characteristics Study Eye:

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

MNV (CNV) Lesion Characteristics Either Eye:

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

Concurrent Ocular Conditions Study Eye :

- Subfoveal and/or juxtafoveal retinal pigment epithelial tear
- Scleral pathology in the superotemporal quadrant (e.g., scleral thinning or calcification)
- Conjunctival pathologies (e.g., pterygium, scarring, thinning, fibrosis) in the superotemporal quadrant
- Any concurrent intraocular condition (e.g., cataract, glaucoma, diabetic retinopathy, epiretinal membrane, amblyopia, or strabismus) 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
- Active intraocular inflammation (grade trace or above)
- Rhegmatogenous retinal tears or peripheral retinal breaks on depressed fundus exam that are untreated, or treated within 3 months prior to the randomization visit
- Aphakia or absence of the posterior capsule Previous violation of the posterior capsule is also an exclusion criterion unless it occurred as a result of yttrium-aluminum garnet (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 exam
- Preoperative refractive error that exceeds 8 diopters of myopia, for subjects who have undergone prior refractive or cataract surgery in the study eye
- Spherical equivalent of the refractive error demonstrating more than 5 diopters of hyperopia
- Preoperative refractive error that exceeds 5 diopters of hyperopia, for subjects who have undergone prior refractive or cataract surgery
- Uncontrolled ocular hypertension or glaucoma (defined as intraocular pressure [IOP] > 25 mmHg or a cup to disc ratio > 0.8, despite treatment with anti-glaucoma medication) and any such condition the investigator determines may require a glaucoma-filtering surgery during a subject's participation in the study
- History or presence of severe posterior blepharitis, recurrent chalazia or hordeolum, severe dry eye syndrome, or severe allergic conjunctivitis
- Ectropion, entropion, ingrowing lashes, 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

Concurrent Ocular Conditions Non-Study (Fellow) Eye

- Non-functioning non-study eye, defined as either:
- BCVA of hand motion or worse 2. No physical presence of non-study eye (i.e., monocular) 3. Legally blind in the subject's relevant jurisdiction

Concurrent Ocular Conditions Either Eye

- Any active or history of uveitis (e.g., idiopathic, drug-associated, or autoimmune-associated uveitis)
- Active or history of keratitis, scleritis, endophthalmitis, or chronic blepharitis
- Suspected or active ocular or periocular infectious conjunctivitis or endophthalmitis
- Active or history of Sjogrens 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:

- Inability to comply with study schedule or procedures as described in the study protocol
- Uncontrolled blood pressure (defined as systolic blood pressure > 180 mmHg and/or diastolic blood pressure > 110 mmHg, while a subject is at rest) If a subject's initial measurement exceeds these values, a second reading should be taken # 30 minutes after the first reading If the subject's blood pressure must be controlled by antihypertensive medication, the subject may become eligible if medication is taken continuously for at least 30 days prior to Day 1
- Active or history of autoimmune diseases, for example, rheumatoid arthritis, lupus, granulomatosis with polyangiitis (Wegner's)
- History of stroke within the last 3 months prior to informed consent
- Atrial fibrillation diagnosed or worsened within the last 3 months prior to informed consent
- History of myocardial infarction within the last 3 months prior to informed consent
- History of other disease, metabolic dysfunction (including uncontrolled diabetes), or clinical laboratory finding (after reviewing the results of the screening laboratory results) giving reasonable suspicion of a disease or condition that contraindicates the use of ranibizumab, aflibercept, or placement of the implant and that might affect interpretation of the results of the study or renders the subject at high risk of treatment complications in the opinion of the investigator
- Confirmed active systemic infection
- Use of any systemic anti-VEGF agents
- Chronic use of oral corticosteroids (> 10 mg/day of prednisone or equivalent)
- Active cancer within 12 months of randomization 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 preceding the informed consent (excluding vitamins and minerals)
- Use of antimitotic or antimetabolite therapy within 30 days or 5 elimination half-lives of the randomization visit
- Requirement for continuous use of any medications or treatments prohibited in the study
- Pregnant or breastfeeding, or intending to become pregnant during the treatment period and for at least 3 months after the final intravitreal injection of ranibizumab or aflibercept, or 1 year after the last implant refill-exchange procedure