ForPatients
by Roche

Age-Related Macular DegenerationNeovascular Age-related Macular DegenerationWet Age-Related Macular Degeneration

A clinical trial to look at how safe an eye implant that releases ranibizumab is for people with wet age-related macular degeneration when refilled every 6 or 9 months – and to find out the long-term effects of the eye implant and ranibizumab

A multicenter, open-label extension study to evaluate the long-term safety and tolerability of the Port Delivery System with ranibizumab in patients with neovascular age-related macular degeneration

Trial Status	Trial Runs In	Trial Identifier
Recruiting	14 Countries	NCT03683251 2020-004427-16 2023-507131-38-00 GR40549

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 multicenter, open-label extension study to evaluate the long-term safety and tolerability of the Port Delivery System with ranibizumab in patients with neovascular age-related macular degeneration

Trial Summary:

This study will evaluate the long-term safety and tolerability of the Port Delivery System with ranibizumab (PDS) (100 mg/mL) in participants with neovascular age-related macular degeneration (nAMD) who have either completed Phase II Study GX28228 (Ladder), Phase III Study GR40548 (Archway), Phase IIIb Study WR42221 (Velodrome), or completed Week 24 visit in Study WR42221 but were not eligible to be randomized in WR42221.
GR40549 Portal Re-Implantation Substudy Lay CTD 28Oct2024.pdf GR40549 Portal Iridex Substudy Lay CTD 28Oct2024.pdf

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT03683251 2020-004427-16 2023-507131-38-00 GR40549
Trial Identifiers

Eligibility Criteria:

ForPatients
by Roche

Gender	Age	Healthy Volunteers
All	# 50 Years	No

1. Why is the Portal clinical trial needed?

Age-related macular degeneration (AMD) causes blurred or reduced central vision in one or both eyes. There are two forms of AMD. They depend on how the back of the eye (known as the retina) is damaged. They are called ‘atrophic AMD’ (also known as ‘dry AMD’) and ‘neovascular AMD’ (also known as ‘wet AMD’). In wet AMD, too much of a protein called VEGF makes unhealthy blood vessels grow in the central area at the back of the eye. These vessels cause swelling and bleeding at the back of the eye. This can lead to vision loss. Wet AMD can be treated by giving an anti-VEGF drug (e.g. ranibizumab), through a needle inserted into the eye. This can be given as often as every 1 to 2 months. Many people find treatment through a needle into the eye a burden. The Port Delivery System (PDS) is an eye implant device. It can release ranibizumab into the eye continuously over time and be refilled at regular intervals. The PDS can remain in the eye long-term unless removed for health reasons. This clinical trial aims to look at the safety and long-term effects of the PDS with ranibizumab in people with wet AMD.

2. How does the Portal clinical trial work?

This clinical trial is recruiting people with wet AMD. People can take part if they have either:

- taken part in and completed the Ladder (GX28228) or Archway (GR40548) clinical trials, without stopping the clinical trial treatment early or leaving the trial early, OR
- taken part in the Velodrome (WR42221) clinical trial and completed either the whole trial or the first 24 weeks of the trial only

People who take part in the Portal clinical trial (participants) will be given the clinical trial treatment PDS ranibizumab refills for around 3 to 5 years. Participants who did not get the PDS eye implant before will receive the implant on Day 1 of the Portal trial. Participants may receive extra doses of ranibizumab through a needle inserted into the eye, 1 or 2 months before each PDS ranibizumab refill. But only if the PDS does not have the desired effect on the participants’ vision and if certain criteria are met. The clinical trial doctor will see participants every 2–3 months during the trial. These visits will include checks of the participants’ eye and general health, and any unwanted effects they may be having. Additional visits may be arranged 1 or 2 months before each PDS ranibizumab refill to check if extra doses of ranibizumab are needed. Participants will receive follow-up calls after being given clinical trial treatment to check on their health. Total time of participation in the clinical trial will be about 3 to 5 years. Participants can stop trial treatment and leave the clinical trial at any time.

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

The main clinical trial endpoint (the main result measured in the trial to see if the drug and PDS has worked) is the number, duration and seriousness of any unwanted effects. The other clinical trial endpoints include:

- The change in the best eyesight a person can have when wearing glasses or contact lenses – known as 'best corrected vision' – over time compared with the start of the trial
- The change in thickness of the retina over time
- The number of participants over time:
    - with very good or poor best-corrected vision
    - with improved or worsened best-corrected vision
    - who need extra ranibizumab treatment given through a needle inserted into the eye between PDS ranibizumab refills
    - who prefer receiving treatment with the PDS compared with a needle inserted into the eye
- How satisfied participants are with treatment

4. Who can take part in this clinical trial?

People can take part in this trial if they can attend all scheduled visits with the clinical trial doctor. People may not be able to take part in this trial if they left the Ladder, Archway or Velodrome clinical trials early or stopped treatment in these clinical trials. Nor can people who have a history of certain medical conditions or other eye diseases and need to take certain treatments during the trial. People who are pregnant or breastfeeding or are planning to become pregnant during or within 1 year after the clinical trial also cannot take part.

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

Everyone who joins this clinical trial will be placed into 1 of 7 groups depending on which trial they previously took part in and whether or not they have the PDS implant:

- Ladder trial participants who have the PDS implant will join **Group 1**
- Archway trial participants who have the PDS implant will join **Group 2**
- Ladder trial participants without the PDS implant will join **Group 3**
- Archway trial participants without the PDS implant will join **Group 4**
- Velodrome trial participants who:
    - only completed the first 24 weeks of the trial will join **Group 5**
    - completed the trial and received PDS ranibizumab refills every 6 months will join **Group 6**
    - completed the trial and received PDS ranibizumab refills every 9 months will join **Group 7**

Participants of this clinical trial will be given:

- **Groups 1 to 4**: PDS ranibizumab refills every 6 months for up to 5 years. Groups 3 and 4 will first have the PDS eye implant surgically inserted into one eye on Day 1 of the trial. A medicine that numbs the eye to prevent the sensation of pain will be used during this procedure (local anaesthetic)
- **Groups 5 and 6**: PDS ranibizumab refills every 6 months for up to 3 years
- **Group 7**: PDS ranibizumab refills every 9 months for up to 3 years

This is an open-label trial. This means everyone involved, including the participant and the clinical trial doctor, will know the clinical trial treatment the participant has been given.

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

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. People who would like to participate 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. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial).

Risks associated with the clinical trial drugs, devices or procedures

Participants may have unwanted effects (an unwanted effect of a drug or medical treatment) from the drug, PDS device, or procedures used in this clinical trial. Unwanted effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly.

Participants will be told about the known unwanted effects of ranibizumab and the PDS, and possible unwanted effects based on human and laboratory studies or knowledge of similar drugs and devices. Participants will be told about any known unwanted effects of having a needle inserted into the eye to give treatment and the surgical eye implant procedures and, where relevant, potential unwanted effects based on human and laboratory studies or knowledge of similar procedures.

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial. Still, the information collected may help other people with similar medical conditions in the future.

For more information about this clinical trial see the **For Expert** tab on this page or follow this link to ClinicalTrials.gov

Trial-identifier: NCT03683251

Inclusion Criteria:

- Previous enrollment in and completion of Study GX28228 (Ladder) or Study GR40548 (Archway), without early treatment or study discontinuation in either study OR Previous enrollment in Study WR42221 (Velodrome) and either not eligible to be randomized in Study WR42221 at Week 24 or completed the study (from the Q24W or Q36W arm)
- Ability and willingness to undertake all scheduled visits and assessments
- For women of childbearing potential: agreement to remain abstinent or use contraceptive measures
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures

Participants must meet the following ocular criteria for the study eye for substudy entry:

- Diagnosis of exudative nAMD within 2 years prior to the enrollment visit
- Previous treatment with at least two anti-VEGF ITV injections (e.g., ranibizumab, bevacizumab, or aflibercept) for nAMD per standard of care within 6 months prior to the enrollment visit
- Demonstrated response to prior anti-VEGF ITV treatment since diagnosis, as evidenced at enrollment by the following:

Overall decrease in nAMD disease activity detected on SD-OCT AND Stable or improved best-corrected visual acuity (BCVA)

- All subtypes of nAMD lesions are permissible (i.e., type I, type II, type III, or mixed forms per optical coherence tomography (OCT) classification) nAMD lesions at the time of diagnosis must involve the macula (6 mm diameter centered at the fovea).
- Sufficiently clear ocular media and adequate pupillary dilation to allow for analysis and grading by the central reading center of FP and SD-OCT images.
- Having experienced septum dislodgement in the original implant while in the main study or after exiting the main study Ocular Inclusion Criteria for Study Eye
- Sufficiently clear ocular media and adequate pupillary dilation to allow for analysis and grading by central reading center

Exclusion Criteria:

- Pregnant or breastfeeding, or intending to become pregnant during the treatment period and for at least 28 days after the last intravitreal injection of ranibizumab or 1 year after the last Implant refill-exchange of ranibizumab
- History of other ocular diseases that give reasonable suspicion of a disease or condition that contraindicates the use of ranibizumab, that might affect interpretation of the results of the study or that renders the participant at high risk for treatment complications
- History of other diseases, 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 that renders the participant at high risk of treatment complications
- Requirement for continuous use of any medications or treatments indicated in the "Prohibited Therapy"

Sub-study 1

Exclusion Criteria Prior Ocular Treatments Study Eye

- History of vitrectomy surgery, submacular surgery, or other surgical intervention for AMD
- Prior treatment with Visudyne, external-beam radiation therapy, or transpupillary thermotherapy
- Previous treatment with corticosteroid ITV injection
- Previous intraocular device implantation
- Previous laser (any type) used for AMD treatment

Either Eye

- Treatment with anti-VEGF agents other than ranibizumab within 1 month prior to the enrollment visit
- Prior participation in a clinical trial involving anti-VEGF drugs within 6 months prior to the enrollment visit, other than ranibizumab

CNV Lesion Charateristics Study Eye

- Subretinal hemorrhage that involves the center of the fovea, if the hemorrhage is greater than 0.5 disc area (1.27 mm2) in size at screening
- Subfoveal fibrosis or subfoveal atrophy

Either Eye

- CNV due to other causes, such as ocular histoplasmosis, trauma, or pathologic myopia

Concurrent Ocular Conditions Study Eye

- Retinal pigment epithelial tear
- Any concurrent intraocular condition (e.g., cataract, glaucoma, diabetic retinopathy, or epiretinal membrane) 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)
- History of vitreous hemorrhage
- History of rhegmatogenous retinal detachment
- History of rhegmatogenous retinal tears or peripheral retinal breaks within 3 months prior to the enrollment 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
- Preoperative refractive error that exceeds 8 diopters of myopia, for participants who have undergone prior refractive or cataract surgery in the study eye
- Intraocular surgery (including cataract surgery) within 3 months preceding the enrollment visit
- 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
- History of glaucoma-filtering surgery, tube shunts, or microinvasive glaucoma surgery
- History of corneal transplant
- History of prior vitrectomy surgery and absence of posterior capsule

Either Eye

- History of idiopathic or autoimmune-associated uveitis
- Active infectious conjunctivitis, keratitis, scleritis, or endophthalmitis

Concurrent Systemic Conditions

- Inability to comply with study schedule or procedures as described in the study protocol
- Uncontrolled blood pressure
- History of stroke within the last 3 months prior to informed consent
- Uncontrolled atrial fibrillation within 3 months of informed consent
- History of myocardial infarction within the last 3 months prior to informed consent
- 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 systemic treatment for a confirmed active systemic infection
- Use of any systemic anti-VEGF agents
- Chronic use of oral corticosteroids
- Active cancer within 12 months of enrollment
- 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 enrollment visit
- History of albinism
- Pregnant or breastfeeding, or intending to become pregnant during the treatment period and for at least 28 days after the last ITV injection of ranibizumab or 1 year after the last implant refill-exchange of ranibizumab

Sub-study 2

Exclusion Criteria (Cohort 1 only):

Concurrent Ocular Conditions-Study Eye

- Any ocular condition that may render the patient at high risk for surgical or treatment complications
- Intraocular surgery (including cataract surgery) within 1 month preceding the enrollment visit
- Any use of medicated intraocular implants (other than the PDS implant), at any time prior to enrollment
- History of rhegmatogenous retinal tears or peripheral retinal breaks within 3 months prior to the enrollment visit
- Any concurrent ocular condition that would require surgical intervention during the study to prevent or treat visual loss
- 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 refill-exchange procedure of the PDS implant
- Ongoing ocular complications that might affect participant safety

Concurrent Ocular Conditions-Either Eye

- Suspected or active ocular or periocular infection
- Any history of uveitis
- Active blepharitis

Concurrent Systemic Conditions

- Recent history (in the last 3 months prior to enrollment) of other disease, other non-diabetic metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a condition that contraindicates the use of ranibizumab or surgical placement of the PDS implant; that might affect interpretation of the results of the study; or that renders the participant at high risk for treatment complications

- Active cancer within the last 12 months, except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, or prostate cancer
- Current systemic treatment for a confirmed active systemic infection - Participation in an investigational trial that involves treatment with any drug or device (with the exception of vitamins and minerals or enrollment in the main study GR40549) within 6 months prior to enrollment.
- Use of antimitotic or antimetabolite therapy within 30 days or 5 elimination half-lives.