

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 Recruiting	Trial Runs In 14 Countries	Trial Identifier NCT03683251 2020-004427-16,2023-507131-38-00 GR40549
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The source of the below information is the publicly available website [ClinicalTrials.gov](https://clinicaltrials.gov). It has been summarised and edited into simpler language.

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.

Hoffmann-La Roche Sponsor	Phase 3 Phase
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Eligibility Criteria:

Gender All	Age >= 50 Years	Healthy Volunteers No
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1. Why is the Portal clinical trial needed?

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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:

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- 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

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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](https://clinicaltrials.gov)

Trial-identifier: [NCT03683251](https://clinicaltrials.gov/ct2/show/study/NCT03683251)