Summary of Clinical Trial Results

A study to compare the Port Delivery System with ranibizumab (with refills every 24 weeks (approximately 6 months)) versus monthly injections of ranibizumab in people living with age-related damage to the back of the eye: End of study report

See the end of this summary for the full title of the study.

About this summary

This is a summary of the results of a clinical trial (called a study in this document) – written for

- members of the public and
- people who took part in the study.

The study started in September 2018 and ended in June 2021. This summary was written after the study had ended and includes all key results of the study.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know about a study treatment. The results from this study may be different from other studies with the same medicine.

- This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.

Thank you to the people who took part in this study

The people who took part have helped researchers answer important questions about age-related damage to the back of the eye and about the study treatment.

Key information about this study

- This study compared different treatments for people who have damage to the layer at the back of the eye that senses light (retina) due to the growth of abnormal blood vessels. This causes swelling in the central part of the retina called the macula, which is responsible for clear vision. Over time, this can lead to a condition called age-related macular degeneration, or wet AMD for short. Another name for wet AMD is neovascular AMD.
- In this study, everyone received ranibizumab treatment in their eye. Ranibizumab is the existing medicine for wet AMD that reduces the swelling in the macula and improves vision.
- Some people received a special formulation of ranibizumab through an eye implant called the “Port Delivery System with ranibizumab” (PDS for short). The PDS is a surgically implanted device designed to deliver a continuous and consistent dose of ranibizumab to maintain vision. In this study, the PDS is refilled every 24 weeks (approximately 6 months). The PDS and the special formulation of ranibizumab are approved for the treatment of wet AMD in the United States.
- Other people received ranibizumab as monthly eye injections, which is approved for the treatment of wet AMD.
- It was randomly decided which treatment each person received.
- This study included 415 people in the United States.
- The main result is that people who had the PDS with refills every 24 weeks (approximately 6 months) maintained similar levels of vision as people who had monthly ranibizumab eye injections. These results are from the entire 96 weeks (approximately 2 years) of the study.
- Overall, eye-related side effects of the PDS were manageable in the clinical trial and overall did not lead to permanent vision loss. These eye-related side effects of the PDS were different from those seen in people receiving eye injections but were more similar to the side effects seen in people who have had other types of eye surgeries (eg, glaucoma drainage devices). Generally, side effects in the body – not including the eye –seen with PDS implant or

surgery were similar to those seen with monthly ranibizumab eye injections.

Contents of the summary

Glossary

Wet AMD (also called neovascular AMD) = age-related damage to the back of the eye (retina) caused by the growth of abnormal blood vessels.

Section 1. What were the results of the study?

Question 1: Did the PDS refilled every 6 months maintain vision at weeks 44 and 48 (11 and 12 months), 60 and 64 (15 and 16 months), and 88 and 92 (22 and 23 months) in people who previously received anti-VEGF medicine (see Section 2, Question 1: “Why was this study done?”) similarly to monthly ranibizumab injections?

In this study, everyone had previously received and had responded to an anti-VEGF medicine, such as ranibizumab, to treat their wet AMD. This means that their vision had already improved before receiving the PDS with the special formulation of ranibizumab or the monthly ranibizumab injections. The researchers wanted to know if the PDS could maintain improvements in people’s vision as well as monthly ranibizumab eye injections. They measured people’s vision by finding out how many letters people could read on a standardized eye chart, which has rows of letters that get smaller from top to bottom.

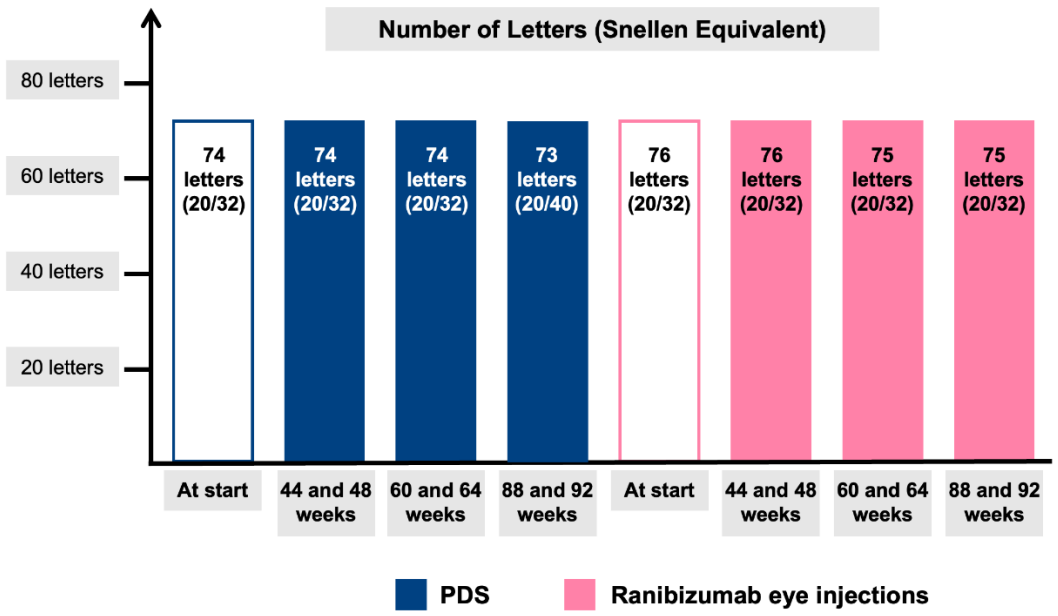
At the start of the study, people in the PDS group and the monthly ranibizumab injection group had 20/32 vision on average. This means that they could see at 20 feet what a person with perfect vision sees at 32 feet. In other words, they could read, on average, 75 letters on a standardized eye chart. After 44 and 48 weeks (approximately 11 and 12 months) of treatment with either PDS or monthly ranibizumab injection, people’s vision was measured again on a standardized eye chart. The average of their vision at weeks 44 and 48 was compared with their vision at the start of the study.

On average, at weeks 44 and 48 (11 and 12 months), the change in people’s vision from the start of the study was similar in the PDS refilled every 6 months and monthly ranibizumab injection groups. This was repeated 2 more times during the study: after 60 and 64 weeks (15 and 16 months) and after 88 and 92 weeks (22 and 23 months).

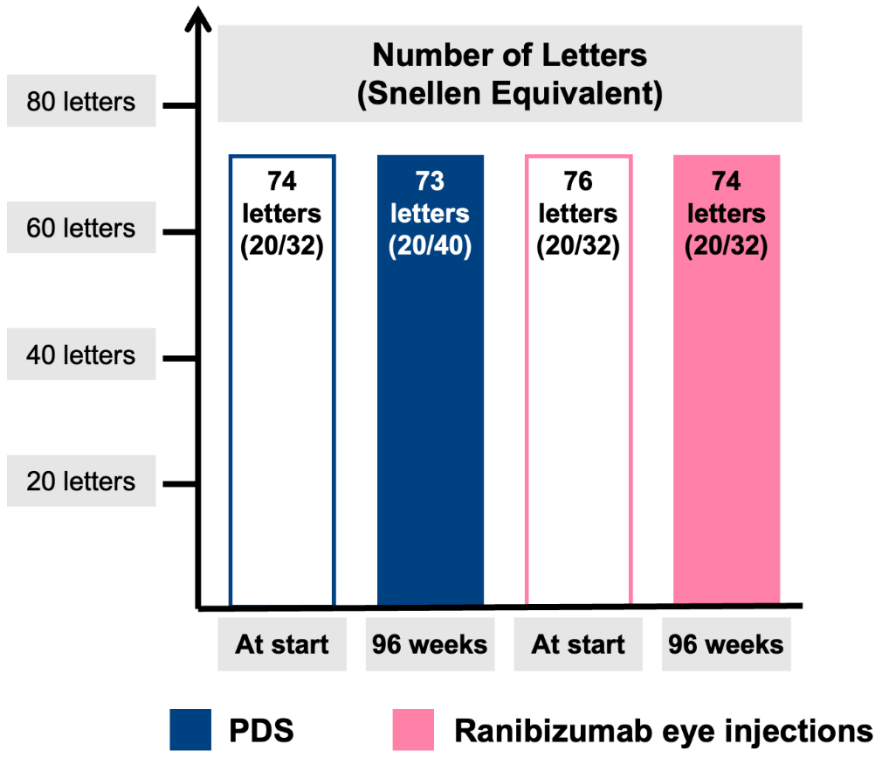
At weeks 60 and 64 (15 and 16 months), the change in vision from the start of the study was similar between the 2 groups. People’s vision was also similar at weeks 88 and 92 (22 and 24 months) on average.

The average vision at the start of the study was similar to the average vision to the end of the study at week 96 (approximately 2 years) in the PDS refilled every 6 months and monthly ranibizumab injection groups.

Average number of letters that people could read on an eye chart at the start of the study and at weeks 44 and 48, 60 and 64, and 88 and 92



Average number of letters that people could read on an eye chart at the start of the study and at week 96

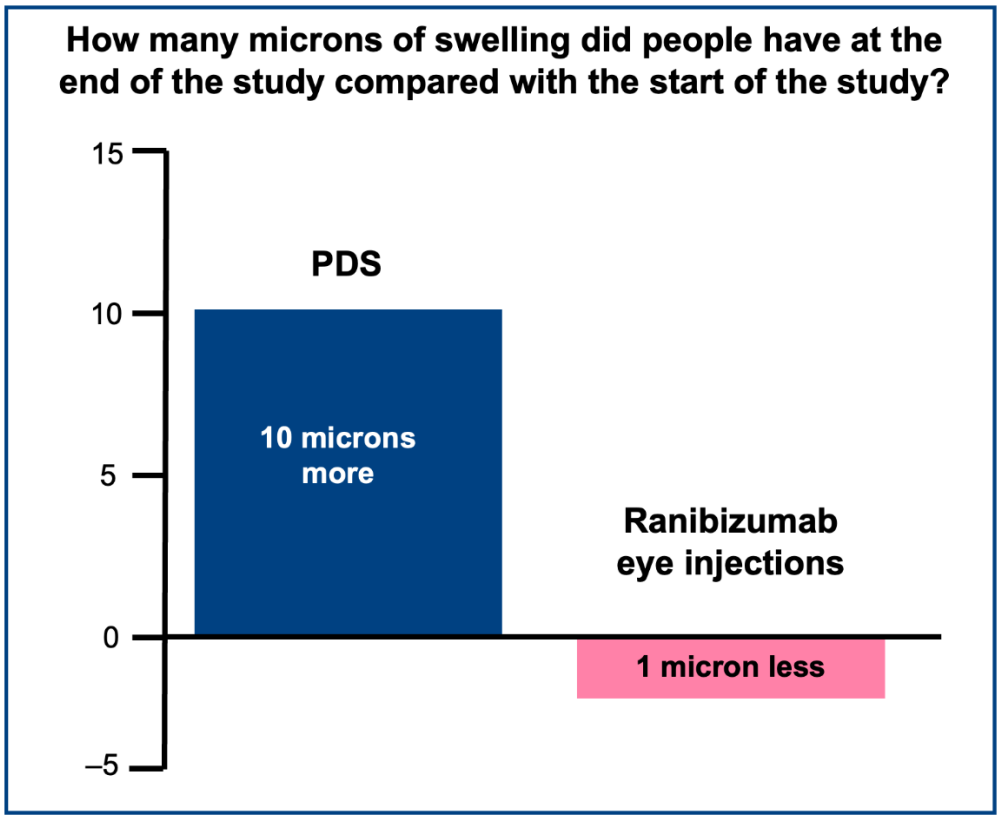


Question 2: Did the PDS refilled every 6 months control swelling in the layer at the back of the eye through 96 weeks (2 years) of treatment similarly to monthly ranibizumab injections?

To see if the PDS could control swelling in the layer at the back of the eye that senses light (retina), researchers measured swelling at every visit during the study. The figure in Section 2, Question 1 ("Why was this study done") shows a healthy eye compared with an eye with wet AMD that has swelling due to blood vessels leaking. The swelling that researchers measured is shown in the picture below.

Researchers measure swelling in microns, which is a unit used to measure very small things. For example, the average width of a human hair is 75 microns, and the thickness of a normal macula is about 250 microns.

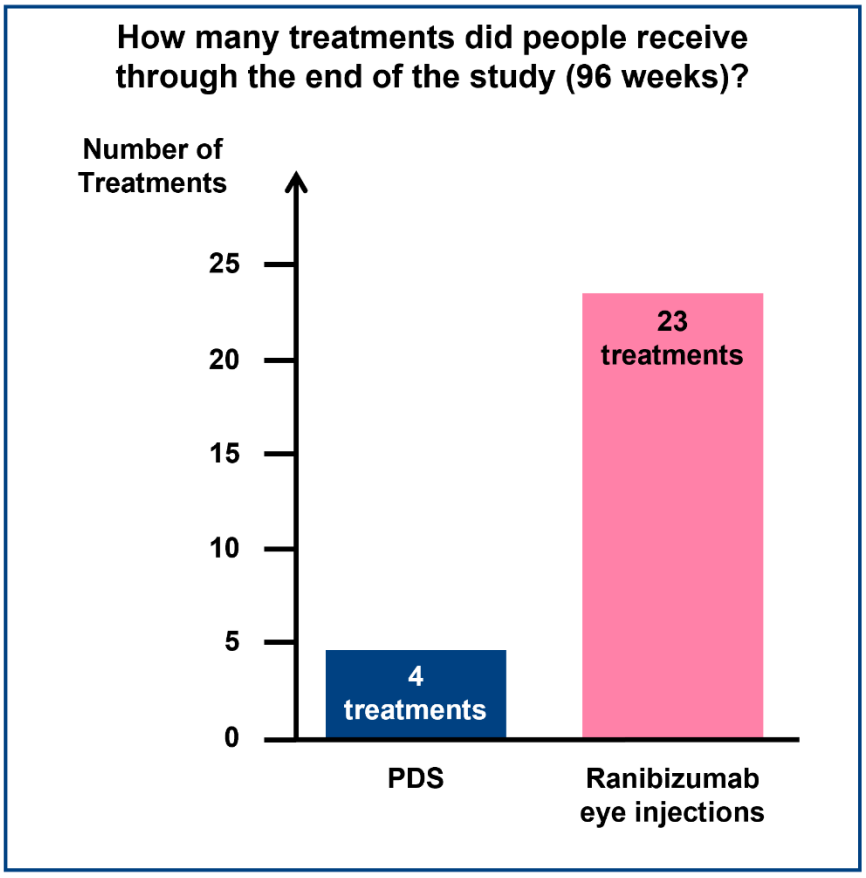
After 96 weeks (approximately 2 years) in both treatment groups, there was little change in the average amount of swelling in the retina during the study. People who received the PDS refilled every 6 months had an average of 10 microns more swelling in the retina. People who received monthly injections had 1 micron less swelling in the retina than at the start of the study.



Question 3: How many treatments did people receive in total over 96 weeks (approximately 2 years) of treatment?

People with the PDS received an average of 4 treatments for their wet AMD in their study eye. This included the first PDS fill with the special formulation of ranibizumab at time of surgery, PDS refills at weeks 24, 48, 72, and 96, and any additional ranibizumab eye injections. People who had monthly ranibizumab eye injections received about 23 treatments on average during this same time period in their study eye.

During the study, people with the PDS received refills every 24 weeks at weeks 24, 48, 72, and 96. Before each refill, people were examined by their doctors to determine if they needed an additional ranibizumab injection. An additional injection, on top of the medicine received via the PDS implant, was needed when the person had a decrease in vision or increase in the swelling of the back of the eye that met thresholds defined by the study. During the first interval from week 1 to week 24, less than 2%, or 2 in 100, of people in the PDS group had received additional ranibizumab injections in their study eye. Through each of the other intervals, approximately 5%, or 5 in 100, of people in the PDS group had received additional ranibizumab injections in their study eye.



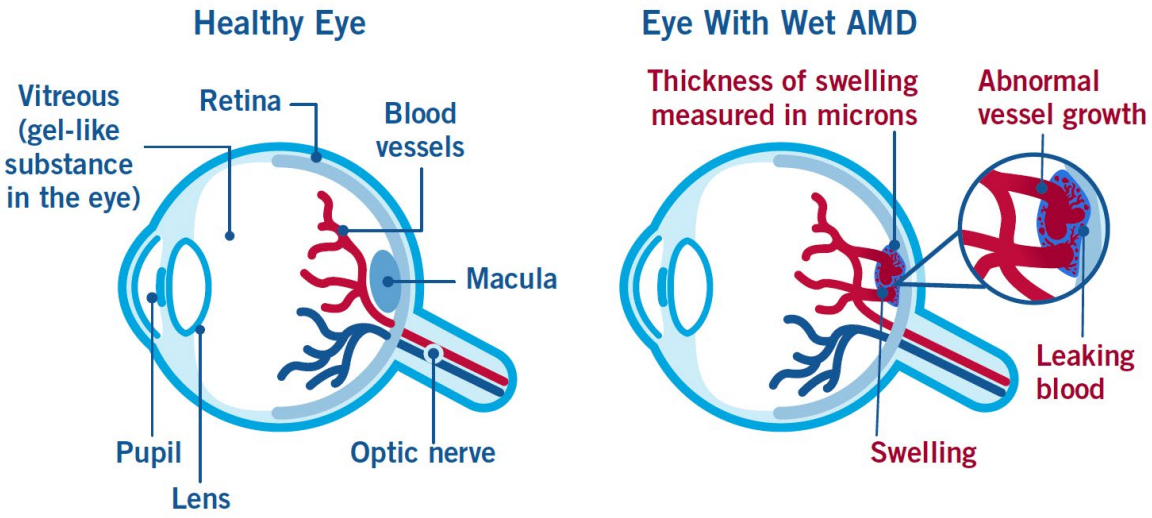
This section only shows the key results from the study. You can find information about the other results on the websites listed at the end of this summary (see Section 8, “Where can I find more information?”).

Section 2. General information about this study

Question 1: Why was this study done?

Some people develop a condition that damages part of the layer at the back of the eye that senses light (retina) as they age. This is called age-related macular degeneration (AMD for short). The macula is an area in the center of the retina that gives you clear vision. In AMD, damage to the macula affects the central part of the vision and may result in permanent blind spots.

One type of AMD is called “wet AMD” or “neovascular” AMD. Wet AMD develops when tiny abnormal blood vessels grow at the back of the eye. These vessels leak blood or fluid in the macula, leading to swelling and scarring.



Currently, people living with wet AMD can receive treatments that block a substance called vascular endothelial growth factor, or VEGF. This substance causes abnormal blood vessels to grow and leak fluid. These treatments are called anti-VEGF medicines and include ranibizumab, brolucizumab, and aflibercept.

People receive anti-VEGF medicines as eye injections. For the best vision and disease control, some people should receive a ranibizumab injection every month. New treatments may allow people to go longer between treatments. One such treatment is the Port Delivery System with ranibizumab (PDS for short). The PDS is surgically implanted into the eye that needs treatment for wet AMD.

Question 2: What were the study treatments?

Ranibizumab is an existing medicine for people living with wet AMD. People receive ranibizumab as often as a monthly eye injection.

- You say this as “rah-nih-bizz-yoo-mab”.
- Ranibizumab is an approved medicine for wet AMD.

The Port Delivery System with ranibizumab (PDS for short) is the treatment that was being studied here.

- The PDS is a permanent **eye implant** that is filled with a special formulation of ranibizumab and surgically placed in the eye by a doctor in a 30–40-minute-long procedure. The procedure is generally carried out on the patient under local anesthesia.
- The PDS implant allows for continuous and consistent release of the medicine over time and at the dose expected to control wet AMD.
- During the study, the PDS was refilled with a special formulation of ranibizumab every 24 weeks (about every 6 months).
- Additional ranibizumab eye injections were given to people in the PDS group when the doctor saw decreased vision or increased swelling at the back of the eye due to wet AMD activity.
- Soon after this study was over, the PDS was approved for the treatment of wet AMD in the United States.

Question 3: What did researchers want to find out?

- Researchers did this study to compare the PDS with monthly ranibizumab eye injections. They wanted to find out if the PDS refilled every 6 months worked as well as monthly ranibizumab injections (see Section 1, “What were the results of the study?”).
- They also wanted to find out how safe the PDS was by checking how many people had side effects with the PDS compared with monthly ranibizumab injections (see Section 5, “What were the side effects?”).

The main question that researchers wanted to answer was:

- Did the PDS refilled every 6 months maintain vision at weeks 44 and 48, 60 and 64, 88 and 92, and 96 in people who previously received anti-VEGF medicine similarly to monthly ranibizumab injections?

Other questions that researchers wanted to answer included:

- Did the PDS refilled every 6 months control swelling at the back of the eye through 96 weeks (approximately 2 years) of treatment similarly to monthly ranibizumab injections?
- How many treatments did people receive in total over the course of the study (96 weeks, approximately 2 years) of treatment?
- How many people with the PDS need additional ranibizumab treatments during the 96 weeks (approximately 2 years) of the study?
- Did the PDS refilled every 6 months have any side effects when compared with monthly ranibizumab injections?

Question 4: What kind of study was this?

This study was a Phase 3 study. This means that the PDS had been tested in a smaller number of people living with wet AMD before this study. In this study, a larger number of people living with wet AMD received either the PDS, refilled every 24 weeks or approximately 6 months, or monthly ranibizumab eye injections (the standard treatment for wet AMD). This was to find out if the PDS refilled every 6 months worked as well as monthly ranibizumab and about the safety of the PDS.

The study was randomized. This means that it was decided by chance, like tossing a coin, which treatment people in the study would receive.

Question 5: When and where did the study take place?

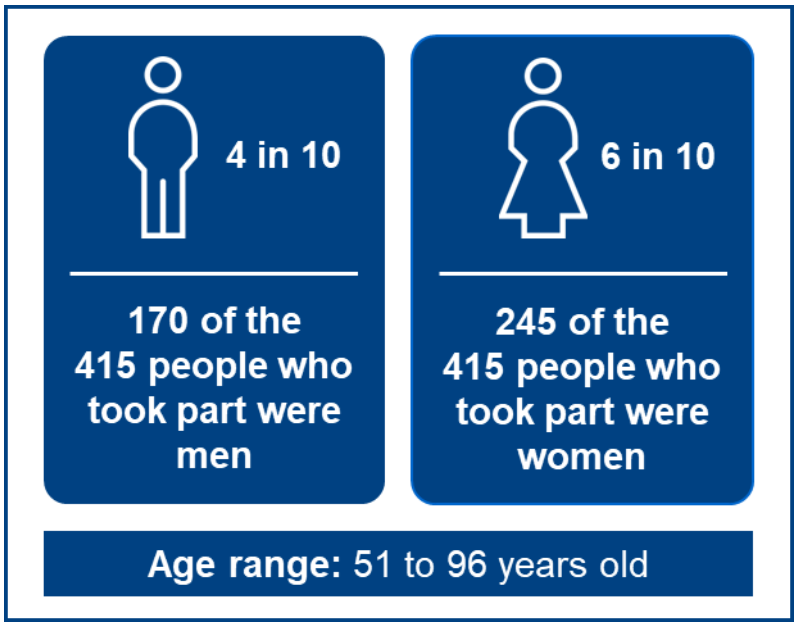
The study started in September 2018 and ended in June 2021. This summary was written after the study ended and includes the main results for the entire study.

The study took place at 78 study centers in the United States.

The study was minimally affected by coronavirus disease 2019 (COVID-19). No one in the PDS group missed a refill due to COVID-19 cases, and only 24% of people in the monthly injection group missed at least 1 injection due to COVID-19.

Section 3. Who took part in this study?

In total, 415 adults living with wet AMD took part in this study.



People could take part in the study if they were aged 50 years or older and if for the study eye they had:

- A new diagnosis of wet AMD within 9 months of selection in the study.
- Received at least 3 previous anti-VEGF treatments, including ranibizumab, bevacizumab, or aflibercept. The most recent anti-VEGF treatment had to be ranibizumab.
- Signs that their previous anti-VEGF treatment was working. This meant that since starting anti-VEGF treatment, people had:
    - Decreased swelling at the back of the eye and
    - Stable or improved vision.
- Good enough vision with correcting lenses to read at least 34 letters on a standard eye chart. This means their visual acuity was 20/200 or better, or they could see at 20 feet what someone with normal vision can see at 200 feet away.

A few reasons why people could **not** take part in the study were:

- If they had received an anti-VEGF medicine other than ranibizumab within a month before starting the study.
- If they had laser therapy to treat wet AMD.
- If they had surgery for wet AMD.
- If they had high blood pressure that was not well controlled.
- If they had a history of stroke, atrial fibrillation, or a heart attack within 3 months before starting the study.
- If they had cancer within 12 months before starting the study, except for appropriately treated cancers of the cervix, prostrate, and skin (non-melanoma).
- If they had been on corticosteroids for a long time.
- If they were pregnant or breastfeeding.

Section 4. What happened during the study?

During the study, people were split into 2 groups to receive the PDS refilled every 6 months or ranibizumab eye injections. The treatments were selected at random by a computer.

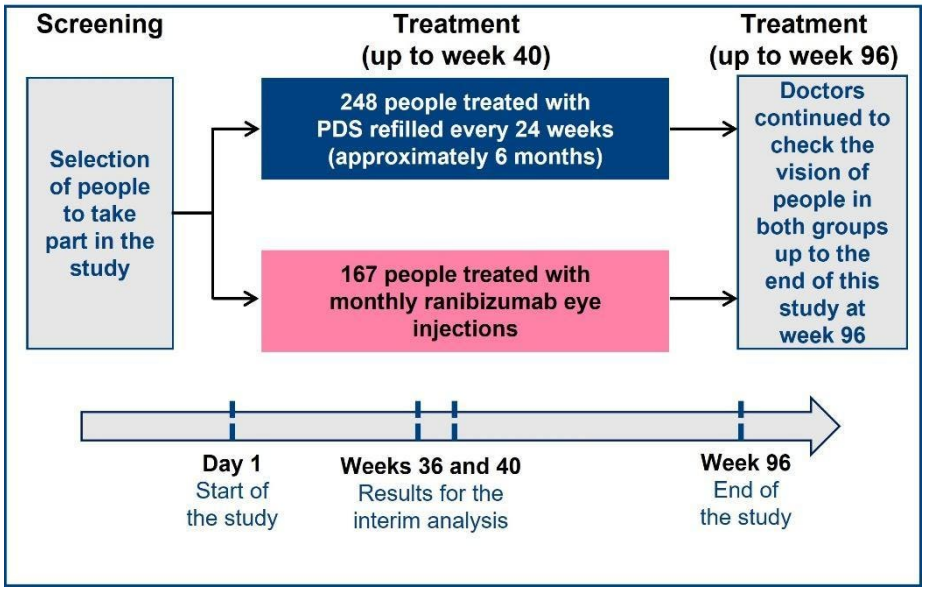
The treatment groups were:

- **PDS** (the study treatment): PDS filled once at the time of the surgery and refilled every 24 weeks (approximately 6 months) in the clinic with 2.0 milligrams of a special formulation of ranibizumab. There were 248 people in this group.
- **Ranibizumab eye injections** (the existing approved treatment): ranibizumab at the approved dose of 0.5 milligrams injected into the eye once a month. There were 167 people in this group.

People in the PDS group were seen by the doctor every month. If they had signs of their wet AMD getting worse like decreased vision or increased swelling at the back of the eye, before a refill was scheduled, they could have additional ranibizumab injections. Refills were done every 24 weeks (approximately 6 months).

People in the ranibizumab group were seen by the doctor and had injections in their eye once a month.

People in this study continued receiving treatment for 96 weeks (24 months). In this summary, we describe the main results, collected at 44 and 48, 60 and 64, 88 and 92, and 96 weeks after the start of the study. The figure below shows more information about what happened in the study.



Section 5. What were the side effects?

Side effects (also known as adverse events) are unwanted medical problems (for example, a headache) that happen during the study.

- They are described in this summary because 1 or more people (in either the PDS or the monthly ranibizumab eye injection group) had these side effects while on study treatments.
- Some of these side effects are caused by study procedures, the study medicine, or the implant itself or may be related to the disease activity.
- Not all of the people in this study had all of the side effects.
- The side effects observed in this study can occur in people who have had another type of eye surgery.

Eye-related side effects of the PDS were manageable in the clinical trial and, overall, did not lead to permanent vision loss. These eye-related side effects of the PDS were different from those seen in people receiving eye injections but were more similar to the side effects seen in people who have had other types of eye surgeries (eg, glaucoma drainage devices). Generally, side effects in the body—not including the eye—seen with the PDS implant or surgery were similar to those seen with monthly ranibizumab eye injections.

During the study, some people decided to stop their study treatment because of side effects.

- By week 96, 10 people in the PDS group stopped taking the study treatment because of side effects.
- One person in the monthly ranibizumab eye injection group left the study by week 96 due to side effects.
- Overall, over 90% of the people completed study eye treatment up to week 96.

Serious and common side effects are listed in the following sections.

Question 1: What were the serious side effects affecting the eyes?

A side effect is considered serious if it is life threatening, needs hospital care, is medically important, or causes lasting problems.

Serious side effects that affected eyes being treated for wet AMD and which may have been related to the PDS implant or surgery or monthly ranibizumab eye injections are shown in the following table.

Serious Side Effects Reported in This Study	**People Who Received the PDS** 248 People	**People Who Received Ranibizumab Eye Injections** 167 People
Defect in the outer layer that covers the white part of the eye (conjunctival erosion)	3 out of 248	None
Decreased sharpness of vision (visual acuity decreased)	3 out of 248	None
Bleeding in the back of the eye in the gel-like substance that fills the eyeball (vitreous hemorrhage)	2 out of 248	1 out of 167
Tear in the layer at the back of the eye that senses light (retina) (retinal tear)	1 out of 248	None
Separation of the layer at the back of the eye that senses light (retina) (retinal detachment)	2 out of 248	None
Cortical cataract	1 out of 248	None
Separation of the layer of blood vessels from its normal location underneath the white part of the eye (choroidal detachment)	1 out of 248	None
Conjunctival bleb	1 out of 248	None
Corneal disorder	1 out of 248	None
Permanent damage of the layer at the back of the eye that senses light (retina) due to severe inflammation from an infection (necrotizing retinitis)	1 out of 248	None
Retinal pigment epithelial tear	1 out of 248	None
Scleral thinning	1 out of 248	None
Decreased vision (visual impairment)	1 out of 248	None
Infection of the eyeball with inflammation of the inside of the eye (endophthalmitis)	4 out of 248	None
A gap in the outer layer that covers the white part of the eye near the incision edge (or stitches) (conjunctival retraction)	3 out of 248	None
Broken bones anywhere on the face (facial bones fracture)	0 out of 248	1 out of 167
Implant moves out of place (implant dislocation)	3 out of 248	Not applicable
Specific part of the implant (the septum) moves out of place (septum dislodgement)	3 out of 248	Not applicable

Question 2: What were the most common side effects?

The 5 most common side effects across both treatment groups in the study are shown in the following table. These side effects can occur in people who have had eye surgery. Although a higher number occurred in the people who received the PDS, the majority were not serious and were mild/moderate in severity and resolved with or without treatment.

Most Common Eye Side Effects Reported in This Study	**People Who Received the PDS** 248 People	**People Who Received Ranibizumab Eye Injections** 167 People
Visible bleeding in the outer layer that covers the white of the eye (conjunctival hemorrhage)	179 out of 248	23 out of 167
Redness in the outer layer that covers the white of the eye (conjunctival hyperemia)	67 out of 248	4 out of 167
Inflammation of the colored part of the eye (iris) (iritis)	52 out of 248	1 out of 167
Eye pain (eye pain)	28 out of 248	13 out of 167
Moving spots in vision (vitreous floaters)	25 out of 248	7 out of 167

Question 3: Were there other side effects?

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary (see Section 8, “Where can I find more information?”).

Section 6. How has this study helped research?

The information presented here is from a single study of 415 people living with wet AMD. These results helped researchers learn more about wet AMD and the PDS.

The PDS refilled every 6 months maintained the vision improvements achieved with previous anti-VEGF injections as well as monthly ranibizumab eye injections and had a similar effect on swelling at the back of the eye. Most people who received the PDS (~95% in each interval) were able to go for each 24-week (approximately 6 months) treatment interval without needing additional eye injections of ranibizumab.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- This means that you should not make decisions based on this one summary. Always speak to your doctor before making any decisions about your treatment.

Section 7. Are there plans for other studies?

The study started in September 2018 and ended in June 2021. This summary includes the entire main results.

Patients who completed this study may have the option to be followed for a longer period of time by joining another study. In this other study, people who have the PDS will continue receiving refills every 24 weeks (approximately 6 months). People who received monthly ranibizumab injections will receive the PDS implant with refills every 24 weeks (approximately 6 months).

A separate study to compare the effect of PDS refilled every 36 weeks (9 months) with PDS refilled every 24 weeks (6 months) in people with wet AMD has started. Similar studies are also planned in people with damage to the back of the eye caused by diabetes (diabetic macular edema and diabetic retinopathy). Another study to compare the effect of PDS refilled every 36 weeks (9 months) with an aflibercept injection in people with wet AMD is also planned.

Section 8. Where can I find more information?

You can find more information about this study on the websites listed below:

- https://clinicaltrials.gov/ct2/show/study/NCT03677934
- https://forpatients.roche.com/en/trials/eye-disorder/amd/a-phase-iii-study-to-evaluate-the-port-delivery-system--47798.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is:
Archway Phase 3 Trial of the Port Delivery System With Ranibizumab for Neovascular Age-Related Macular Degeneration 2-Year Results
Regillo C et al. *Ophthalmology*; epub March 2, 2023

Question 1: Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form: https://forpatients.roche.com/en/trials/eye-disorder/amd/a-phase-iii-study-to-evaluate-the-port-delivery-system--47798.html
- Contact a representative at your local Genentech, Inc. or Roche office.

If you took part in this study and have any questions about the results, speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment, speak to the doctor in charge of your treatment.

Question 2: Who organized and paid for this study?

This study was organized and paid for by F. Hoffmann-La Roche Ltd, who have their headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is “A Phase III Study to Evaluate the Port Delivery System With Ranibizumab Compared With Monthly Ranibizumab Injections in Participants With Wet Age-Related Macular Degeneration (Archway).”

The study is known as “Archway”.

- The protocol number for this study is GR40548.
- The ClinicalTrials.gov identifier for this study is NCT03677934.
- Portions of these data were presented online at Angiogenesis, Exudation, and Degeneration, Virtual, February 2022; The Association for Research in Vision and Ophthalmology, Colorado, USA, May 2022; Retina World Congress, May 2022; Macula Society Annual Meeting, Florida, USA, June 2022; and EURETINA Congress, Hamburg, Germany September 2022.