Summary of Clinical Trial Results

A study examining a new medicine called faricimab for treating people with damage to the retina (macular edema) due to a blood clot in the main central vein of the eye (CRVO) or the main branch of the smaller blood vessels (hemiretinal vein) within the eye (HRVO)

See Section 8 (page 14) at the end of this summary for the full title of the study.

About this summary

This summary describes the results of a clinical trial (also called a study), written for:

- Members of the public, and
- People taking part in the study.

This summary is based on information known at the time of writing (February 2024). More information may now be available.

The study started in March 2021 and finished in July 2023. This summary presents the results for the second part of the study that were analyzed in August 2023.

No single study can tell us everything about the risks and benefits of a medicine. It takes a lot of people in many studies to find out everything we need to know about a new medicine. 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 helped doctors to answer important questions about people with leaky blood vessels in their retina (macular edema) due to a blood clot in the main central vein of the eye (called central retinal vein occlusion, or CRVO for short) or the main branch of the smaller blood vessels (called hemiretinal vein occlusion, or HRVO for short) and whether the new medicine faricimab could help.

Key information about this study

- This study compared a new medicine called faricimab (also known as Vabysmo™) with a medicine called aflibercept (also known as Eylea®) that is already used to treat people who have leaky blood vessels in their retina (macular edema) caused by a blood clot in the main vein of the eye. This condition is called central retinal vein occlusion (CRVO, for short) if the whole retina is affected by abnormalities, or hemiretinal vein occlusion (HRVO, for short) if only half of the retina is affected by abnormalities.
- The aim of this study was to find out if faricimab improved vision as well as aflibercept and to find out if faricimab given at flexible treatment intervals improved vision.
- In the first part of the study, people were given either faricimab eye injections or aflibercept eye injections once a month for 6 months. It was decided by chance which treatment each person was given.
- In the second part of the study, all people from the first part of the study were given faricimab eye injections at flexible treatment intervals (every month, every 2 months, every 3 months, or every 4 months), depending on their CRVO or HRVO symptoms, for 12 months
- This study included 729 people in 22 countries.
- This summary describes the key results from the second part of the study. People who received faricimab eye injections at flexible treatment intervals had improved vision.
- Most people could go 3 to 4 months between faricimab eye injections.
- Faricimab side effects were mostly mild and easily treated.
- No new or unexpected side effects were reported.
- There is another summary available describing key results for the first part of the study.

Contents of the summary

Glossary

Ang-2: a protein that plays a role in the growth and leakiness of blood vessels, and in inflammation

Central retinal vein occlusion (CRVO): a blood clot in the main vein of the eye that leads to abnormalities affecting the entire retina

Hemiretinal vein occlusion (HRVO): a type of CRVO where only half of the retina (either the top or bottom 'hemisphere') is affected by abnormalities

Macula: the central part of the retina that provides sharp, clear vision for activities such as reading, driving, and recognizing faces and colors

Macular edema: swelling in the retina due to leaking blood vessels

Retina: the thin layer of light-sensitive nerve cells that lines the back of the eye and sends signals through the optic nerve to the brain for processing

VEGF-A: a protein that plays a role in the growth and leakiness of blood vessels

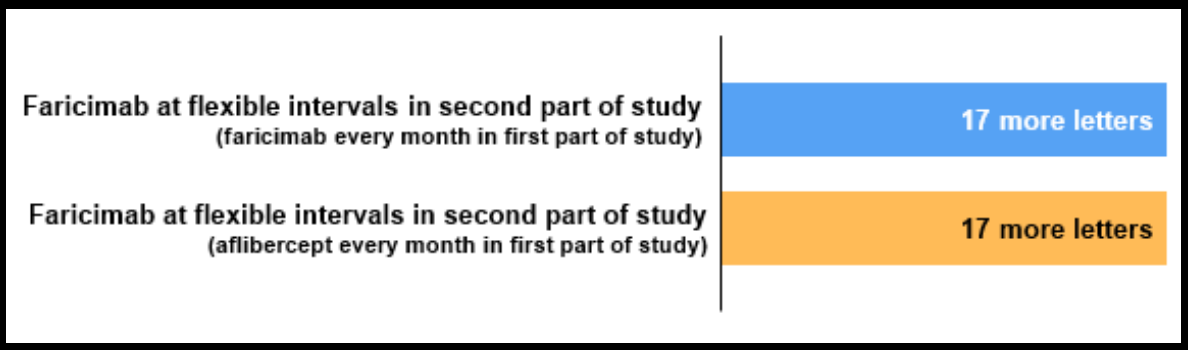
Section 1: What were the results of the study?

Question 1: Was there a change in a person's best vision after 18 months (at the end of the second part of the study) compared to the start of the study?

Doctors looked at whether a person's vision changed from the start of the study. For this, the people wore their corrective lenses and their vision was tested by finding out how many letters they could read on a standardized eye chart. This chart has rows of letters, bigger on the top and then gradually smaller towards the bottom. The study doctors compared the results of eye tests taken after 18 months (at the end of the second part of the study) with eye tests taken at the start of the study.

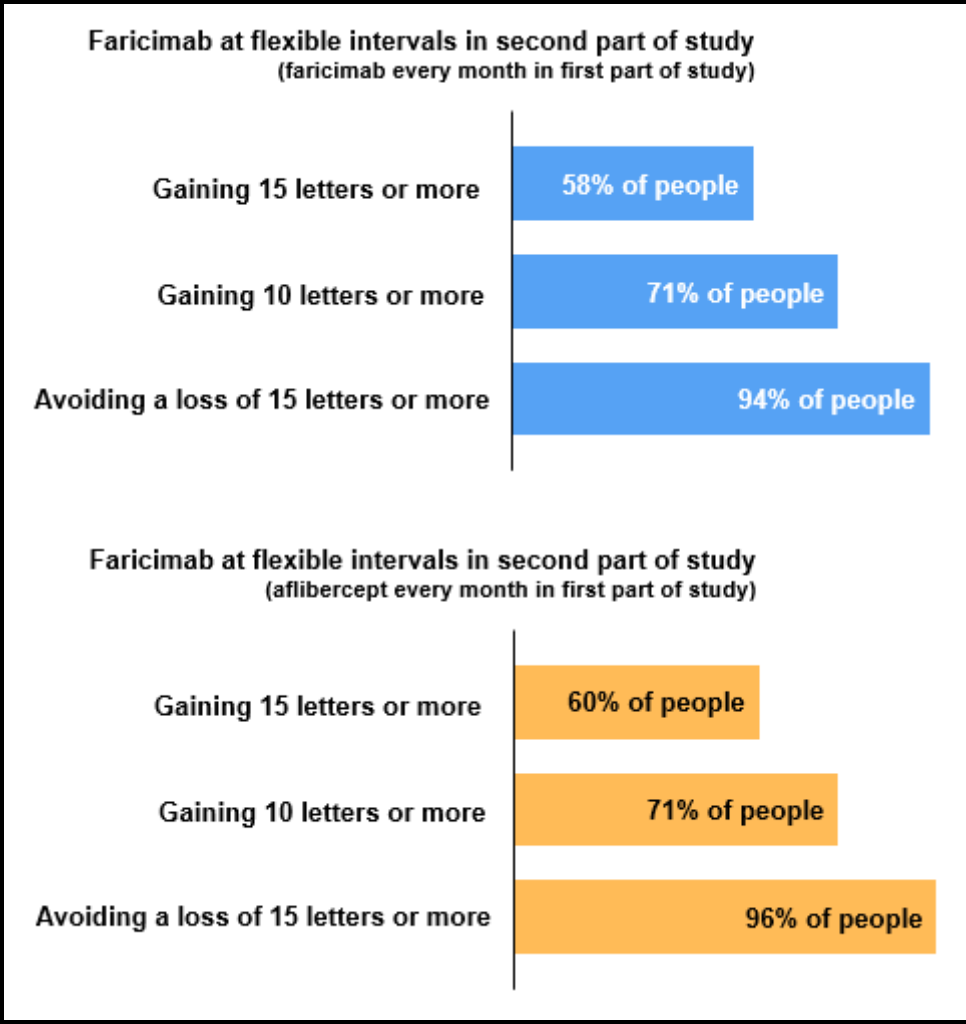
On average, people who were given faricimab at flexible intervals in the second part of the study saw 17 more letters on an eye chart than when they started the study. These results are shown below in Figure 1.

Figure 1: Was there a change in the measure of a person's best vision with correcting lenses after 18 months (at the end of the second part of the study) compared to the start of the study?



For people who were given faricimab at flexible intervals in the second part of the study, 58% and 60% of people saw an additional 15 letters or more since the beginning of the study. Almost all the people who received faricimab at flexible treatment intervals in the second part of the study avoided a loss of vision of 15 letters or more. These results are shown below in Figure 2.

Figure 2: How many people gained vision or avoided loss of their vision after 18 months (at the end of the second part of the study)?

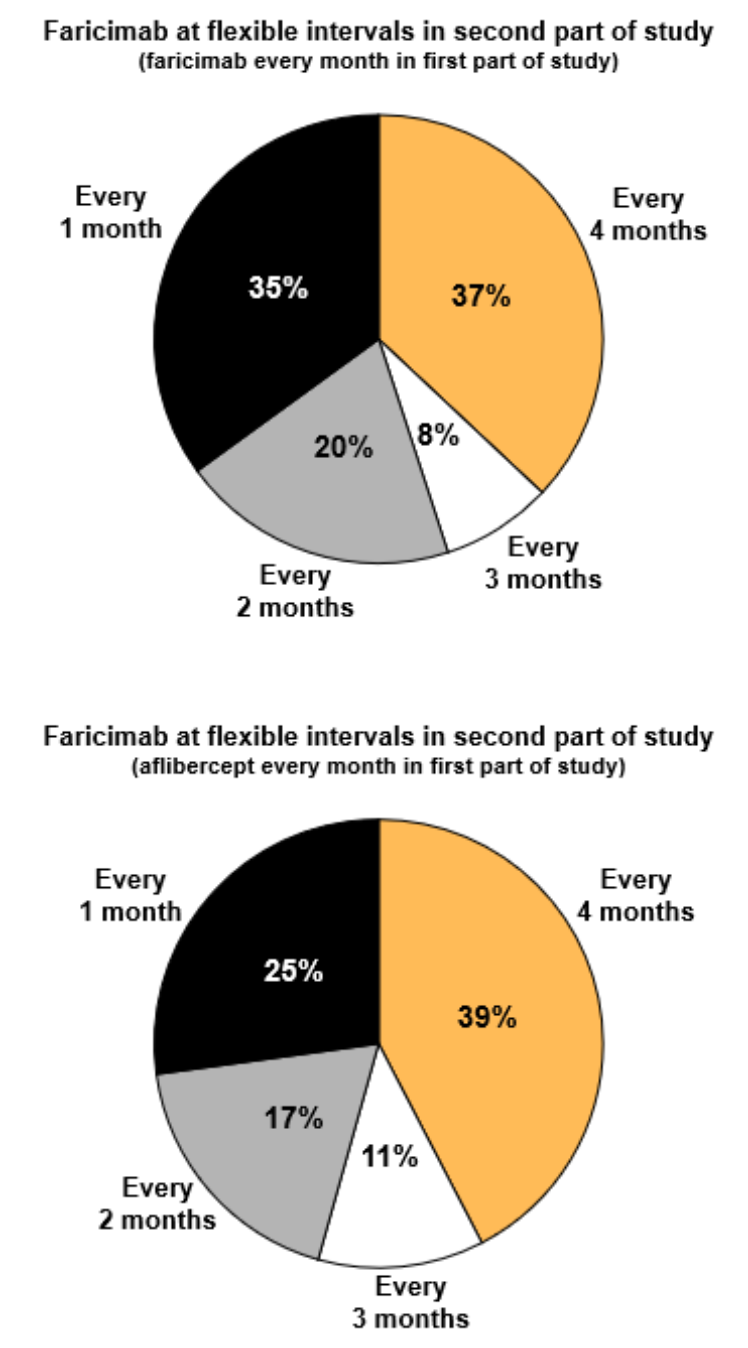


In the second part of the study, all people received faricimab at flexible intervals. The study doctors could change the time between faricimab injections, depending on a person's CRVO or HRVO symptoms. People with worsening CRVO or HRVO symptoms received faricimab more often, and people with improving CRVO or HRVO symptoms received faricimab less often. People could have faricimab injections every month, every 2 months, every 3 months, or every 4 months.

- After 18 months (at the end of the second part of the study), around 4 out of 10 people (40%) were receiving faricimab injections every 4 months, and around 1 out of 10 people (10%) were receiving faricimab every 3 months.
- About 2 out of 10 people (20%) were receiving faricimab every 2 months, and around 1 out of 3 people (33%) were receiving faricimab every month.

These results are shown below in Figure 3.

Figure 3: How many people were able to go longer than 2 months between faricimab eye injections?



This section only shows the key results from the second part of the study. Additional information about all other results will be released at a later stage.

Section 2: General information about this study

Question 1: Why was this study done?

Arteries and veins carry blood throughout your body, including your eyes. Retinal vein occlusion occurs when the veins that carry blood away from the nerve cells in the retina get blocked. A blockage in the main vein is called a central retinal vein occlusion (CRVO). The blockage can lead to blood and fluid spilling into the retina causing a condition called macular edema . In rare cases, only half of the eye (either the top or bottom 'hemisphere') is affected, this is called hemiretinal vein occlusion (HRVO). Both CRVO and HRVO usually only affect one eye.

The goal of treating macular edema caused by CRVO or HRVO is to stop blood and fluid from leaking into the retina. Medicines such as ranibizumab (Lucentis®) and aflibercept (Eylea®) eye injections have been developed to slow down macular edema. Other treatments that can reduce swelling and stabilize vision in CRVO or HRVO include steroid injections and laser treatments.

Existing medicines have improved vision for many people with macular edema caused by CRVO or HRVO, but they usually require eye injections every month for a long time. Newer medicines, such as faricimab (Vabysmo™), that work in a different way, may help to reduce CRVO or HRVO symptoms with fewer injections.

Question 2: What was the medicine being studied?

This study is looking at 2 medicines.

- Aflibercept – an existing treatment.
- Faricimab – the medicine that is being studied.

Aflibercept (Eylea®) is an existing medicine for people with macular edema caused by CRVO or HRVO. Many people who receive aflibercept need to have eye injections every month.

- You say this as *"ah-flib-er-sept".*
- Aflibercept stops a protein called VEGF-A from working. Blocking VEGF-A reduces fluid leakage and can prevent new abnormal blood vessels growing in the eye.

Faricimab is the medicine that is being tested in this study. Faricimab is also injected into the eye, but it works in a different way than aflibercept.

- You say this as *"far-ih-see-mab".*
- Like aflibercept, faricimab blocks VEGF-A, but it also blocks another protein called Ang-2. Like VEGF-A, blocking Ang-2 also reduces fluid leaking from blood vessels. Reducing the amount of fluid leaking from blood vessels may reduce the amount of swelling in the macula.
- By blocking two proteins that cause macular edema due to CRVO or HRVO, faricimab may be able to more effectively protect vision with fewer eye injections.

Question 3: What did the study doctors want to find out?

In the first part of the study, study doctors wanted to find out if vision changes were similar in people who received faricimab and those who received aflibercept (there is another summary available describing key results for the first part of the study).

In the second part of the study, study doctors wanted to find out if faricimab given at flexible treatment intervals improved vision. (see Section 1 "What were the results of the study?", page 4).

They also wanted to find out how safe faricimab given at flexible intervals is for people with macular edema caused by CRVO or HRVO. To test this, they looked at the number of side effects and how serious the side effects were (see Section 5 "What were the side effects?", page 10).

Question 4: What kind of study was this?

This was a 'Phase 3' study. This means that before this study, faricimab was tested in a smaller number of people with macular edema to make sure that faricimab is effective and safe. This study was run to see if the results held up in a larger group of people. The people tested in the earlier study had macular edema due to diabetes, which is similar to macular edema due to CRVO or HRVO. You can find more information about this earlier study on the website listed below:

- https://clinicaltrials.gov/study/NCT02699450

The results of this Phase 3 study helped health authorities decide that faricimab should be approved for people with macular edema due to CRVO or HRVO. A medicine may only be made available to patients after positive Phase 3 study results and registration by healthcare

regulators, such as the Food and Drug Administration (FDA) and the European Medicines Agency (EMA).

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

The study started in March 2021 and ended in July 2023.

This study took place at 192 centers in 22 countries, including Argentina, Australia, Austria, Brazil, China, Czech Republic, France, Germany, Hong Kong, Hungary, Israel, Italy, Japan, Korea, Poland, Portugal, Russia, Singapore, Spain, Taiwan, the United Kingdom, and the United States.

The study started and continued during the COVID-19 pandemic, but the pandemic did not have a major impact on the results.

Section 3: Who took part in this study?

In total, 729 people with macular edema caused by CRVO or HRVO took part in this study.

Around 54% of the participants (393 people) were men and about 46% of the participants (336 people) were women. At the start of the study, people were, on average, 65 years of age.

People could take part in the study if they:

- Had swelling in the macula caused by CRVO or HRVO that happened in the last 4 months.
- Had macula edema.
- Could read between 73 and 19 letters on a standard eye chart, which means that they have vision between 20/40 to 20/400.
- Had clear eyeballs and their pupils could be dilated with special eye drops to allow for good photos of the retina to confirm the CRVO or HRVO and macular edema.

Section 4: What happened during the study?

In the first part of the study, people were randomly split into 2 groups.

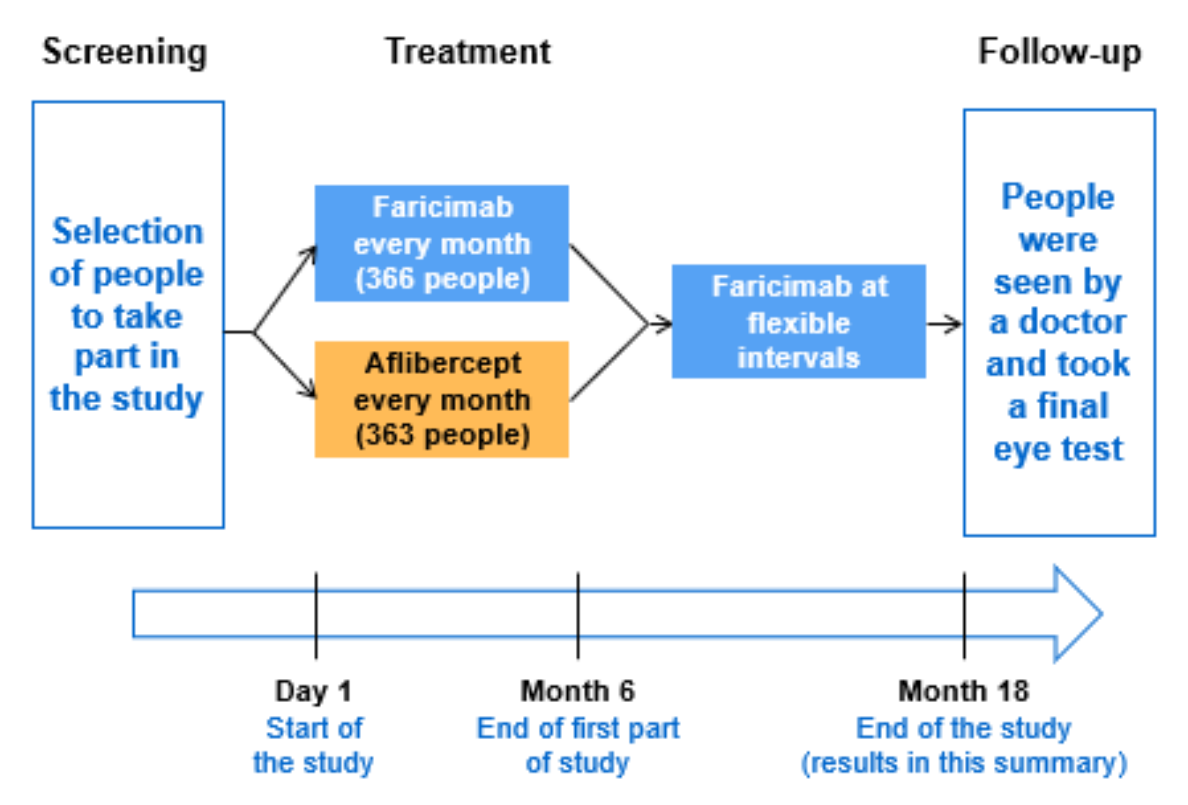
The groups were:

- **Faricimab:** this group received 6 milligrams of faricimab injected into their eye once every month for 6 months.
- **Aflibercept:** this group received 2 milligrams of aflibercept injected into their eye once every month for 6 months.

In the second part of the study (after the first 6 months), all people received 6 milligrams of faricimab injected into their eye at flexible intervals (every month, every 3 months, or every 4 months), depending on their CRVO or HRVO symptoms, for 12 months.

There is a diagram showing what happened during the study below (see Figure 4).

Figure 4: What happened during the study?



Section 5: What were the side effects?

Side effects (also known as adverse reactions) are medical problems (such as a headache or dizziness) that can happen during a study. This section describes the side effects reported during the study so far:

- Some side effects may be related to the medicines used, the injection procedure, or the disease itself.
- Not all of the people participating in this study had all of the side effects.
- Side effects can vary from mild to serious and may differ from person to person.

During the second part of the study, when all people were given faricimab at flexible intervals, the side effects caused by faricimab were mostly mild and could be easily treated and resolved.

Only 14 out of 701 people (about 2%) stopped receiving faricimab due to side effects.

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

Question 1: What serious side effects were reported?

A side effect is considered serious if it is life-threatening, causes vision loss, needs hospital care, or causes lasting problems.

During the second part of the study when all people were given faricimab at flexible intervals, a low number of people had at least one serious side effect in the treated eye. Overall, 7.2% and 3.5% of people had a serious side effect.

A relatively low number of people (8.4% and 12.0%) had a serious side effect that didn't involve their eyes.

Table 1 below shows the number of people with the six most common serious side effects during this study.

Table 1: What serious side effects were reported?

Serious side effects reported in this study	**Faricimab at flexible treatment intervals in second part of study** (faricimab every month in first part of study) (359 people total)	**Faricimab at flexible treatment intervals in second part of study** (aflibercept every month in first part of study) (342 people total)
Serious side effects in the treated eye	26 out of 359 (7.2%)	12 out of 342 (3.5%)
Worsening of their CRVO or HRVO (retinal vein occlusion)	5 out of 359 (1.4%)	3 out of 342 (less than 1%)
New swelling in the macular (cystoid macular edema)	5 out of 359 (1.4%)	1 out of 342 (less than 1%)
Blockage of the retinal artery (retinal artery occlusion)	None	2 out of 342 (less than 1%)
Swelling of the macular (macular edema)	3 out of 359 (less than 1%)	None
A small hole in the macular (macular hole)	1 out of 359 (less than 1%)	1 out of 342 (less than 1%)
New blood vessel growth in the retina (retinal neovascularization)	1 out of 359 (less than 1%)	1 out of 342 (less than 1%)

Question 2: What were the most common side effects reported?

During the second part of the study, when all people were given faricimab at flexible intervals, 130 out of 359 people (36%) and 118 out of 342 people (around 35%) had at least one side effect in the treated eye.

- Most of these side effects were mild or moderate in severity.
    - Mild side effects may cause discomfort but do not disrupt normal daily activities, while moderate side effects may cause discomfort that does affect or reduce normal daily activities.

Table 2 below shows the six most common side effects during the second part of the study.

Table 2: What were the most common side effects reported?

Most common side effects in the treated eye	**Faricimab at flexible treatment intervals in second part of study** (faricimab every month in first part of study) (359 people total)	**Faricimab at flexible treatment intervals in second part of study** (aflibercept every month in first part of study) (342 people total)
High pressure inside the eye (intraocular pressure increased)	17 out of 359 (4.7%)	15 out of 342 (4.4%)
Cloudy patches develop on lens of eye (cataract)	14 out of 359 (3.9%)	15 out of 342 (4.4%)
New swelling in the macular (cystoid macular edema)	17 out of 359 (4.7%)	10 out of 342 (2.9%)
Swelling of the macular (macular edema)	10 out of 359 (2.8%)	14 out of 342 (4.1%)
Vitreous coming away from the retina at the back of the eye (vitreous detachment)	6 out of 359 (1.7%)	14 out of 342 (4.1%)
Worsening of their BRVO (retinal vein occlusion)	11 out of 359 (3.1%)	8 out of 342 (2.3%)

Question 3: Were there any 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 (page 14).

Section 6: How did this study help research?

The results described in this summary are from a single study of 729 people with macular edema caused by CRVO or HRVO. These results helped study doctors learn more about faricimab and its effects on macular edema due to CRVO or HRVO.

The main result from the second part of the study is that people who received faricimab at flexible treatment intervals gained vision.

Most people could go 3 to 4 months between faricimab eye injections.

Faricimab side effects were mostly mild and easily treated. No new or unexpected side effects were reported.

Section 7: Are there plans for other studies?

An identical study of 553 people with macular edema due to a blood clot in one of the branched veins of the eye (called branch retinal vein occlusion, or BRVO for short) took place at the same time as this one. The results of both studies are similar so far. Together, these studies will help study doctors to collect information from 1282 people with macular edema over 18 months.

Section 8: Where can I find more information?

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

- https://www.clinicaltrials.gov/study/NCT04740931
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-000441-13/DE
- https://forpatients.roche.com/en/trials/eye-disorder/rvo/a-study-to-evaluate-the-efficacy-and-safety-of-faricima-34453.html

If you would like to find out more about the design of this study, the full title of the scientific paper is: “BALATON and COMINO: Phase III Randomized Clinical Trials of Faricimab for Retinal Vein Occlusion”. The authors of the scientific paper are Lars-Olof Hattenbach, Francis Abreu, Pablo Arrisi, Karen Basu, Carl J. Danzig, and others. The paper is published in a medical journal called *Ophthalmology Science*, volume number 3, and can be found online here:
DOI: https://doi.org/10.1016/j.xops.2023.100302.

If you would like to find out more about the results for the first part of the study, the full title of the scientific paper is: “Efficacy and Safety of Faricimab for Macular Edema due to Retinal Vein Occlusion: 24-Week Results from the BALATON and COMINO Trials”. The authors of the scientific paper are Ramin Tadayoni, Liliana P Paris , Carl J Danzig, Francis Abreu, Arshad M Khanani, and others. The paper is published in a medical journal called *Ophthalmology*, and can be found online here:
DOI: https://doi.org/10.1016/j.ophtha.2024.01.029.

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 For Patients platform and fill out the contact form: https://forpatients.roche.com/en/trials/eye-disorder/rvo/a-study-to-evaluate-the-efficacy-and-safety-of-faricima-34453.html
- Contact a representative at your local Genentech, Roche, or Chugai office.

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

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

Question 2: Who is organizing and paying for this study?

This study is being 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 Study to Evaluate the Efficacy and Safety of Faricimab in Participants With Macular Edema Secondary to Central Retinal or Hemiretinal Vein Occlusion”.

The study is known as ‘COMINO’.

The protocol number for this study is GR41986.

The ClinicalTrials.gov identifier for this study is NCT04740931.

The EudraCT number for this study is 2020-000441-13.