Summary of Clinical Trial Results

Testing a new medicine (galegenimab) to find out if it is effective for a type of eye disease (geographic atrophy secondary to age-related macular degeneration)

See the end of the 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).

This summary is written for:

- Members of the public
- People who took part in the study

This summary is based on information known at the time of writing.

The study started in June 2019 and stopped early – in October 2022 – because the medicine being studied did not work as well as expected.

A single study cannot tell us everything about the risks and benefits of a medicine. It takes many people in several 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.**

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Thank you to the people who took part in this study

The people who took part in this study have helped researchers answer important questions about geographic atrophy secondary to age-related macular degeneration (AMD), and the medicine that was studied, galegenimab.

Key information about this study

- This study was done to find out if a new medicine was effective in people with a type of eye disease, geographic atrophy secondary to AMD.
- People got the study medicine, galegenimab, by injection into the eye. Some people in the study received a "sham" injection – which did not contain any medicine. It was decided by chance (randomly) who got which treatment.
- This study included 373 people in one country, the USA, among whom 372 received at least one galegenimab injection or sham control.
- The main finding was that galegenimab was not effective for geographic atrophy secondary to AMD.
- Five out of 224 people (2%) treated with galegenimab had serious side effects thought to be caused by the treatment. People with sham treatments did not report any treatment-related serious side effects.
- Twenty-two people had side effects that were not serious, but researchers thought they were caused by the study treatment. This included 21 out of 224 people (9%) with galegenimab treatment and one out of 148 people (1%) with sham treatment.
- This study was stopped early (terminated) because researchers did not see any benefit from this treatment.

1. General information about this study

Why was this study done?

Age-related macular degeneration (AMD) is an eye problem that can cause vision loss in people as they age. In the advanced states, there are two forms of AMD: dry AMD and wet AMD.

Dry AMD causes parts of the eye to slowly wear out and is called "geographic atrophy." It gets more common as people get older. At age 70, about 1% of the people have it. By age 90, about 11% of the people have it.

People with geographic atrophy experience several symptoms that can lead to blindness. In the beginning, they may have difficulty recognizing faces, seeing in the dark, and reading. Later, geographic atrophy may cause loss of the ability to see in the center of the field of vision. This disease usually affects both eyes.

The disease causes cells in the back of the eye (the retina and associated retinal pigment epithelium) to gradually die. There are now two approved treatments for geographic atrophy. The new treatments do not restore vision that has already been lost, or completely stop disease progression. Therefore, it is important to continue research for new medicines.

Researchers have been studying a medicine called "galegenimab" that may be useful for geographic atrophy secondary to AMD. This study was done to test galegenimab in people with geographic atrophy – to find out if galegenimab was effective.

What was the study medicine?

The study medicine was called "**galegenimab**." It was also known as "**FHTR2163**," "**RO7171009**," and "**anti-HtrA1**."

Galegenimab is made of an antibody, a protein that is very specific in choosing to bind to one other protein in the body. Galegenimab was designed by scientists to bind and inactivate the HtrA1 protein.

The HtrA1 protein is made naturally in our bodies, including in our eyes. In the eyes, it is thought to help maintain clear vision. But, if someone has too much HtrA1 in their eyes, especially as they get older, it causes problems. Researchers believe that too much HtrA1 can contribute to geographic atrophy secondary to AMD.

By binding to HtrA1 and "turning off" HtrA1, galegenimab may be useful for treating people who have geographic atrophy secondary to AMD.

What did researchers want to find out?

In this study, researchers compared the results of giving people sham treatments and real treatments – to learn about the effects of the real medicine. Sham treatments were made to look like the real treatment but did not contain any medicine.

The main question that researchers wanted to answer was:

Was galegenimab an effective treatment for geographic atrophy secondary to AMD?

What kind of study was this?

Phase 2 study

In Phase 1 studies, researchers learn about how much medicine people can tolerate and what the side effects are. Then, if it is safe to do so, they move on to Phase 2 studies. In Phase 2 studies, the medicine is given to a larger group and to those who have the disease. Researchers want to find out if the treatment is effective for the disease, and to take a further look at its safety.

Randomized study

This was a type of study where there was more than one treatment group, and it was decided by chance who joined which treatment group. It was like flipping a coin – a computer decided who joined which group. That means, the personal preferences of people did not influence the decision. This was done to "reduce bias" in the study results, as people did not control who got which treatment.

Sham-controlled, single-masked study

Some people got fake treatments that looked just like the actual treatment but did not contain any real medicine. These were "sham" treatments. People in the study were "masked," which means they did not know which treatment they were receiving. Researchers did this to prevent any "bias" from affecting the results. Bias could happen if people started to feel better simply because they expected the new treatment to work, and not because it was actually effective. Keeping people masked was a way to protect the real results and keep out the expectations of the people.

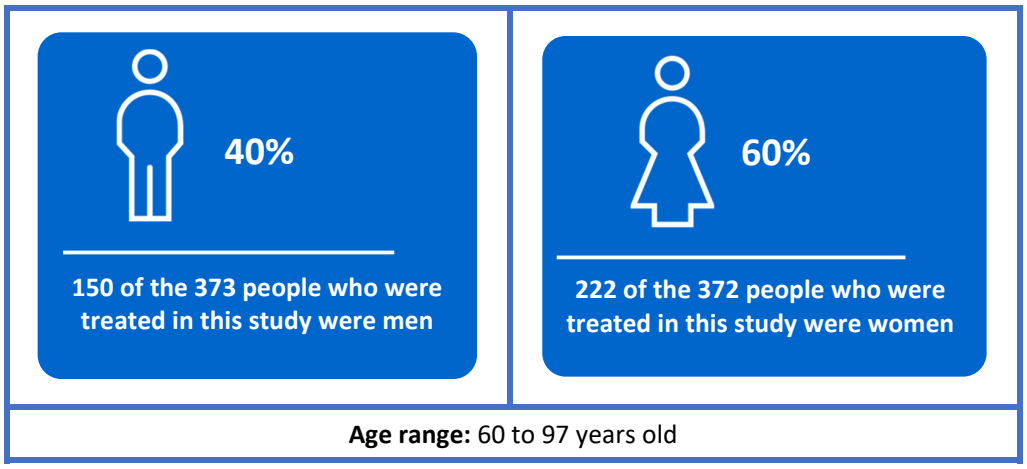
When and where did the study take place?

The study started in June 2019 and stopped early. The study sponsor decided to stop all studies looking at galegenimab for people with geographic atrophy secondary to AMD. This summary presents the results of the study up until it was stopped in October 2022.

The study took place at 77 study centers at 71 study sites in one country – the USA.

2. Who took part in this study?

Three hundred and seventy-two people with geographic atrophy secondary to AMD enrolled and received at least one galegenimab injection or sham control treatment in this study.



People could take part in this study if they met all the following conditions:

- They were at least 60 years old when they signed the informed consent form.
- One eye was selected to be the study eye. The study eye and the non-study eye met all the requirements for vision and disease for this study.

People could not take part in the study if they met any one of the following conditions:

- If they had geographic atrophy for reasons other than being secondary to AMD.
- If they had current eye healthy conditions or past eye health history which were not allowed in this study.
- If they had general health conditions, medical history, current or past use of medicines, that were not allowed in this study.

3. What happened during the study?

Screening:
The screening period lasted about 3 months. During this time, researchers did medical exams, took images of the eyes using specialized equipment, and asked questions to see if people interested in the study met the conditions for joining the study.

Treatment:
The treatment period lasted under 1 ½ years. Those who met the conditions for joining the study were randomized into one of four groups. Treatments were given by injection into the eye (intravitreal injections), once every four or eight weeks. Galegenimab injections penetrated the eye, while sham injections did not. The treatment groups were:

- Group1: Galegenimab 20 milligrams (mg) was given once every four weeks (Q4W). The treatment lasted 68 weeks.
- Group 2: Sham treatment was given Q4W. The treatment lasted 68 weeks.
- Group 3: Galegenimab 20 mg was given once every eight weeks (Q8W). The treatment lasted 64 weeks.
- Group 4: Sham treatment was given Q8W. The treatment lasted 64 weeks.

Data collection:
Researchers compared the size of the disease area in the eye at baseline and at 72 weeks – in each of the four treatment groups. They noted the general health of the person and any side effects seen in the eye due to the study treatments. Fluid from the eyes and blood from the vein (usually the arm) were collected throughout the study for tests.

Follow-up:
There was a final study visit at 76 weeks. Once again, researchers checked the general healthy and eye health of people in the study.

4. What were the results of the study?

Researchers found a certain side effect of the treatment – inflammation of the eye – present at a high rate. This caused people to experience sudden pain, redness, swelling, or sensitivity to light.

Because of the side effects, researchers decided to look at the study results early. They wanted to find out if there was benefit from the treatment – that was greater than the burden of the side effects. Unfortunately, they did not find galegenimab to be effective for the treatment of geographic atrophy secondary to AMD.

This study was stopped early – it was "terminated" because researchers did not see any benefit from this treatment.

Of the 372 people who joined the study and received treatments, 224 were treated with galegenimab and 148 received sham treatments.

Question: Was galegenimab an effective treatment for geographic atrophy secondary to AMD?

Researchers collected images of the eye with specialized equipment – before treatment and at several timepoints after treatment.

The measure of effectiveness of the treatments was done in 337 people:

- Group 1: Galegenimab Q4W, 138 people
- Group 3: Galegenimab Q8W, 67 people
- Group 2 and 4: Sham Q4W and sham Q8W, 132 people

Not everyone enrolled in the study at the same time. Because the study had stopped early, people who joined the study later did not proceed far in the study and missed the chance to have eye images taken at later time points. That meant that while 303 people had eye images taken when they reached Week 24 on the study, only 185 were taken at Week 72 because fewer people reached Week 72 on the study.

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see Section 8).

5. What were the side effects?

Side effects are medical problems (such as having a headache) that happened during the study.

- If they were seen in this study, they are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Not everyone in any one study will have all of the side effects.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies.
- Serious and common side effects are listed in the following sections if they were seen in this study.

Serious side effects

A side effect is considered "serious" if it is life-threatening, results in death, needs hospital care, causes lasting problems, or requires an intervention to avoid any of them. An intervention is when a doctor gets involved to take care of a situation.

Five out of 372 people (1%) had a serious side effect that was thought to be caused by the study treatment, all of them were side effects affecting the eye (ocular side effects).

- Four people had inflammation that was not caused by an infection (aseptic ocular inflammation) in different parts of the eye:
    - Two had inflammation inside the eye coming from the middle layer of the eye (uveitis)
    - One had redness, swelling or pain of the colored part of the eye and nearby areas (iridocyclitis)
    - One had inflammation of the gel-like substance inside the eye (vitritis)
- One person had inflammation that was caused an infection (septic inflammation) in the eyeball (endophthalmitis)

There were no deaths in this study that were related to the study treatment.

Six of the 224 people who received galegenimab (3%) decided to stop their treatments because of side effects thought to be caused by the study treatments. These were all inflammation of the eye (ocular side effects).

Fourteen of the 224 people who received galegenimab (8%) decided to delay the next dose (dose interruption) because of treatment-related side effects.

Side effects considered to be caused by the study treatment

During this study, 22 people had 32 side effects that were not serious, but researchers believed they were caused by the study treatments. Among the 22 people, one person received sham treatment and 21 received galegenimab. The side effects are listed below. Some people had more than one side effect and are represented on more than one line.

- Thirteen people had aseptic ocular inflammation:
  - Six had redness, swelling or pain of the colored part of the eye and nearby areas (iridocyclitis)
  - Five had inflammation of the gel-like substance inside the eye (vitritis)
  - Two had redness, swelling or pain of the colored part of the eye (iritis)
  - Four people: The pressure in the eye was higher than usual (intraocular pressure increased; ocular hypertension)
- Two people:
  - Blood showing in the white part of the eye (conjunctival hemorrhage)
- Several side effects were seen only once in the study:
  - The lens of the eye became cloudy (cataract)
  - Eye discomfort (ocular discomfort)
  - Abnormal blood vessels of the light-sensitive layer at the back of the eye (retinal vasculitis)
  - Inflammation of the sclera, which is the white part of the eye (scleritis)
  - Blurred vision
  - One or more tiny moving shadow present in your vision, caused by the gel-like substance inside the eye (vitreal cells)
  - One or more tiny moving shadow present in your vision, caused by the gel-like substance inside the eye (vitreous floaters)

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.

6. How has this study helped research?

The information presented here is from a single study of 372 people with geographic atrophy secondary to AMD who were treated in this study. These results helped researchers learn more about this disease and the study medicine, galegenimab.

A single study cannot tell us everything about the risks and benefits of a medicine. It takes many people in several studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

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- **Always speak to your doctor before making any decisions about your treatment.**

7. Are there plans for other studies?

There are no plans for any new studies to look at galegenimab in people with geographic atrophy secondary to AMD.

8. Where can I find more information?

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

- https://clinicaltrials.gov/study/NCT03972709
- https://forpatients.roche.com/en/trials/eye-disorder/amd/a-study-assessing-the-safety--tolerability--and-efficac-97970.html

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/About.html
- Contact a representative at your local 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.

Who organized and paid for this study?

This study was organized and paid for by Genentech, Inc., South San Francisco, CA, USA. Genentech is part of F. Hoffmann-La Roche Ltd., with headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is:

> A phase 2, multicenter, randomized, single-masked, sham-controlled study to assess safety, tolerability, and efficacyon intravitreal injections of FHTR2163in patients with geographic atrophy secondary to age-related macular degeneration.

- The study is known as "GALLEGO."
- The protocol number for this study is GR40973.
- The ClinicalTrials.gov identifier for this study is NCT03972709.