Clinical Trial Results – Layperson Summary

A study to look at how safe a study medicine was for patients – when taken at different doses - and how this medicine was processed through the body

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; we will refer to the clinical trial as a "study" in this document.

This summary is written for:

- members of the public
- patients who took part in the study

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

The study started in September, 2017, and finished in November, 2018. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. Many patients volunteer in several studies to help us 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.

Contents of the summary

Thank you to the people who took part in this study

The patients who took part have helped researchers to answer important questions about an eye disease and a study medicine for this disease.

Key information about this study

- This study was done to find out what was the safe dose for a new medicine.
- Patients with a certain eye disease called “age-related macular degeneration’ took part in this study.
- Patients were injected in their eye with a medicine called FHTR2163 – different patients got different amounts of the medicine.
- Researchers wanted to know what dose or how much of the medicine was safe for patients to get.
- Researchers also wanted to know what happened to the medicine in the body.
- This study included 28 patients in USA.
- The main finding was that all doses tested were safe for patients.
- Two patients had serious medical problems which were not believed to be side effects related to the study medicine.
- At the time this summary was written, the study was completed and researchers had decided that the highest dose tested could be used in further studies of this medicine.

1. General information about this study

Why was this study done?

The “macula” is a specialized part of the retina – the macula and the retina are parts of the eye that allow you to see. As people grow older, sometimes their eyesight fails. This can be due to an eye disease known as “age-related macular degeneration” where the macula can no longer do its job properly. We will call this disease by a short name – “**AMD**”.

As time goes by, AMD can become worse in some patients. One way it can become worse is when small parts of the macula start dying. This condition is known as “AMD with geographic atrophy”. Once again, we will shorten the name of this disease to “**AMD with GA**”.

Patients who have AMD with GA can go blind, and we need to find treatments for this disease. Researchers have studied the eyes of patients who have this disease and found a buildup of a certain protein in the area where the disease is located. This protein is known as **HtrA1**. Researchers wanted to find out if they could make a medicine that could reduce the effect of HtrA1, and if doing so would help patients with their vision.

What was the study medicine?

In this study, a new medicine known as **FHTR2163** was given to patients. This medicine is also known as RO7171009, but we will use the first name throughout this summary.

- FHTR2163 is a type of medicine known as an antigen-binding fragment, or “**Fab**” for short.
- FHTR2163 works by binding and destroying the HtrA1 protein made in the eyes of patients who have the eye disease, AMD with GA.
- FHTR2163 is a study medicine which means it is new and being studied in patients.

What did researchers want to find out?

The main questions that researchers wanted to answer were:

1. **How safe was FHTR2163 when it was injected into the patient's eye?**
   Researchers wanted to know what side effects could be caused by FHTR2163 in the eye as well as in the rest of the body.
2. **What was the largest dose of FHTR2163 that could be safely given to a patient?**
   From this study, researchers wanted to find out what dose they should stay below in future studies to reduce side effects.

Other questions that researchers wanted to answer were:

3. **What happens to FHTR2163 in the body?**
   After patients were given FHTR2163, researchers were interested to know what amount of this medicine could be found in the body. They also wanted to know how long the medicine stayed in the body. Such information could be used to decide how much of the medicine to give to patients in the future to reduce the number of side effects or maybe to increase the effectiveness of the medicine.
4. **Does FHTR2163 cause any reaction in the immune system of the body?**
   FHTR2163 is a medicine that consists of the Fab protein which is found in the immune system of the body. Researchers wanted to find out what effects this type of medicine had on the immune system of the patient.

What kind of study was this?

Phase 1 study

This was a Phase 1 study, which means that this was one of the first studies for the study medicine. A small number of patients who had AMD with GA got the medicine and the researchers did medical tests to find out about the effects of FHTR2163 on the patients.

Open label study

This was known as "open label" which means that doctors and patients knew which medicine the patients were getting.

When and where did the study take place?

The study started in September, 2017, and finished in November, 2018. This summary was written after the study had ended.

USA - the study took place at 11 study centers across the United States of America.

2. Who took part in this study?

In this study, **28 patients** affected by AMD with GA got the study medicine. All patients were adults; the youngest patient was 66 years old and the oldest patient was 91 years old. The average age was 79 years. Fifteen patients (54%) were females and 13 (46%) were males.

Patients could participate if:

- They had a certain level of vision remaining. Patients on this study could not be completely blind.
- They had AMD with GA, and the disease could be measured and had to be of a certain size.
- They were healthy enough to participate in this study. Patients with health conditions that made tests unsafe were excluded.

Patients could not participate if:

- They had certain other eye diseases.
- They had undergone certain types of eye treatments or certain types of eye surgeries.
- Patients with certain diseases in other parts of the body were also not allowed to take part in this study.

3. What happened during the study?

During the study, patients were given different doses of the study medicine.

- The medicine was given to the patient through an injection into the eye, called an intravitreal injection or **ITV injection**.
- Only one eye was injected – this was called the "study eye".

Single ascending dose study:

- The first part of this study was called "single ascending dose study". That means each patient only got one injection of the study medicine in one eye.
- Three patients got the medicine at the lowest dose, and researchers observed them for two weeks.
- If the low dose was safe, the next group of 3 patients got the next higher dose. Once again, researchers observed the patients for two weeks.
- The process was repeated until 15 patients got 5 different doses of the study medicine.
- **Three patients each got 1 mg, 3 mg, 10 mg, 15 mg, or 20 mg of FHTR2163**.

Multiple dose study:

- The second part of this study was called “multiple dose study”. That means each patient got multiple doses of the study medicine.
- Each patient got one injection in their study eye, then a second injection at 4 weeks, and a third injection at 8 weeks.
- A total of 13 patients took part in this second part of the study.
- **Twelve patients got a total of 3 injections with 20 mg of the study medicine each time, 4 weeks apart**.
- **One patient got 2 injections and stopped treatment after the second injection because of medical problems. The medical problems were not believed to be side effects related to the study medicine.**

4. What were the results of the study?

Researchers had asked four questions before they started this study. Here are the results of what they found.

Question 1: How safe was FHTR2163 when it was injected into the eye of patients?

Based on the results from this study, researchers decided that FHTR2163 was safe and could be tolerated by patients who got a single injection or multiple injections.

Question 2: What was the largest dose of FHTR2163 that could be safely given to a patient?

Researchers were not able to find out what the largest dose of FHTR2163 was that could be injected into the eye of a patient. This was because the highest dose that they tested was safe, and they did not continue to increase the dose beyond that to find the dose that became unsafe.

Question 3: What happened to FHTR2163 in the body?

Researchers found higher amounts of the study medicine in the eye than in blood samples taken from the body. The study medicine stayed long enough in the body to possibly be a useful medicine.

Question 4: Does FHTR2163 cause any reaction in the immune system of the body?

Researchers tested blood samples and found 3 of the 28 patients (or 11% of the patients) had antibodies made by their immune system against the study medicine. Because the number of patients was small, researchers did not have enough results to make a statement regarding the effect of this observation.

5. What were the side effects?

Side effects (also known as “adverse reactions”) are unwanted medical problems (such as a headache) that happen during the study.

- Not every patient in a study has all of the side effects seen in the study.
- Common side effects and serious side effects are listed in the following sections.

Most common side effects

Side effects in the eye

- Thirteen of the 28 patients in this study (46%) had a medical problem in their study eye – this was the eye that was injected in each patient.
- One of the 28 patients (4%) had a medical problem in the eye that was not injected.
- None of the medical problems in the one eye of all 14 patients were thought to be side effects related to the study treatment.
- The most common medical problems in the study eye were bleeding on the outside surface of the eye in 7 patients (25%), blood vessels in the eye that became larger in 4 patients (14%), and eye pain in 2 patients (7%).

Side effects in the body

- Thirteen of the 28 patients in this study (or 46%) had a medical problem in their body.
- The most common medical problems that happened while patients were on the study were the common cold in 2 patients (7%), skin cancer in 2 patients (7%), and skin ulcer in 2 patients (7%).
- None of these medical problems were thought to be side effects related to the study drug.

Serious side effects

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

- During this study, no serious side effects were reported in the eye.
- Two patients (or 7% of the patients) had a serious medical problem in the body.
- One of these patients had a loop of the intestine in the stomach twist around itself – this condition is known as “volvulus”. This serious medical problem was not thought to be a side effect related to the study medicine. The patient later died from a heart attack – this was not related to the study medicine either.
- The other patient got severe diarrhea (viral gastroenteritis) which cleared up one day later.

6. How has this study helped research?

The results presented here are from a single study of FHTR2163 in patients who have AMD with GA. These results helped researchers learn more about the disease and the study medicine.

This was the first time this new study medicine was given to patients. The results showed FHTR2163 to be safe for further use and investigation in patients.

7. Are there plans for other studies?

More studies are planned to look at the safety and effectiveness of FHTR2163 in patients who are affected by AMD with GA. Remember that this medicine is also known as RO7171009.

A new study that started in June, 2019, is expected to be completed by March, 2022, and will enroll 285 patients (https://clinicaltrials.gov/ct2/show/NCT03972709)

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/NCT03295877
- https://forpatients.roche.com/en/trials/eye-disorder/amd/safety-and-tolerability-study-of-ro7171009-in-participants-with-.html

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Fill out a contact form online at: https://forpatients.roche.com/
- Or 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 I, Multicenter, Open-Label, Single-Dose, Dose-Escalation and Multiple-Dose Study of the Safety, Tolerability, Pharmacokinetics, and Immunogenicity of Intravitreal Injections of FHTR2163 in Patients With Geographic Atrophy Secondary to Age-Related”.

- The protocol number for this study is: GR39821.
- The ClinicalTrials.gov identifier for this study is: NCT03295877.