Summary of Clinical Trial Results

A study to look at how safe different doses of a new study medicine (RO7303509) were for healthy people to take – 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 (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 September 2020 and finished in July 2022. This summary was written after the study had ended.

No single study can 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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Contents of the summary

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 RO7303509, a new study medicine.

Key information about this study

- This study was done to find out how safe was it for people to get a new medicine at different doses.
- People were given either the study medicine (RO7303509) or a placebo. It was decided by chance which treatment each person was given.
- This study included 49 healthy people in one country – the USA.
- The main finding was that researchers found RO7303509 to be safe for people at the doses tested in this study – when a single dose was given to healthy people.
- No one in this study had any serious side effects caused by the treatments.
- Five out of 36 people who got RO7303509 – and 3 out of 13 people who got placebo – had a side effect that was not serious and went away (resolved) quickly – but was thought to be caused by the treatments.

1. General information about this study

Why was this study done?

Connective tissue gives support, structure, strength, shape, and protection to tissues and organs in the body. **Systemic sclerosis** (**SS**) is a disease that causes abnormal **scarring** in the connective tissues – similar to what happens after an injury.

People with SS have thick and stiff connective tissues – that may be swollen and painful. There is increased collagen made. **Collagen** is a structural protein, and extra collagen causes hardening of the connective tissues. Doctors are able to see this as scar tissue or "**fibrosis**".

Many people with SS have a good prognosis - they live a full and productive life. However, some people die from this disease when the lung, heart, or kidney becomes involved.

SS is known to be an **autoimmune disease**. It happens when your white blood cells (immune cells) are triggered – by mistake – and they start an "immune response". During this immune response, white blood cells release different types of signaling proteins (**cytokines**). Some of the cytokines can affect genes and proteins in the cell – and start a "wound-healing response" – resulting in extra collagen – and the accumulation of scar tissue.

Researchers have identified several cytokines that play a role in SS. They are also developing study medicines that could interfere with cytokines and stop the fibrosis process. **RO7303509** is one such study medicine. Researchers are testing RO7303509 to see if it could be useful in SS.

This study was done to find a dose of RO7303509 that was safe to give to healthy people. Results from this study would be useful for dosing in studies done after this one.

What was the medicine being studied?

This study looked at a medicine and a placebo.

RO7303509

- This study medicine is also known as "MTBT1466A".
- RO7303509 is an antibody, a protein that only binds to one molecule.
- RO7303509 has been designed to bind to **TGFβ3**, pronounced as "T-G-F-beta-3".
- TGFβ3 is a cytokine.
- When TGFβ3 is bound by RO7303509, TGFβ3 becomes inactive.
- By stopping TGFβ3 from being active in the body, RO7303509 may be able to interfere in the fibrosis process in people who have SS disease

Placebo

- Everyone in this study got a treatment. The treatment contained the study medicine (RO7303509), or a placebo.
- The placebo looked like the real medicine but did not contain any medicine. This means it had no medicinal effects on the body.
- Researchers compared treatments with RO7303509 to the placebo – so they could show which side effects of the treatment were actually caused by RO7303509.

What did researchers want to find out?

The main question that researchers wanted to answer was:

1. How safe was it for people to get a single treatment of RO7303509 – given at different doses to different groups of people?

What kind of study was this?

Here are some features of this study.

Phase 1 study
This was a "Phase 1" study, which means that this was an early study looking at RO7303509. A small number of healthy people got treatments. Researchers did medical tests on the people to find out more about the treatments.

Dose-escalation study
Each new group of people who joined the study received the next higher dose of the treatment. The decision to increase the dose level – "dose escalation" – was made after reviewing safety results from people who had already been treated at the lower dose levels.

Randomized study
A computer randomly decided which person got RO7303509 and who got placebo. Researchers and people had no control over this.

Double-blind study
The researchers and people in the study did not know who was getting RO7303509 and who was getting the placebo. That made it a double-blind study.

Placebo-controlled study
Some people got RO7303509 while others got a placebo. This was done so that the treatment with RO7303509 could be compared to the treatment with placebo – to find out the real effect of RO7303509.

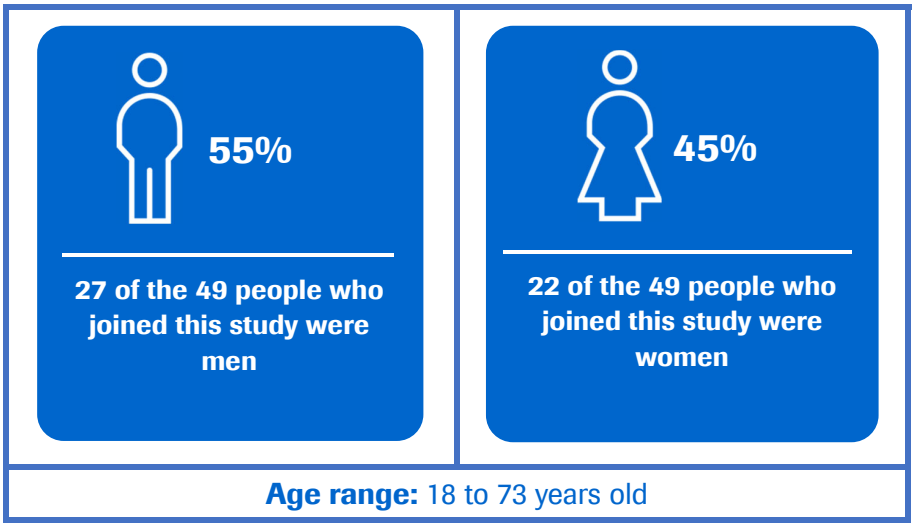
When and where did the study take place?

The study started in September 2020 and finished in May 2022. This summary was written after the study had ended.

The study took place at one study center in the USA.

2. Who took part in this study?

Forty-nine healthy people took part in this study.



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

- They were between 18 and 75 years old.
- They weighed 50-150 kg.
- They met a certain height-to-weight ratio (body mass index: 18-32 kg/m^2).
- They were able to follow study instructions and signed a consent form.
- They met the health requirements for this study.
- They were able to stop using alcohol, tobacco, nicotine products, and illegal drugs while on the study.
- Men and women agreed to use birth control during the study. Men could not donate sperm for some time after dosing.

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

- Women who were pregnant, breastfeeding, or intended to become pregnant during the study.
- Recent history of major surgery or plans for one in the near future.
- History of health condition – or a current health condition – from a list of conditions not allowed in this study.
- Illegal drug use in the past 12 months or tobacco and nicotine use in the last 3 months.
- Recent use of prescription medicines not allowed in this study.
- Recent participation in another clinical trial.

3. What happened during the study?

Screening
Researchers asked people questions and did tests to decide whether they could take part in this study. This happened during 35 days before the study started.

Checking in
People checked into the study center on Day -1. This was one day before they got their treatments.

Randomization
On Day 1, people were selected by chance to get either the study medicine or placebo. They got their treatment on Day 1. They stayed at the study center from Day -1 to Day 3.

Follow-up
People returned to the clinic several times for follow-up visits, until Day 85.

Dose escalation
When enough information was available to show that a dose level was safe, researchers started the process all over to enroll people for the next higher dose group.

Treatment groups

- Intravenous treatment (**IV**) delivered through a vein for 25 people in Groups A, B, and C. This included 18 who got RO7303509 and 7 who got placebo.
- Subcutaneous treatment (**SC**) delivered through an injection under the skin for 24 people in Groups D, E, and F. This included 18 who got RO7303509 and 6 who got placebo.
- IV and SC doses of RO7303509 were given in milligram amounts (**mg**).

Treatment Group	Dose	People who got RO7303509	People who got placebo
A	50 mg IV	6	2
B	150 mg IV	6	3
C	240 mg IV	6	2
D	240 mg SC	6	2
E	675 mg SC	6	2
F	1200 mg SC	6	2
		Total = 36 people	Total = 13 people

4. What were the results of the study?

Everyone in the study received one treatment. Most of the people came to all their follow-up visits and completed the study. Only 4 people dropped out of the study before completing all their follow-up visits, for which one subject was replaced in Cohort B.

Question 1: How safe was it for people to get a single treatment of RO7303509 – given at different doses to different groups of people?

Researchers looked at people who got RO7303509 between 50 and 1200 mg. There were no deaths in this study and nobody dropped out of the study because of side effects.

- Nobody got a serious side effect thought to be caused by the IV or SC treatments.
- Some people got a side effect that was not serious but was thought to be caused by the study treatments.
- Nobody withdrew from the study because of side effects.
- All side effects went away (**resolved**).

The results in this study showed that a single dose of RO7303509 was safe for people to get at the doses tested in this study. These results are from a small group of healthy people and may differ for another group of people.

5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happened during the study.

- If they are described in this summary, it is because the study doctor believes the side effects were related to the treatments in the study.
- Not all of the people in any one study get all of the side effects listed for that study.
- 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, or those that appear on the medicine leaflet.
- If any serious and common side effects were experienced in this study, they will be listed in the following sections.

Serious side effects

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

During this study, nobody got a serious side effect.

During this study, there were no deaths. Nobody dropped out of the study because of side effects from study treatments.

Most common side effects

During this study, some people got a side effect that was not serious – but doctors thought it was caused by the study treatment. The side effects were:

- Infusion-related reactions (IRR) in 3 people among the 25 who got IV treatments
    - One out of 18 people (6%) who got RO7303509
    - Two out of 7 people (29%) who got placebo
    - IRR can be any of several symptoms from getting an IV, such as itchy skin, rash, swelling, redness, sore site, fever, chills, and shortness of breath, among others.
- Injection-site reactions (ISR) in 5 people among the 24 who got SC treatments
    - Four out of 18 people (22%) who got RO7303509
    - One out of 6 people (17%) who got placebo
    - ISR can be any of several symptoms from getting an injection, such as pain, itching, and swelling around the injection site, among others.

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 49 healthy. These results helped researchers learn more about the study medicine. There was no benefit from the medicine to people in this study.

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7. Are there plans for other studies?

At the time of writing this summary, another study looking at RO7303509 had started.

8. Where can I find more information?

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

https://www.isrctn.com/ISRCTN13175485

https://forpatients.roche.com/en/trials/healthy-volunteers/a-study-to-look-at-how-safe-different-doses-of-a-new-study-medic.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 the study is: A phase 1a, randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability, and pharmacokinetics of single ascending doses of RO7303509 in healthy volunteers.

- The protocol number for this study is GA42285.
- The ISRCTN clinical trial number for this study is 13175485.