Summary of Clinical Trial Results

A study to look at two generations of a medicine (zinpentraxin alfa) – that were manufactured in two different ways – how do they move through the body, from absorption to elimination

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 2022 and stopped early – in October 2022 – because the study sponsor decided to end the program for developing this medicine. This summary was written after the study had stopped.

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.

- **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 people who took part in this study have helped researchers answer important questions about zinpentraxin alfa.

Key information about this study

- This study was done to compare two generations of a study medicine, how they moved through the body, from absorption to elimination.
- People in this study were given first and second generation zinpentraxin alfa, a medicine under development for lung disease, manufactured in two different ways.
- This study included 44 people in one country, the USA.
- The main finding was that after giving the same dose to people, the second generation zinpentraxin alfa was found to have a higher concentration present in the blood, compared to the first generation zinpentraxin alfa.
- No one in this study experienced any serious side effects. Six people (14%) experienced side effects that were not serious, but study doctors thought they might be caused by the study medicine.
- This study stopped early because the study sponsor decided to end the program for developing this medicine.

1. General information about this study

Why was this study done?

Idiopathic pulmonary fibrosis (IPF) is a type of lung disease. There is “fibrosis” which is a process that generates scar tissue. This stiffens the lungs and makes it difficult to breathe. The fibrosis gets worse over time. Only 20% to 40% of people live past 5 years after diagnosis.

Currently available treatments are not very effective in slowing down the disease. In addition, they come with side effects that some people do not tolerate well. There is a need for more effective treatments with fewer side effects.

Zinpentraxin alfa is a study medicine being developed for IPF. It is a man-made version of pentraxin-2 (PTX-2), which is a naturally circulating protein in the body.

PTX-2 travels around the body, and attaches to dead or damaged cells, and scar tissue. It aids special cells in the spleen and liver to get rid of the debris. This helps to turn off inflammation and fibrosis, and stimulates the creation of more healing cells.

People with IPF have lower levels of PTX-2 in their blood, compared to healthy people. By injecting zinpentraxin alfa into the bloodstream, you can increase the levels of PTX-2 in the blood and at the sites where the disease is active. This could help decrease fibrosis.

In the beginning, researchers started working with zinpentraxin alfa that was made one way. This was the "first generation" zinpentraxin alfa. Later, the manufacturing process was improved. Then, the "second generation" zinpentraxin alfa became available. That means the medicine is made in two ways.

This study was done to compare how the first and second generation of the study medicine behaved in the body. Results from this study would help researchers predict the concentration of the first and second generation medicine in the body, at any given time after getting the medicine.

What was the study medicine?

The study medicine, **zinpentraxin alfa**, is also known by other names:

- RO7490677
- PRM-151
- Recombinant human pentraxin-2 (rhPTX-2)

In this study, people got the first and second generation zinpentraxin alfa.

What did researchers want to find out?

Researchers wanted to compare how the medicines – created by the two manufacturing processes – behaved in the body.

The main questions that researchers wanted to answer were:

1. How does the body handle the first and second generation zinpentraxin alfa when given through an IV?
2. What were the side effects of a single dose of zinpentraxin alfa?
3. Does the body have any immune response to zinpentraxin alfa?

What kind of study was this?

Pharmacokinetic study
This is a type of study that looks at how a medicine moves through the body. It studies how quickly and effectively the medicine is absorbed by the body, distributed within it, broken down, and finally eliminated from the body. It helps in understanding how often and what dose of the study medicine should be given to maintain the desired concentration in the body.

Phase 1 study
This was a small study to find out some basic information that would be helpful to know about the study medicine.

Randomized study
It was decided by chance who joined which treatment group. It was like flipping a coin to decide which group to join. This was done to reduce bias in the study results.

Double-blind study
Neither the people in the study nor the researchers knew who was receiving which treatment. This was done to reduce bias in the study results.

Crossover study
People in the study were randomized into Group 1 to receive Treatment A, and Group 2 to receive Treatment B. After a "washout period" to allow the first treatment to leave the body, each group “crossed over” (or switched) to the other treatment. This type of study allowed researchers to compare different treatments in the same person. It was also designed to show that the treatment sequence does not affect the results.

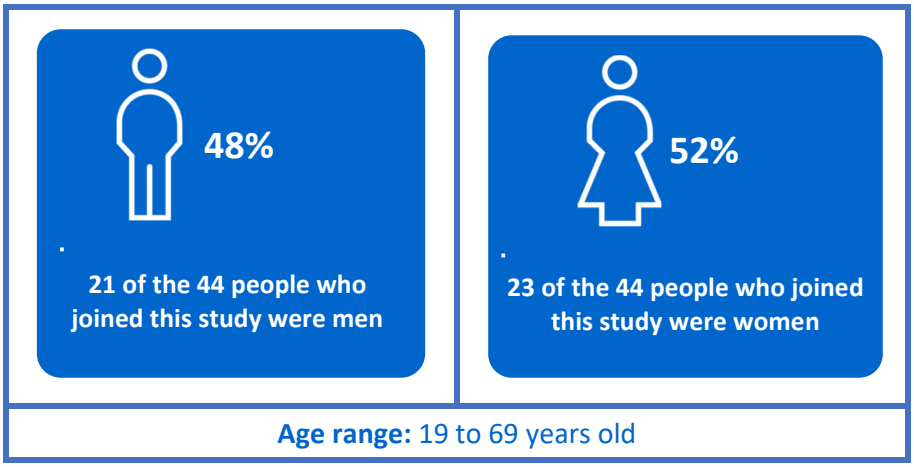
When and where did the study take place?

The study started in June 2022 and stopped early because the study sponsor decided to end the program for developing this medicine. This summary presents the results of the study up until it was stopped in October 2022.

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

2. Who took part in this study?

Forty-four healthy people took part in this study.



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

- Males and females between 18 and 70 years old who agreed to use birth control during and after the study for a specified time
- Females were not pregnant or breastfeeding
- They met the height to weight ratio (BMI 18-36 kg/m^2)
- In good health (medical history, ECG test, vital signs, blood test results)
- Negative results for drug and alcohol tests

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

- History or presence of health conditions not allowed in study
- Previously received zinpentraxin alfa
- Recent surgery, hospitalization, or surgery planned within a restricted period
- History of drug or alcohol addiction within the past year
- Use of any medicine (prescription, over-the-counter, vaccinations, or investigational) during a restricted period
- Use of tobacco or nicotine-containing products during a restricted period
- Eating or drinking anything with alcohol or caffeine, during a restricted period
- Participating in strenuous exercise during the week before the study started
- Blood donation, blood loss, or received blood products during a restricted period
- Females who were pregnant, producing milk (lactating), or breastfeeding

3. What happened during the study?

Screening: Researchers asked questions and did medical tests to see if people interested in joining the study met all the study conditions. This happened up to 35 days before the study started.

Treatment: There were two treatments that were given into the vein through an IV (intravenously):

- Treatment A: first generation zinpentraxin alfa
- Treatment B: second generation zinpentraxin alfa

Treatment groups: People were randomized to join one of two groups. The treatments were given in the following order to each group:

- Group 1: Treatment A, followed by B
- Group 2: Treatment B, followed by A

What happened: One day before treatment (Day -1), people checked into the study center. On treatment day (Day 1), they were randomized into two groups and received their first treatment. On Day 8, they got their second treatment. On Day 15, they went home.

Each treatment (A, B) (one single dose) was given at least 7 days apart. This was the "washout" period that allowed for the medicine to become undetectable in the body before the next treatment.

Researchers collected blood samples, did medical tests, and asked questions at several time points before and after dosing.

4. What were the results of the study?

Question 1: How does the body handle the first and second generation zinpentraxin alfa when given through an IV?

Researchers measured zinpentraxin alfa present in blood samples that were collected throughout the study. They were interested to know how the body handled the medicine over time.

Peak exposure is the highest concentration of a medicine that is found in the body after a person has been given the medicine dose. At peak exposure, the medicine found in blood reaches the maximum concentration possible for the dose given.

Total exposure is a measure of the amount of medicine that the body is exposed to, over time. It takes into account the concentration of the medicine, and the length of time the medicine stays in the body. This number tells researchers how much of the medicine the body is exposed to, over the course of the treatment.

In this study, researchers found that the peak exposure and total exposure were slightly higher following the second generation zinpentraxin alfa formulation – in comparison to the first generation formulation.

The time it took for the blood concentrations to fall to half of the peak level – were similar for the first and second generation zinpentraxin alfa.

Question 2: What were the side effects of a single dose of zinpentraxin alfa?

Researchers looked at side effects, and any changes in blood test results, heart rate measures, vital signs, and physical exams.
Seven side effects were reported by six people (14%) that were thought to be caused by zinpentraxin alfa. Two people (5%) had side effects after the first generation zinpentraxin alfa, and four people (9%) after the second generation zinpentraxin alfa. Side effects are discussed in detail in Section 5.

Question 3: Does the body make any immune response to zinpentraxin alfa?

Researchers checked for antibodies against zinpentraxin alfa. They tested blood samples before and after treatments. Sometimes, your body can treat a medicine like a threat and have an immune response to try and get rid of the medicine. That would affect how the medicine works. Everyone in this study was negative to such antibodies before and after dosing.

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 feeling dizzy) 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.
- Everybody in a study will not 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, or those that appear on the medicine leaflet.
- 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, needs hospital care, or causes lasting problems.

There were no serious side effects during this study.

There were no deaths due to side effects.
Two people (5%) left the study because of side effects following the second generation zinpentraxin alfa.

Most common side effects

Six people (14%) reported a total of 7 side effects that were not serious, but study doctors thought they might be caused by zinpentraxin alfa.

Side effect	Among 44 people who got first generation zinpentraxin alfa	Among 44 people who got second generation zinpentraxin alfa
Symptoms like fever, chills, rash, breathing difficulties, nausea, and headache. – during or soon after an infusion (infusion-related reaction)	-	2 people (5%)
Reaction such as redness and pain in the area where medicines or fluids have been put into the blood through the skin (infusion site reaction)	1 person (2%)	1 person (2%)
Blood test abnormal (an increase in alanine aminotransferase, a liver enzyme)	-	1 person (2%)
Blood test abnormal (an increase in aspartate aminotransferase, a liver enzyme)	-	1 person (2%)
Headache	1 person (2%)	-

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 44 healthy people. These results helped researchers learn more about the first and second generation zinpentraxin alfa.

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.

- **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.**

7. Are there plans for other studies?

At the time of writing this summary, no more studies looking at zinpentraxin alfa were planned.

8. Where can I find more information?

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

- https://www.isrctn.com/ISRCTN59409907
- https://forpatients.roche.com/en/trials/respiratory-disorder/ipf/a-phase-1-double-blind--randomized--two-arm--two-way-crossover--.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 1 double-blind, randomized, two-arm, two-way crossover, sequential two-stage study to assess the pharmacokinetic comparability of first and second generation RO7490677 (recombinant human pentraxin-2; rhPTX-2) drug products in healthy subjects

The protocol number for this study is:

GP44111

The “International Standard Randomized Controlled Trial Number” for this study is:

ISRCTN59409907