Summary of Clinical Trial Results

What happens to a medicine (pralsetinib) when given to people with unhealthy livers

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 December 2021 and finished in October 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.

- **This means that you should not make decisions based on this one summary.**
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Contents of the summary

Thank you to the people who took part in this study

The people who took part have helped researchers answer important questions about liver disease and its effect on pralsetinib, the study medicine.

Key information about this study

- This study was done to find out how the health status of the liver affects the total amount of study medicine, pralsetinib, found in blood after dosing.
- People with healthy livers and those with different stages of liver disease were given pralsetinib.
- Researchers measured pralsetinib in blood samples collected at different times before and after pralsetinib dosing.
- This study included a total of 29 people in the USA.
- The main finding was that the overall pralsetinib found in blood was similar between people with healthy livers and those with moderate and severe liver disease. However, the highest amount of pralsetinib found in blood was slightly lower in people with severe liver disease.
- In this study, there were no serious side effects. One person with severe liver disease and another with healthy liver function – had side effects that were not serious but doctors thought they were caused by the study medicine. The side effects went away (resolved) by the end of the study.
- Overall, the effect of moderate and severe liver disease on the amount of pralsetinib in the blood was small.

1. General information about this study

Why was this study done?

When people take a dose of medicine, health and function of the liver can affect the amount of medicine that can be measured in blood. This study was done to find out how liver function – healthy versus moderate and severe liver disease – affected the amount of the study medicine in the body.

What was the study medicine?

Pralsetinib is a medicine that has been approved for a type of lung cancer and a type of thyroid cancer. It is an inhibitor of "rearranged during transfection" (RET) proteins that have mutations (oncogenic proteins) or are stuck together (fusion proteins). That means, pralsetinib slows or stops the activity of those proteins that have changed in a way that helps the cancer grow.

What did researchers want to find out?

The main question that researchers wanted to answer was:

1. How does pralsetinib behave in the body when given to people with moderate or severe liver disease – in comparison to people with healthy liver function?

What kind of study was this?

There are several ways to describe this study.

Phase 1 study
This was a "Phase 1" study to gather information about the study medicine. A small number of healthy people - and those with moderate and severe liver disease – were given the study medicine. Information from this study may be used to guide other studies with more people or to help your doctor give the medicine safely to people with liver disease.

Open-label study
Researchers and people in the study knew that they were receiving the study medicine, pralsetinb. That made it an "open-label" study.

Single dose study
People in the study received a single dose of the study medicine.

Parallel group study
People joined one of three study groups. The liver health status of each group was different – this is what was being compared between the groups – while all groups received the same study medicine. This made it a "parallel group" study.

When and where did the study take place?

The study started in December 2021 and finished in October 2022. This summary was written after the study had ended.

The study took place at four study centers across one country – the USA.

2. Who took part in this study?

Twenty-nine people took part in this study.

		Group 1 Healthy liver function	Group 2 Moderate liver disease	Group 3 Severe liver disease	All
Number of people		14	9	6	29
Average age (years)		57	57	61	58
Sex	**Male**	10 (71%)	7 (78%)	5 (83%)	22 (76%)
	Female	4 (29%)	2 (22%)	1 (17%)	7 (24%)

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

- Women who were not pregnant or breastfeeding, and could not become pregnant
- Men who were sterile or used birth control, and agreed not to donate sperm for 14 days after dosing
- Between 18 and 74 years old
- Met a certain height to weight ratio (BMI 17-38 kg/m^2)
- In good health other than for liver disease for people in Groups 2 and 3
- Tested negative for drug abuse

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

- Sickness during the 2 weeks before study start (infections, surgery, or hospital stays) – unless it was because of liver disease (Groups 2 and 3)
- A history of having surgical or artificial shunts
- A history of, or current health issues that were not allowed
- A history of drug, alcohol, or nicotine use during a period when it was not allowed
- Exposure to medicines from a list of medicines that were not allowed
- Use of food/drinks from a list of items not allowed 3 days before study start
- Strenuous exercise within 2 days before study start
- Donating or receiving blood products during a period when it was not allowed

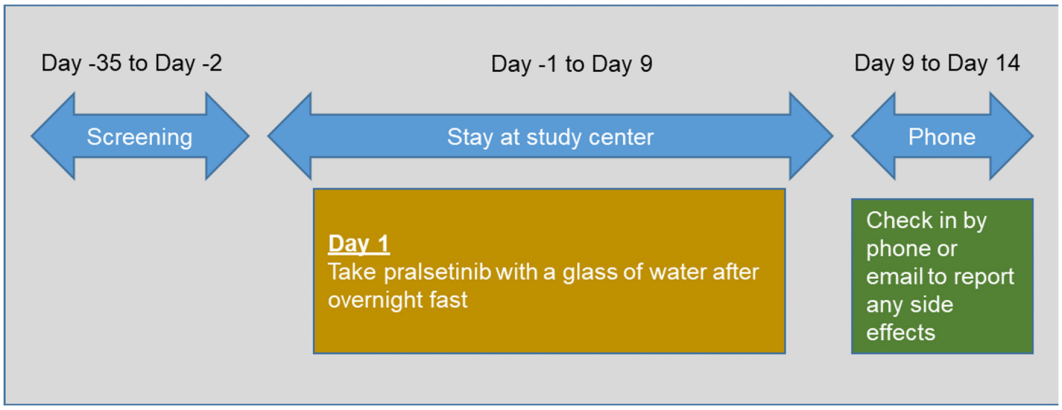
3. What happened during the study?

Study staff examined (**screened**) the people who wanted to join the study – for up to 35 days before the study started.

Those people who passed the screening were able to join the study – they checked into the study center one day before getting the medicine – this was **Day –1**. Study staff collected blood samples, asked questions, and did medical tests to determine the person's medical status before the study medicine was given.

People joined one of three groups, based on the results of their liver function test:

- Group 1: Healthy liver function
- Group 2: Moderate liver disease
- Group 3: Severe liver disease



Treatment on Day 1

On Day 1, after fasting overnight for at least 8 hours, people in the study took pralsetinib with water in the morning – and fasted for another two hours after taking pralsetinib. People could drink water freely at all times except during an hour before and two hours after taking pralsetinib.

What happened after the treatments

- The study center staff collected blood samples before and at several time points after treatment. Medical examinations were performed throughout the study
- The people stayed at the study center until Day 9, and then they went home.
- They talked on the phone with study staff up to Day 14 to report any side effects.

4. What were the results of the study?

Question 1: How does pralsetinib behave in the body when given to people with moderate or severe liver disease – in comparison to people with healthy liver function?

- The main finding was that the overall pralsetinib found in the body was similar between people with healthy livers and those with moderate and severe liver disease.
- However, the highest amount of pralsetinib in the blood was lower in people with severe liver disease.

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.

- They are described in this summary 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 experience 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.
- If serious and common side effects were seen 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.

- There were no serious side effects seen in this study.
- No one withdrew from the study because of side effects.

Most common side effects

During this study, two people had side effects that were not serious but the study staff thought they were caused by the study medicine.

- One person in Group 1 (healthy liver function) had a headache.
- One person in Group 3 (severe liver disease) had an abnormal electrocardiogram (ECG) test result.
- Both side effects went away by the end of the study.

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 29 people, 15 of whom had moderate or severe liver disease, and the remaining 14 people had healthy livers. These results helped researchers learn more about how pralsetinib behaves in the body of people with healthy livers and those with moderate and severe liver disease.

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7. Are there plans for other studies?

Studies with pralsetinib are still happening.

8. Where can I find more information?

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

- https://doi.org/10.1186/ISRCTN38890848
- https://forpatients.roche.com/en/trials/metabolic-disorder/hepatic-insufficiency/a-study-to-evaluate-the-processing-by-the-body-and-safety-of-pra.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, open-label, single-dose study to evaluate the pharmacokinetics and safety of pralsetinib in subjects with moderate or severe hepatic impairment compared to healthy subjects.

- The protocol number for this study is GP43163.
- The International Standard Randomized Controlled Trial Number (ISRCTN) identifier for this study is 38890848.