# Summary of Clinical Trial Results

## How does the body process a cancer medicine (pralsetinib) – when it is taken together with another medicine (cyclosporine)

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 February 2022 and finished in April 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 have helped researchers answer important questions about the medicine studied – pralsetinib.

## Key information about this study

- This study was done to find out the effect taking a second medicine known to potentially interfere with the first medicine.
- In this study, people were given the medicine being studied (called pralsetinib) – with or without cyclosporine. Cyclosporine belongs to a group of medicines known to interfere with a protein that pumps pralsetinib out of the body.
- This study included 15 people at one study center in USA.
- The main finding was that taking cyclosporine with pralsetinib increased the amount of pralsetinib in the body – in comparison to taking pralsetinib alone.
- There were no serious side effects caused by the study medicine.

# 1. General information about this study

### Why was this study done?

There are several proteins in the human body that can affect the amount of medicine that gets in the body – after a person takes the medicine by mouth.

One such protein is "P-glycoprotein" or "**P-gp**", found on cells lining the gut. P-gp is able to pump out certain medicines that people take. The medicines are pumped from inside the cells into the gut for removal in the feces. The medicines that Pgp can pump out are called "substrates of P-gp".

Pralsetinib is a medicine taken by mouth that is pumped out by P-gp – **pralsetinib is a substrate of P-pg**. That means pralsetinib must be given to people at a higher dose than the amount needed in the body.

Researchers have already found out how much pralsetinib to give to people for it to be effective. Today, pralsetinib is an approved medicine used by doctors for treating patients with certain types of cancer.

Doctors watch what other medicines people take while taking pralsetinib. Taking other medicines could affect the amount of pralsetinib in the body. "**Drug-drug interaction**" is a term used to describe when one medicine affects another medicine.

Cyclosporine is a medicine that may cause drug-drug interaction with pralsetinib. Cyclosporine belongs to a group of medicines known to interfere with P-gp – **cyclosporine is an inhibitor of P-gp**.

If cyclosporine interferes with P-gp, then P-gp will not be able to pump out pralsetinib as well as in the absence of cyclosporine. This will increase the amount of pralsetinib in the body – compared to when pralsetinib is taken alone.

In this study, researchers wanted to find out how much pralsetinib is absorbed into the body when taken together with a medicine that interferes with P-gp – such as cyclosporine.

## What were the study medicines?

This study looked at two medicines.

**Pralsetinib:**

- "RET receptor tyrosine kinase" or "**RET kinase**" is a protein in cells that can become overactive (**aberrant**) which causes uncontrolled cell growth and cancer.
- Pralsetinib is a medicine that interferes with (inhibits) RET kinase – it is a **RET kinase inhibitor**.
- Pralsetinib is an approved medicine given to patients who have certain types of lung and thyroid cancers that test positive for defective RET kinase.
- A protein, P-glycoprotein (**P-gp**), found on cells lining the gut, pumps out pralsetinib for removal in the feces. This makes pralsetinib a **P-gp substrate**.

**Cyclosporine:**

- Cyclosporine is a medicine that calms the immune system – it is an "**immunosuppressive agent**".
- Cyclosporine is given to people with certain types of diseases that have inflammation, and it is also given after an organ transplant.
- Cyclosporine interferes with the P-gp pump. This makes cyclosporine a **P-gp inhibitor**.
- When a P-gp inhibitor medicine is taken together with a P-gp substrate medicine, there could be a drug-drug interaction.

## What did researchers want to find out?

Researchers did this study to compare the amount of pralsetinib absorbed into the body when it was taken with cyclosporine – in comparison to when pralsetinib was taken alone.

**The main question that researchers wanted to answer was:**

1. What was the effect of a single dose of cyclosporine – on a single dose of pralsetinib?

**Another question that researchers wanted to answer included:**

2. How safe was it to give pralsetinib with cyclosporine – in comparison to giving pralsetinib alone?

## What kind of study was this?

This was a "**Phase 1**" study, which means that this was a small study to answer some basic questions about pralsetinib. A small number of healthy people got the treatments. The researchers did medical tests to collect information about the treatments.

This was an "**open-label study**". That means the researchers and people who took part in the study knew which medicine the people were getting.

This was a "**fixed sequence**" study. That means everyone in the study got their treatments in the same order – that was already decided by the researchers.

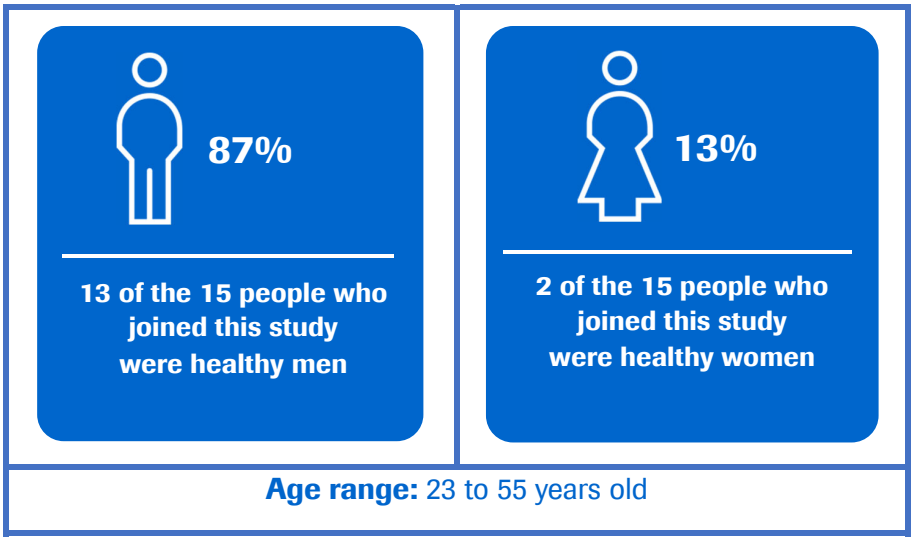
### When and where did the study take place?

The study started in February 2022 and finished in April 2022. This summary was written after the study had ended.

The study took place at one study center in USA.

## 2. Who took part in this study?

Fifteen healthy people took part in this study.




**People could take part in the study if:**

- They were men who agreed they would not donate sperm for 90 days out from the last dose of the study medicine. They also agreed to use methods to prevent their partners from getting pregnant for 90 days out from the last dose of the study medicine.
- They were women who could not get pregnant, were not pregnant, and were not breastfeeding.
- They were between the ages of 18 and 55 years.
- They had a certain height to weight ratio.
- They tested negative for coronavirus and human immunodeficiency virus (HIV).

**People could not take part in the study if:**

- They had health issues that excluded them from the study.
- They recently used medicines that were not allowed.
- They had stomach or intestinal surgery that would have changed the absorption or removal (by P-gp) of the study medicine.
- They had a recent history of drug or alcohol addiction, or nicotine use.
- They had recently participated in another study so that it was possible that there was some other study medicine remaining in their bodies.
- They planned to do strenuous exercise while on the study.

## 3. What happened during the study?

Doctors 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 joined the study – they checked into the study center one day before getting the medicine – this was **Day -1**.

### Treatment on Day 1

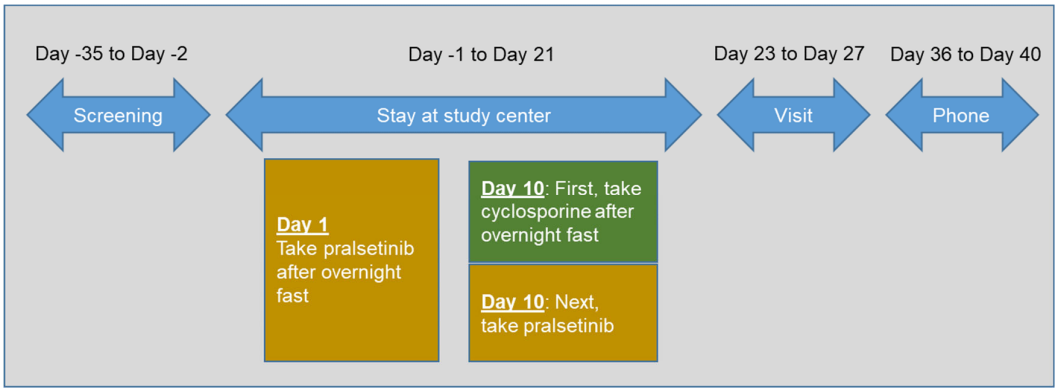
On Day 1, everyone got pralsetinib pills – taken with water in the morning – after fasting overnight for 10 hours.

### Treatment on Day 10

On Day 10, everyone got cyclosporine pills, followed by pralsetinib pills – taken with water in the morning – after fasting overnight for 10 hours.

### What happened after the treatments

- The study center staff collected blood and urine samples before treatment – and at several time points after the first and second treatments. Medical examinations were performed throughout the study
- The people stayed at the study center until Day 21, and then they went home.
- They returned for a follow-up visit between Day 23 and Day 27.
- They talked on the phone with study staff sometime between Day 36 and Day 40.



## 4. What were the results of the study?

### **Question 1:** What was the effect of a single dose of cyclosporine – on a single dose on pralsetinib?

Researchers looked at the level of pralsetinib in the blood – when it was taken alone on Day 1. This was compared to the level of pralsetinib in the blood – when it was taken with cyclosporine on Day 10.

There was a 9-day "**washout**" before the second dose – this was the time allowed for the first dose taken on Day 1 to disappear from the body. Tests were done to make sure pralsetinib was absent in the blood before the second dose was taken on Day 10.

Researchers looked at the amount of medicine (concentration) as well as how long (time) the medicine was present in blood.

- The body was exposed to 81% more pralsetinib when taken together with cyclosporine – in comparison to when pralsetinib was taken alone.
- The highest concentration of pralsetinib in the body increased by 48% when taken together with cyclosporine – in comparison to when pralsetinib was taken alone.

### **Question 2:** How safe was it to give pralsetinib with cyclosporine – in comparison to giving pralsetinib alone?

This was a small study of 15 people. The side effects seen in this study were consistent with the side effects reported in previous studies for pralsetinib.

When pralsetinib was combined with cyclosporine, there were more side effects in comparison to pralsetinib given alone.

This section only shows the key results from this study. You can find information about all other results on the websites listed 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 this study had 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.

### 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 reported in this study.

Nobody stopped taking their medicine because of side effects and there were no deaths.

### Most common side effects

Six of the 15 people in this study (40%) reported a total of 9 side effects that were not serious – but were thought to be caused by the study medicine.

Some people had more than one side effect.

The most common side effect was constipation, experienced by 3 people in the study. The other 6 side effects were only seen one time:

- Feeling sick to the stomach (nausea).
- Abnormal liver test (alanine aminotransferase increased).
- Abnormal liver test (aspartate aminotransferase increased).
- Abnormal blood test (neutropenia).
- Rapid heartbeat (palpitations).
- Redness to the skin (flushing).

### 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 15 healthy volunteers. These results helped researchers learn more about drug-drug interactions that could happen when pralsetinib is taken with a medicine that is a P-gp inhibitor – such as cyclosporine.

Researchers learned how much more pralsetinib becomes available in the body when taken with cyclosporine, a P-gp inhibitor medicine.

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## 7. Are there plans for other studies?

Other 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://www.isrctn.com/ISRCTN57377850

https://forpatients.roche.com/en/trials/cancer/how-does-the-body-process-a-cancer-medicine--pralsetinib----when.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, fixed-sequence study to evaluate the effect of a single dose of cyclosporine on the single dose pharmacokinetics of pralsetinib in healthy subjects.

- The protocol number for this study is GP43162.
- The clinical trial number for this at ISRCTN registry is 57377850.