Summary of Clinical Trial Results

A study to look at if a certain type of medicine affected how the body processed the study medicine (RO6953958) and how safe the study medicine was in healthy people

Full title: A non-randomized, open-label, single sequence, two-period study to investigate the effect of CYP3A inhibition on the pharmacokinetics of RO6953958 in healthy participants.

The protocol number for this study is: BP43293

About this summary

This is a summary of the results of a clinical trial (called a 'study' in this document) – written for:

- members of the public and
- people who took part in the study.

This summary is based on information known at the time of writing (July 2023). More information may now be known.

The study started in October 2021 and finished in January 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 lots of people in many 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 have helped researchers to answer important questions about how the body processed the study medicine and if this process was affected by other medicines.

Key information about this study

- This study was done to look at how medicines that stop a certain protein called CYPA3 from working, affect how the body processes the study medicine and the safety of the study medicine under these conditions.
- The study was done in 2 parts. In Part 1, people were given the study medicine only. In Part 2, people were given the study medicine with another medicine called itraconazole.
- The study included 16 people in the United States.
- The main finding was that itraconazole affected and altered how the body processed the study medicine. Researchers think that the study medicine should not be given with other medicines that stop a certain protein, called CYPA3, from working.
- Overall, the study medicine was well-tolerated and most side effects were mild.
- None of the people taking part in the study had a serious side effect.

1. General information about this study

Why was this study done?

People with psychiatric conditions and/or conditions that affect brain development (known as neurodevelopmental disorders, or NDDs) can also have sleep issues. This makes daily life more difficult for people with these conditions and their caregivers.

Nerves in the brain control the body's internal clock so that you wake and do not feel too sleepy during the day, and you feel tired and sleep when it is dark. When you sleep, your body slows down its activity, and your temperature drops slightly. When it is time to wake up, the body produces more of a molecule called vasopressin (you say this as 'vay–zo–press–in') that activates the nerves in the brain and tells the body to get ready for the day. This is known as the sleep-wake cycle, or circadian (you say this as 'ser–cay–dee–an') rhythm.

Sleep issues in people with psychiatric disorders and/or NDDs may be due to the circadian and vasopressin system not working correctly. The study medicine is an experimental drug that blocks the activation of nerves by vasopressin in the brain and may help correct sleep/wake cycles in people with psychiatric disorders and/or NDDs.

Before a medicine can be given to patients, researchers study it to learn more about how it is processed in the body and how other medicines may affect this process. When medicines interact with each other, this may cause one of the medicines to not work very well or have worse side effects. So, in this study, researchers wanted to find out how a medicine called itraconazole (you say this as 'in·truh·ko·nuh·zl) affected how the body processed the study medicine. Itraconazole stops a certain protein called CYPA3 from working. Researchers think this may increase how much the study medicine gets into the blood and how long it remains in blood. This information is important to know before the study medicine can be given to patients.

What was the medicine being studied?

A medicine called 'RO6953958' was the focus of this study.

- The study medicine works by blocking the activity of nerves in the brain that are involved in the body's sleep/wake cycle.
- The study medicine was tested at one dose level when taken on a full stomach, with or without itraconazole.

What did researchers want to find out?

- Researchers did this study to compare how the body processed the study medicine when given with or without itraconazole (see section 4 "What were the results of the study?").
- They also wanted to find out how safe the medicine was – by checking how many people had side effects and seeing how serious they were during this study (see section 5 "What were the side effects?").

The main question that researchers wanted to answer was:

1. Did itraconazole affect how the body processed the study medicine?

What kind of study was this?

This study was a 'Phase 1' study, which means that this was one of the first studies in people for the study medicine. A small number of healthy people (without conditions that affect their sleep) took the study medicine, and the researchers did medical tests on the people who took part to find out more about the study medicine.

The study was done in 2 parts. Both parts of the study were 'open-label'. This means that both the people taking part and the study doctors knew what study medicines people were taking.

In Part 1, the people taking part took the study medicine only. Then, in Part 2, they took the study medicine and itraconazole.

When and where did the study take place?

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

The study took place at one study centre in one country (the United States).

2. Who took part in this study?

In this study, 16 healthy people took part.

People who took part in the study were between 20 and 53 years of age. 9 of the 16 people (56%) were male and 7 of the 16 people (44%) were female.

People could take part in the study if they:

- Had a body weight that was healthy to slightly obese based on their body mass index, or BMI.
- Were considered generally healthy and well (without conditions that affect their sleep).

People could not take part in the study if they:

- Have had certain medical conditions that may affect their ability to complete the study.
- Have had certain medical conditions that affect how medicines are processed through the body.

3. What happened during the study?

During the study, everyone was given the study medicine once in Part 1 and then once in Part 2.

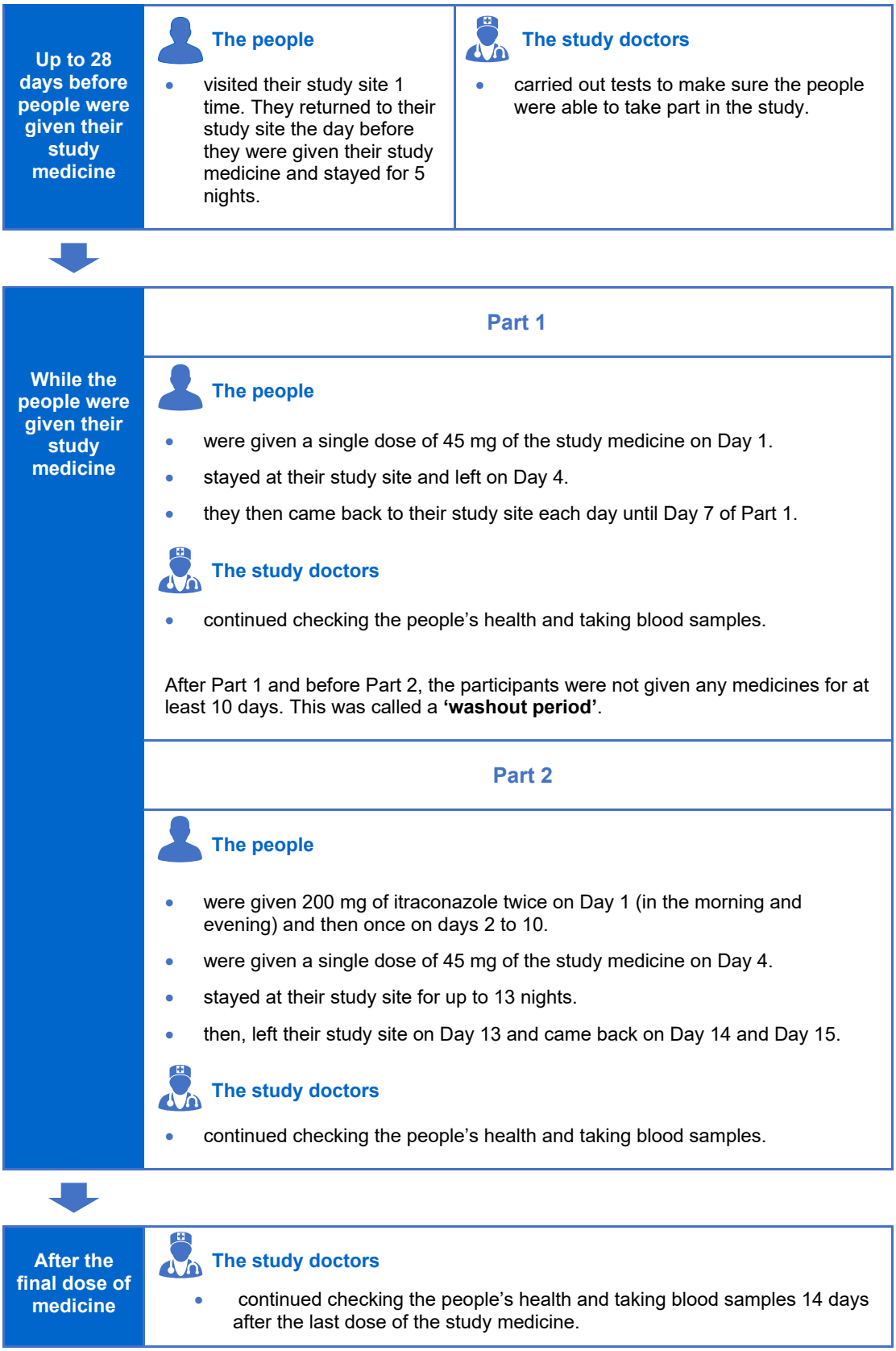
In **Part 1**, everyone was given:

- A single dose of 45 milligrams (mg) of the study medicine taken by mouth (swallowed) on a full stomach.

In **Part 2**, everyone was given:

- A dose of 200 mg of **itraconazole** twice on Day 1, and a dose of 200mg of **itraconazole** once on days 2 to 10 - taken by mouth (swallowed) on a full stomach.
    - Itraconazole was given in the morning and then 12 hours later in the evening of Day 1. Then, it was given once a day, in the morning of Day 2 to Day 10.
- A single dose of 45 mg of the study medicine on Day 4 on a full stomach.

When the study finished, the people who took part were asked to go back to their study centre for more visits – to check their overall health. This image shows more information about what happened in the study:



4. What were the results of the study?

Did itraconazole affect how the body processed the study medicine?

Researchers looked at whether taking a medicine that stopped the protein CYPA3 from working, like itraconazole, affected how the body processed the study medicine. They also looked at whether taking itraconazole affected how the body processed the parts of the study medicine that remained after the body had broken it down (known as 'metabolites' – you say this as 'meh-tab-oh-lytes').

To answer this question, the study doctors took blood samples at different times after the people who took part in the study were given the study medicine. In these samples, the researchers measured:

- The **highest level** of the study medicine and specific metabolites that were detected in the blood.
- The **total level** of the study medicine and specific metabolites that were detected in the blood.

They then compared the results from Part 1 (where people were only given the study medicine) to Part 2 (where they were given the study medicine with itraconazole).

The researchers found that:

- The **highest level** and the **total level** of the study medicine and one of the metabolites was higher after the study medicine was given with itraconazole in Part 2, compared to when only the study medicine was given in Part 1.
- The **highest level** and the **total level** of the other metabolite was lower after people were given the study medicine with itraconazole in Part 2, compared to when only the study medicine was given in Part 1.
- The study medicine should not be given with a medicine like itraconazole. This is because it affected and altered how the body processed the study medicine.

5. What were the side effects?

Side effects (also known as 'adverse reactions' are unwanted medical problems (such as feeling dizzy) that happen 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.

Serious side effects

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

None of the people taking part in this study had a serious side effect or died during the study due to side effects that may have been related to the study medicine.

During the study, none of the people taking part decided to stop taking the study medicine because of side effects. But, 1 of the people taking part left the study before finishing Part 2 because of a side effect. So, the results for Part 2 include 15 participants.

Side effects

During this study, all side effects were mild or moderate. Around 31% of people taking the study medicine had a side effect that was not considered serious.

The side effects that happened during the study are shown in the following table.

Side effects reported in this study	**People taking the study medicine in Part 1** (16 people total)	**People taking the study medicine with itraconazole in Part 2** (15 people total)
A skin condition that causes acne-like bumps to form, usually on the face, scalp, chest, and upper back	6% (1 out of 16)	None
Abnormal dreams	None	6% (1 out of 15)
Feeling dizzy	None	6% (1 out of 15)
Feeling sleepy or drowsy	None	6% (1 out of 15)
Impaired vision	6% (1 out of 16)	None

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 16 healthy people. These results helped researchers learn more about how the body processed the study medicine and if it was affected by medicines, like itraconazole, that stop CYPA3 from working, and how safe the study medicine is under these conditions.

- Itraconazole affected and altered how the body processed the study medicine.
- The highest level and total level of the study medicine and one of its metabolites was higher when it was given with itraconazole. For another metabolite the total level was lower when the study medicine was given with itraconazole.
- Overall, in both parts of the study, the study medicine was well-tolerated, and most side effects were mild.

- There were no serious side effects, no one stopped treatment due to side effects, and no one died due to study treatment.
- About 31% (5 out of 16) of people who took part in the study had a side effect that was not considered serious.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many 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?

The company (F. Hoffmann-La Roche Ltd) is evaluating whether to run further studies with the study medicine.

8. Where can I find more information?

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

- https://forpatients.roche.com/en/trials/neurodevelopmental-disorder/a-study-to-investigate-the-effect-of-enzyme-inhibition-on-the-bo.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/trials/neurodevelopmental-disorder/a-study-to-investigate-the-effect-of-enzyme-inhibition-on-the-bo.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 organised and paid for this study?

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.