Summary of clinical trial results

A study to look at how a single dose of risperidone was processed through the body when taken with multiple doses of ralmitaront

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) – 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.

The study started in October 2021 and stopped early – in September 2022 – because researchers had enough information about the study medicines. There was also no justification for more participants to be given the study medicines, because the potential risks outweighed the benefits of continuing the study. This summary was written after the study had ended.

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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**

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about the medicines studied – 'risperidone' and 'ralmitaront'.

Key information about this study

- Risperidone is an approved medicine for treating problems with the mind, moods or behaviour (known as 'psychiatric disorders'), such as schizophrenia and schizoaffective disorder
- Ralmitaront is a new investigational medicine – which means it has not been approved for any illness or disorder
- This study looked at the effect of multiple doses of ralmitaront on how the body processes and gets rid of a single dose of risperidone in healthy people
- In this study, a single dose of risperidone was given on its own on Day 1. Then, ralmitaront was given daily from Day 6–15, and risperidone on Day 14
- By taking blood samples over time, researchers could see if the body processed risperidone differently when it was taken on its own or with ralmitaront
- This study included 10 people in 1 country
- The main finding was that higher levels of risperidone were seen in the blood and more quickly after it was taken with ralmitaront compared when risperidone was taken on its own. However, researchers could not be sure this was not due to chance, because fewer people took the study medicines than planned
- No-one taking risperidone and ralmitaront had serious side effects

1. General information about this study

Why was this study done?

Dopamine and serotonin are chemicals that carry messages between brain cells. These chemicals are important for controlling different functions such as memory and mood. An abnormal increase in dopamine activity has been linked to schizophrenia. Drugs that target dopamine are known to help manage symptoms of schizophrenia. Medicines called antipsychotics, such as risperidone, are the standard treatment, which work by blocking the effect of dopamine on the brain.

The main purpose of this study was to see if a drug interaction exists when the study medicines, ralmitaront and risperidone, are taken together. A drug interaction means one drug alters how another drug works or how it is processed in the body. A drug interaction may cause one of the drugs to not work very well or may make side effects worse.

Risperidone is approved for use in many countries for treating problems with the mind, moods or behaviour (known as 'psychiatric disorders'), such as schizophrenia and schizoaffective disorder. Ralmitaront is a new investigational medicine – this means that it is not approved for sale by any national health authority, including in the United States by the U.S. Food and Drug Administration. Lab tests show ralmitaront balances the level of dopamine in the brain and has the potential to be used to treat schizophrenia.

In the future, people could be given risperidone and ralmitaront together to see how safe it is and how well it works to treat schizophrenia. If ralmitaront is taken with risperidone, ralmitaront may increase the amount of risperidone that gets to the brain. If this happens, risperidone may have a larger effect on the brain and may cause more side effects. To avoid unwanted side effects, the timing of when each dose of risperidone is given to people may need to be adapted in situations where risperidone is given alongside ralmitaront treatment.

What were the study medicines?

This study looked at two medicines:

- **Risperidone** – existing medicine
- **Ralmitaront** – the medicine that was studied

'Risperidone' is an existing medicine given to people with psychiatric disorders.

- You say this as 'ris-PER-i-doan'
- Risperidone may change brain activity by sticking to proteins found on the surface of brain cells. This changes how the brain responds to the chemicals dopamine, serotonin and norepinephrine. Changing how much the brain responds to these chemicals can help treat psychiatric disorders.

'Ralmitaront' is the experimental medicine that was studied here – it works in a different way to risperidone.

- You say this as ral-MIT-a-ront'
- Ralmitaront works by partially blocking the TAAR1 receptor – a protein found on the surface of brain cells. This changes how the brain responds to dopamine and serotonin
- This may mean that ralmitaront could reduce symptoms of schizophrenia

What did researchers want to find out?

- Researchers did this study to look at the effect of multiple doses of ralmitaront on how the body processes and gets rid of a single dose of risperidone in healthy people (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, when taking each of the medicines during this study (see Section 5 'What were the side effects?')

The main questions that researchers wanted to answer were:

1. Does the amount of risperidone in the blood change when it is taken with ralmitaront?
2. Does the time taken for risperidone to reach maximum levels in the blood change when it is taken with ralmitaront?
3. Does ralmitaront change the way the body breaks down and gets rid of risperidone?

What kind of study was this?

This study was a 'phase I' study, which means that this was one of the first studies for ralmitaront. A small number of healthy people (without any psychiatric disorder) took ralmitaront on its own, then with risperidone, and the researchers did medical tests on the people who took part to find out more about how the study medicines affected each other.

This was an 'open label' study. This means that both the people taking part in the study and the study doctors knew which of the study medicines people were taking.

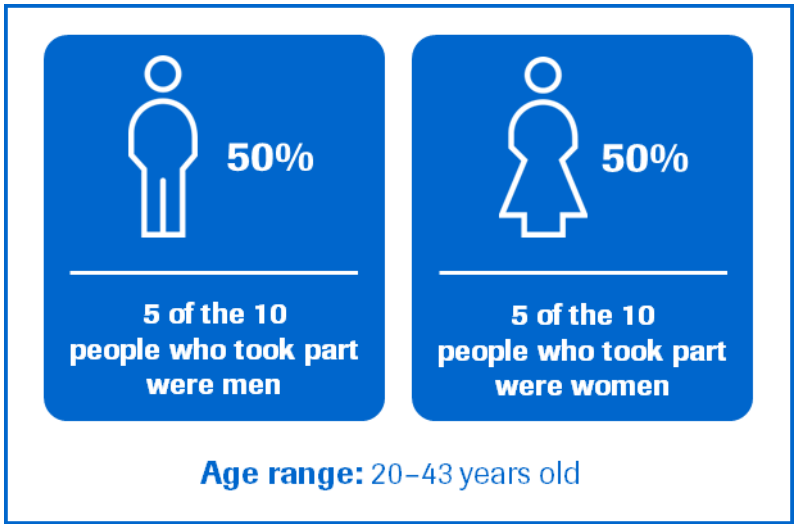
When and where did the study take place?

The study started in October 2021 and stopped early because researchers had enough information about how the study medicines interacted with each other, and to avoid giving more healthy people the study medicines because potential risks outweighed the benefits of continuing the study. This summary presents the results of the study up until it was stopped in September 2022. This summary was written after the study had ended.

The study took place at one study centre in the US.

2. Who took part in this study?

In this study, 10 healthy people took part.



People could take part in the study if:

- They were 18–55 years old, inclusive
- They had a healthy body weight (body mass index of 18–30kg/m^2)
- They agreed to use effective contraception (if necessary)

People could not take part in the study if:

- They had (or recently had) a fever or certain allergies, infections, or diseases such as high or low blood pressure, heart conditions, kidney disease, liver disease, cancer, or problems with the mind, moods or behaviour
- They were taking or had recently taken certain medicines or vaccines
- They were or had recently taken part in one or more clinical study
- They smoked and were not able to not smoke during the study (due to staying at the clinic site)
- They had a strict diet so could not have regular meals
- They were pregnant or breastfeeding

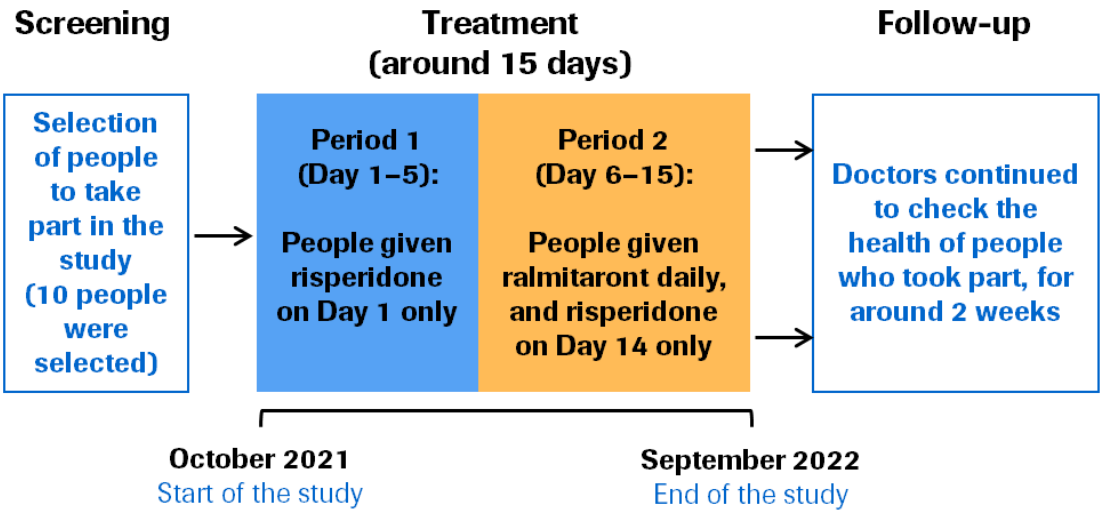
3. What happened during the study?

During the study, people were given risperidone (existing medicine) and ralmitaront (the experimental medicine).

People were given:

- **Risperidone** as a tablet taken by mouth on Day 1 and Day 14 of the study
- **Ralmitaront** as a tablet taken by mouth from Day 6–15 of the study

The study stopped early. After people finished taking their medicine for this study, they were asked to go back to their study centre for more visits – to check their overall health. The study flowchart shows all stages planned for the study. Look below to see more information about what happened in the study.



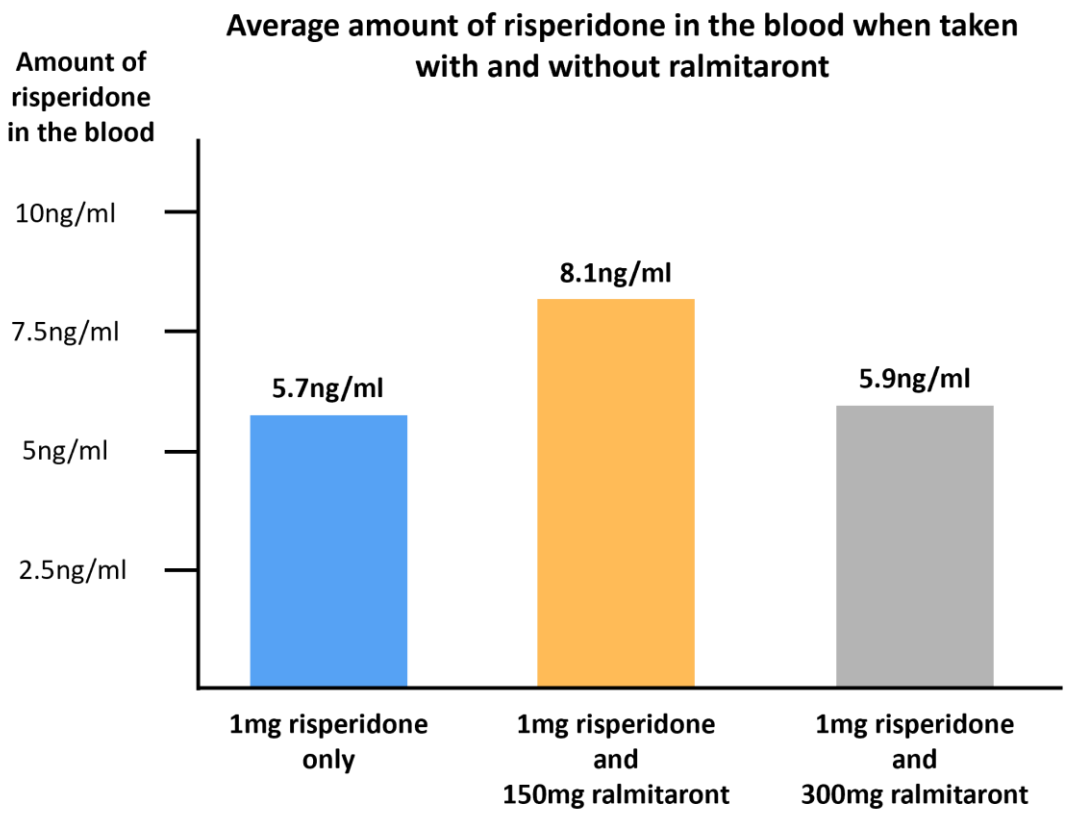
4. What were the results of the study?

Question 1: Does the amount of risperidone in the blood change when it is taken with ralmitaront?

Researchers looked at how much risperidone was in samples of blood over time when it was taken on its own and when it was taken with ralmitaront.

- The average highest amount of risperidone in the blood when it was given on its own was 5.7ng/mL
- The average highest amount of risperidone in the blood was:
  - 8.1ng/mL when it was given with 150mg ralmitaront
  - 5.9ng/mL when it was given with 300mg ralmitaront

Because fewer people were in this study than planned, researchers could not be certain if the higher amount of risperidone seen in the blood when it was taken with ralmitaront (compared to when taken on its own), was due to chance or not.

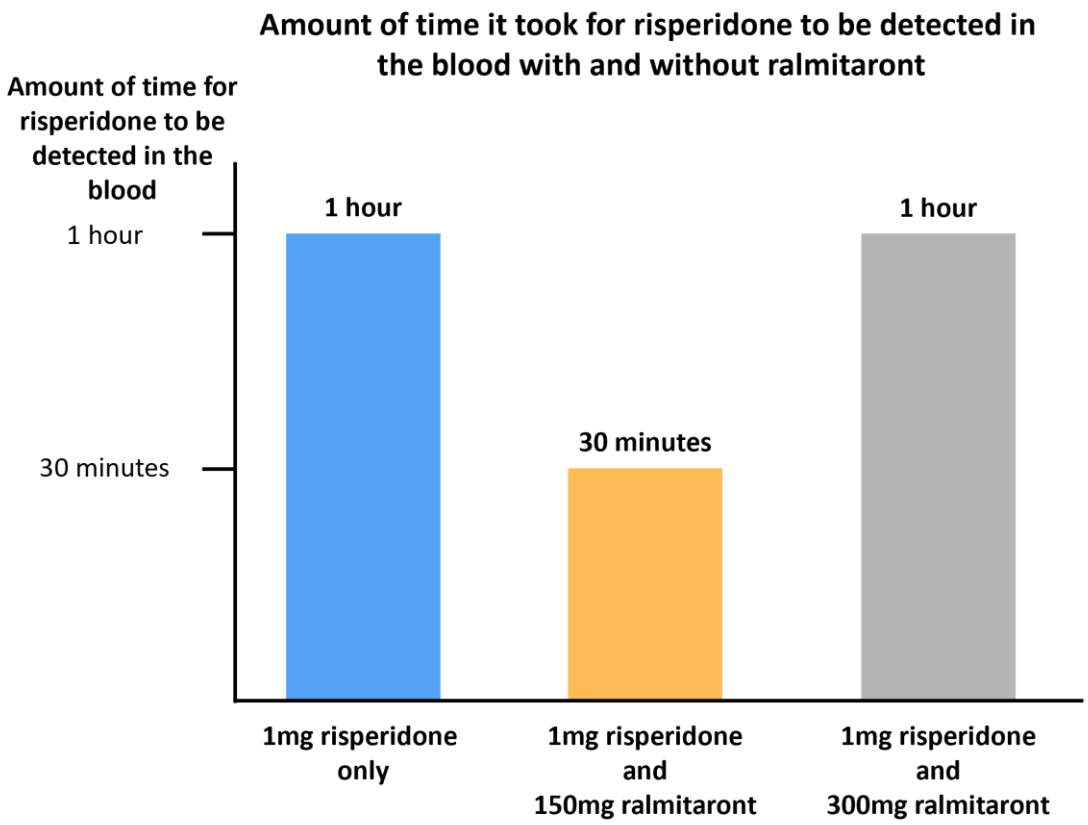


Question 2: Does the time taken for risperidone to reach maximum levels in the blood change when it is taken with ralmitaront?

Another piece of information that researchers collected was the amount of time it took for risperidone to reach maximum levels in the blood.

- When given on its own, maximum risperidone levels were seen 1 hour later
- Maximum risperidone levels were seen:
  - 30 minutes later when given with 150mg ralmitaront
  - 1 hour later when given with 300mg ralmitaront

Because fewer people were in this study than planned, researchers could not tell if the shorter time it took to detect maximum levels of risperidone in the blood when it was taken with ralmitaront (compared to when taken on its own), was due to chance or not.

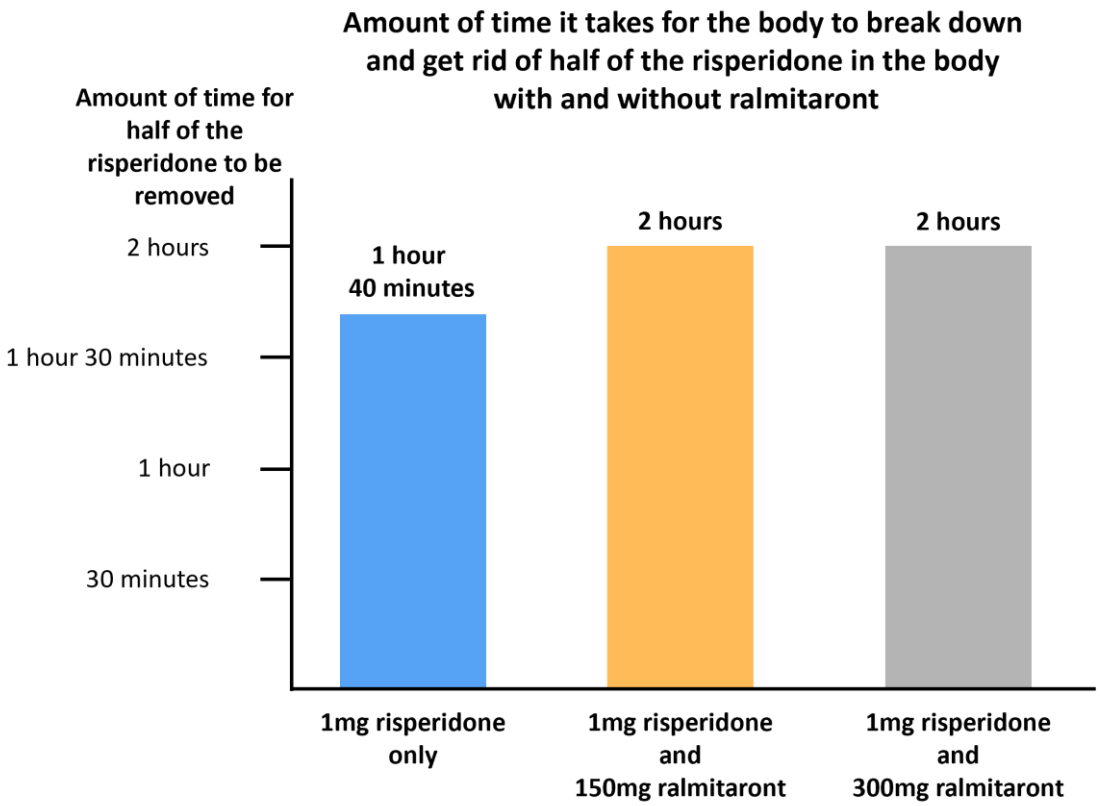


Question 3: Does ralmitaront change the way the body breaks down and gets rid of risperidone?

Another piece of information that researchers collected was the amount of time it took for the body to break down and get rid of half the risperidone.

- When given on its own, it took an average of 1 hour and 40 minutes
- When given with either 150mg or 300mg of ralmitaront, it took 2 hours

Because fewer people were in this study than planned, researchers could not tell if the shorter time it took for the body to get rid of half the risperidone when it was taken with ralmitaront (compared to when taken on its own), was due to chance or not.



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 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
- Side effects may be mild to very serious any 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 leaflets
- 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.

During this study, no-one had serious side effects.

No-one in this study died due to side effects that may have been related to one of the study medicines.

No-one decided to stop taking their medicine because of side effects.

Most common side effects

During this study, around 1 in 2 people (50%) had a side effect that was not considered serious.

The most common side effects are shown in the following table, which includes side effects that affected at least two people. Some people had more than one side effect – this means that they are included in more than one row in the table.

Most common side effects reported in this study	**When taking risperidone** (10 people total)	**When taking ralmitaront** (10 people total)	**When taking risperidone and ralmitaront** (10 people total)
Headache	10% (1 out of 10)	10% (1 out of 10)	0% (0 out of 10)
Rash with flat and raised areas	0% (0 out of 10)	0% (0 out of 10)	20% (2 out of 10)
Skin allergy (dermatitis)	0% (0 out of 10)	10% (1 out of 10)	10% (1 out of 10)
Skin rash (caused by a reaction to the study drug)	0% (0 out of 10)	0% (0 out of 10)	20% (2 out of 10)

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 ten healthy people. These results helped researchers learn more about how the body processes risperidone and ralmitaront when taken together.

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?

At the time of writing this summary, no more studies looking at risperidone and ralmitaront are planned.

8. Where can I find more information?

You can find more information about this study on the following website:

- https://forpatients.roche.com/ en/trials/psychiatric-disorder/schizophrenia/a-study-to-evaluate-the-safety--tolerability--processing-by-the-.html#formedicalprofessionals

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/psychiatric-disorder/schizophrenia/a-study-to-evaluate-the-safety--tolerability--processing-by-the-.html#formedicalprofessionals
- 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.

Full title of the study and other identifying information

The full title of this study is: 'A single-center, single-sequence, open-label, two-period study to investigate the safety, tolerability, pharmacokinetics and pharmacodynamic effects of the combination of multiple doses of ralmitaront with a single dose of risperidone in healthy subjects'.

- The protocol number for this study is: BP43026