Summary of Clinical Trial Results

A study to look at how safe different doses of RO7444973 were for people with MAGE A4-positive solid tumours, what happens to this medicine in the body, and how well it works

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 December 2021 and stopped early – in July 2023 – because the medicine being studied was removed from the body by the person's immune response.

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

Glossary

- Melanoma-associated antigen A4 = MAGE A4

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about MAGE A4-positive solid tumours and the medicine studied – 'RO7444973'.

Key information about this study

Why was this study done?

- This study was done to look at how safe different doses of RO7444973 were for people with MAGE A4-positive solid tumours
- Researchers also looked at what happens to this medicine in the body, and how well it works against MAGE A4-positive solid tumours
- RO7444973 was given to people for the first time in this study

Which medicines were being studied and who took part?

- In this study, people were given the medicine being studied (called 'RO7444973')
- This study included 22 people in 6 countries

What were the results?

- The main findings were:
  - Around 9% of people (2 out of 22 people) taking RO7444973 had serious unwanted effects
  - 86% of people (19 out of 22 people) taking RO7444973 had non-serious unwanted effects
  - An immune response against RO7444973 was found in 77% of people (17 out of 22 people)
    - RO7444973 was removed more quickly from the body in people with this immune response than in people without the immune response
  - No-one in the study had cancer that shrank or disappeared after being given RO7444973
- This study stopped early because most people developed an immune response against RO7444973. Research into RO7444973 as a treatment for cancer was stopped

1. General information about this study

Why was this study done?

Solid tumours are cancer cells that grow in organ systems throughout the body. New treatments are needed that can target solid tumours without damaging healthy cells. Researchers have found a possible target called 'melanoma-associated antigen A4', or 'MAGE A4'.

MAGE A4 can be part of the surface layer of cancer cells. MAGE A4 is thought to be a good target because it is found on various solid tumours, such as non-small cell lung cancer, head and neck cancer and others. But healthy body cells do not have MAGE-A4 on them. This means healthy cells may not be affected by treatment.

The immune system's cells scan the body for signs of disease. The immune system is the body's natural defence, protecting the body from foreign or harmful substances such as bacteria and viruses. Immune cells check the surface of a cell, which lets them 'see' inside cells of the body. This helps them remove cancerous, infected or diseased cells. Immune cells do not usually spot MAGE-A4 as a target on cancer cells.

Immunotherapy is a type of medicine that helps a person's own immune system attack cancer cells. In this study, researchers looked at an immunotherapy that uses MAGE A4.

What was the medicine being studied?

'RO7444973' is the medicine that was studied here.

- RO7444973 connects to MAGE A4 on cancer cells and links them to cancer-killing cells of the immune system
- This may mean that RO7444973 could work as a treatment for MAGE A4-positive solid tumours
- RO7444973 was given to people for the first time in this study, so it was tested at different doses

What did researchers want to find out?

- Researchers did this study to see how safe RO7444973 was – by checking how many people had unwanted effects and seeing how serious they were, when taking it (see Section 4 'What were the results of the study?' and Section 5 'What were the side effects?')
- They also wanted to find out what happened to RO7444973 in the body, and if it may be useful for treating some types of solid tumours (see Section 4 'What were the results of the study?')

The main questions that researchers wanted to answer were:

1. What were the number and seriousness of unwanted effects?
2. What was the maximum dose of RO7444973 that could be given before people had unacceptable unwanted effects, the best dose to give as a treatment for cancer, and how often should it be given?

Other questions that researchers wanted to answer included:

3. How does RO7444973 work in the body and what effects does it have?
4. How well does RO7444973 work against MAGE A4-positive cancers?
5. How does RO7444973 get to different parts of the body, and how does the body change and get rid of it?

What kind of study was this?

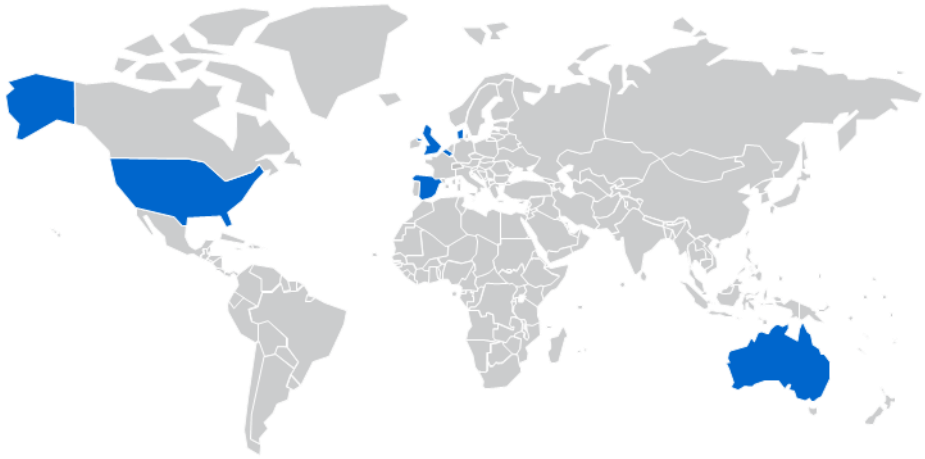
This study was a 'Phase 1' study, which means that this was one of the first studies for RO7444973. A small number of people with MAGE A4-positive solid tumours took RO7444973 and the researchers did medical tests on the people who took part to find out more about RO7444973.

This was an 'open-label' study. This means everyone involved, including the participant and the study doctor, know which study treatment the participant is given.

When and where did the study take place?

The study started in December 2021 and stopped early – in July 2023 – because the medicine being studied was removed from the body by the immune response. This summary presents the results of the study up until it was stopped in July 2023.

The study took place at 9 study centres – across 6 countries in Australia, Europe and North America. The following map shows the countries where this study took place.



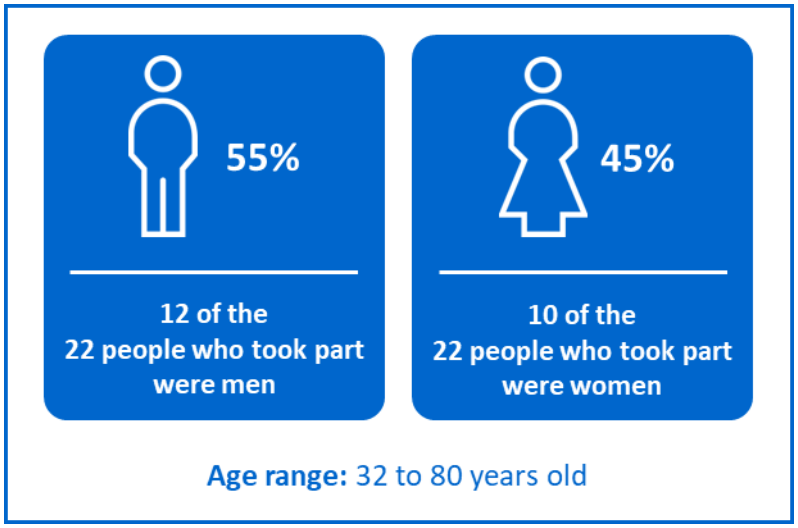
- Australia
- Belgium
- Denmark
- Spain
- United Kingdom
- United States of America

2. Who took part in this study?

In this study, 23 people took part. They all had a solid tumour that could not be taken out or completely removed with surgery. The tumour may have spread to other parts of the body.

One person left the study before being given any treatment and is not included in the results below.

More information on the people who took part is given below.



People could take part in the study if they:

- Were at least 18 years of age
- Had cancer with MAGE A4
- Had been given standard treatment for their cancer, and had no further treatment options available to them

People could not take part in the study if they had:

- Certain medical issues, such as high blood pressure, heart disease, epilepsy, or uncontrolled infections
- Been given certain anti-cancer treatments within 1 month before starting the study

3. What happened during the study?

The study was in 3 parts. Everyone was given RO7444973, as a drip into a vein (infusion).

To look at how safe RO7444973 was to give to people, very small amounts, or doses, were first given. These very low doses were not expected to have any effect on a person's cancer.

In Part 1, 2 people were given RO7444973 every 3 weeks:

- 1 person was given the lowest dose used in the study, then
- 1 other person was given a very low dose

When these very low doses were shown to be safe enough in Part 1, more people were given the same low doses in Part 2, to confirm the safety results. Then, once the low doses were shown to be safe enough, Part 2 looked at the safety of increasingly higher doses of RO7444973.

Some people were given the full dose each time – known as 'fixed doses' and some people were given 'step up' doses. Step up doses start with a lower dose which is increased over time. Using step up doses can be a safer way to give the first doses of a medicine than fixed doses.

In summary, for Part 2, 20 people were given RO7444973 every 3 weeks:

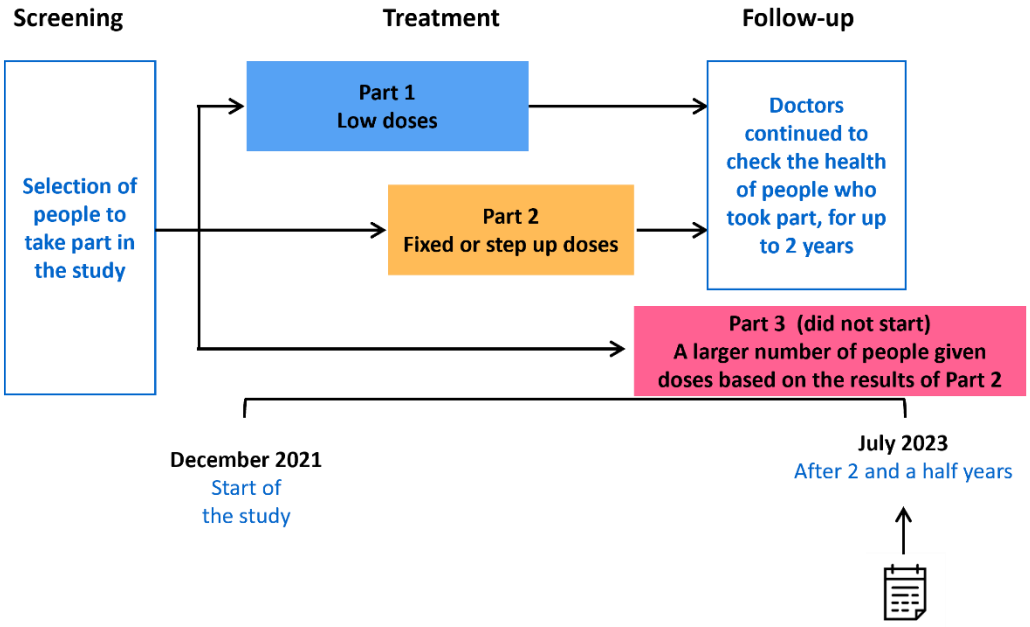
- 9 people were given a very low dose (the same dose as a person was given in Part 1)
  - 5 people were given fixed doses
  - 4 people were given step up doses
- Then, 5 people were given a higher dose starting with step up doses
- Then, 6 people were given the highest dose starting with step up doses

In Part 2, researchers also looked at the effects of different dose levels of RO7444973 on the body. This was to understand what dose level a person would need if RO7444973 was to work as a treatment for cancer.

Part 3 planned to look at how safe the best dose of RO7444973 was and how well it worked in a larger number of people with MAGE A4-positive solid-tumours. This part was not started due to the results of Parts 1 and 2.

The study stopped early because some people had an immune response against RO7444973. 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, and the symbol shows the point where the study was stopped.



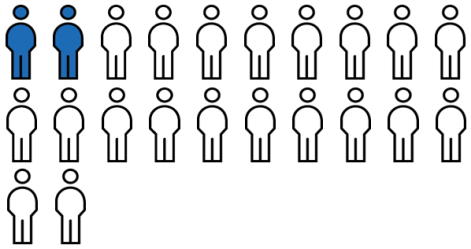
4. What were the results of the study?

Question 1: What were the number and seriousness of unwanted effects?

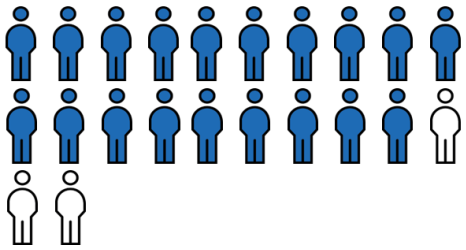
Unwanted effects are medical problems (such as feeling dizzy) that happen during the study.

- They are described in this summary because the study doctor believes the unwanted effects were related to the treatments in the study
- Not all of the people in this study had all of the unwanted effects
- Unwanted effects may be mild to very serious and can be different from person to person
- An unwanted effect is considered 'serious' if it is life-threatening, needs hospital care, or causes lasting problems

2 out of 22 (9%) people had serious unwanted effects related to RO7444973



19 out of 22 (86%) people had non-serious unwanted effects related to RO7444973



See Section 5 'What were the unwanted effects?' for more information about the type of unwanted effects that people had.

Question 2: What was the maximum dose of RO7444973 that could be given before people had unacceptable unwanted effects, the best dose to give as a treatment for cancer, and how often should it be given?

Researchers wanted to look at the maximum dose of RO7444973 that could be given before people had unacceptable unwanted effects. They also wanted to find out if people had fewer unwanted effects if step up doses were given compared with fixed doses.

A small number of people joined the study before it was stopped. This means that these questions could not be answered.

Question 3: How does RO7444973 work in the body and what effects does it have?

Researchers looked in the blood for 'antibodies' to RO7444973. Antibodies are proteins that form part of the body's natural defence against infection or other foreign substances.

Antibodies against RO7444973 were found in 17 out of 22 people (77%), after they had been given RO7444973.

The antibodies may affect how well RO7444973 works by removing it from the body more quickly than in people without the antibodies.

Information on how much RO7444973 was in the body and if people made antibodies against RO7444973 was available for 19 people in the study. 12 out of these 19 people had antibodies against RO7444973 that removed it from the body. This would stop RO7444973 from being able to work as a treatment for cancer.

Question 4: How well does RO7444973 work against MAGE A4-positive cancers?

No-one in the study had cancer that shrank or disappeared after being given RO7444973.

12 out of 22 people (55%) had cancer that did not get better or worse.

9 out of 22 people (41%) had cancer that got worse – this was not related to being given RO7444973.

Results were not available from 1 person (5%).

Question 5: How does RO7444973 get to different parts of the body, and how does the body change and get rid of it?

Another piece of information that researchers collected was the level of RO7444973 in the blood.

Maximum levels of RO7444973 in the blood were reached just after RO7444973 had been given as a drip into the vein over 2 hours.

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 'Where can I find more information?').

5. What were the unwanted effects?

- It is important to be aware that the unwanted effects reported here are from this single study. Therefore, the unwanted effects shown here may be different from those seen in other studies
- Serious and common unwanted effects are listed in the following sections

Serious unwanted effects

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

During this study, 2 out of 22 (9%) people had a serious unwanted effect considered related to the study medicine. This was a skin rash with flat and raised areas.

Some people died during the study. 12 out of 22 people (55%) died due to their cancer getting worse, and not due to unwanted effects that may have been related to the study medicine.

During the study, no-one decided to stop taking their medicine because of unwanted effects.

Most common side effects

During this study, around 9 out of every 10 people (86%) had an unwanted effect that was not considered serious.

The most common side effects are shown in the following table – these were seen in at least 1 in every 20 people (5% or more). Some people had more than one unwanted effect – this means that they are included in more than one row in the table.

Most common unwanted effects reported in this study	**People taking RO7444973** (22 people total)
Rash with flat and raised areas	50% (11 out of 22)
Itching	36% (8 out of 22)
A low level of white blood cells	23% (5 out of 22)
A reaction to the study medicine, known as 'cytokine release syndrome'	23% (5 out of 22)
Feeling tired or weak	18% (4 out of 22)
Rash	18% (4 out of 22)
Skin flaking or peeling	14% (3 out of 22)
Higher than usual levels of 'ALT' in the blood, which can indicate liver damage	9% each (2 out of 22 each)
Higher than usual levels of 'AST' in the blood, which can indicate liver, heart, or kidney damage	
A low number of red blood cells	
Back pain	
Difficulty pooping	
Frequent, watery stools	
Dry mouth	
Dry skin	
Redness of skin	
Decreased number of a type of white blood cells	
Dry and crusty nose	
Wanting to throw up	
Sensations of tingling, burning, pricking, or numbness in the skin	
Inflamed and sore mouth	

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 'Where can I find more information?'.

6. How has this study helped research?

The information presented here is from a single study of 23 people with solid tumours. These results helped researchers learn more about RO7444973.

7. Are there plans for other studies?

At the time of writing this summary, no more studies looking at RO7444973 are planned.

8. Where can I find more information?

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

- https://clinicaltrials.gov/ct2/show/results/NCT05129280
- https://forpatients.roche.com/en/trials/cancer/solid-tumors/a-study-to-evaluate-safety--pharmacokinetics--and-preli-17129.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/cancer/solid-tumors/a-study-to-evaluate-safety--pharmacokinetics--and-preli-17129.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.

Full title of the study and other identifying information

The full title of this study is: 'An Open-Label, Multicenter, Phase I Study to Evaluate Safety, Pharmacokinetics, and Preliminary Anti-Tumor Activity of RO7444973 in Participants with Unresectable and/or Metastatic Mage A4 Positive Solid Tumors'.

- The protocol number for this study is: BE43244
- The ClinicalTrials.gov identifier for this study is: NCT05129280
- The EudraCT number for this study is: 2021-000624-35