Summary of Clinical Trial Results

A study to look at how safe different doses of RO7293583 were for people with skin cancer (melanoma), how best to give RO7293583, and how the body breaks it down and processes it

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 (participants).

This summary is based on information known at the time of writing (April 2023).

The study started in October 2020 and stopped early – in July 2022 – because the drug company (Roche) decided to prioritise the development of other, potentially more impactful medicines, and not because too many participants had concerning side effects.

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 = Melanoma is a type of skin cancer that develops in the cells (melanocytes) that produce melanin — the pigment that gives your skin and eyes its colour

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about melanoma and the medicine studied – RO7293583.

Key information about this study

- This study was done to look at:
    - the highest dose of RO7293583 that could safely be given, and the safest way to give it
    - the number and seriousness of side effects when RO7293583 was given with or without a pre-treatment medicine
    - how the body processes RO7293583.
- This study included 20 people in 6 countries.
- The main finding was that RO7293583 (up to 0.4mg) given every 3 weeks into a vein was well-tolerated and side effects were manageable with or without medical care.
- It took 3 to 5 days for the amount of RO7293583 in the blood to reduce by half; almost half of all participants made antibodies against RO7293583 that likely stopped RO7293583 from working properly.
- 8 out of 20 participants taking RO7293583 had a serious side effect.
- The study was discontinued and did not include as many participants as planned because the drug company (Roche) decided to prioritise the development of other, potentially more impactful medicines, and not because too many participants had concerning side effects.

1. General information about this study

Why was this study done?

Melanoma is a type of cancer that usually develops in the skin. Melanoma can also develop in other areas of your body, such as the eye or inside the mouth or nose, although rare.

Cancers are 'staged' to describe how much they have grown. When diagnosed at early stages (stages 0 to II), melanoma is usually treated with surgery. At later stages (stages III to IV), melanoma has grown (known as 'advanced') or spread to other organs in the body (called 'metastatic') and is harder to treat. Current treatments for advanced and metastatic melanoma that cannot be removed by surgery aim to reduce symptoms and extend life. These include chemotherapy, radiotherapy, targeted therapies for melanoma with a specific change (mutation), and immunotherapies. These treatments have improved disease outcomes for people with advanced or metastatic melanoma. However, they do not work for everyone, or they stop working after a time, and the cancer returns. They do not work well for types of metastatic melanoma that affect the eyes and the inner lining of the body (for example, the mouth, nose and genitals).

New medicines are needed for advanced or metastatic melanoma that cannot be removed with surgery and/or do not respond to current therapy.

What were the study medicines?

An experimental drug called **RO7293583** was the focus of this study.

- RO7293583 is called an experimental drug because health authorities have not approved it for the treatment of advanced and/or metastatic melanoma.
- RO7293583 attaches to a protein called TYRP1 on melanoma cells. It also attaches to cancer-killing cells of the immune system. This brings the two types of cells closer together.
- This may mean that RO7293583 will help the immune cells find and destroy melanoma cells.
- This study was the first time RO7293583 was given to people.

Obinutuzumab is an existing medicine given to people with certain types of cancer called lymphoma and leukaemia – in which a type of white blood cells, called 'B-cells', become cancerous.

- You say this as 'oh-bi-noo-too-zoo-mab'.
- It is an experimental pre-treatment medicine in this study as it is not approved for treating melanoma.

Tocilizumab is an existing medicine to treat people with a side effect called 'cytokine release syndrome', which can happen shortly after being given medicine as an infusion (into a vein).

- You say this as 'to-ci-li-zoo-mab'.
- It is called a 'rescue medicine' and is not a treatment for melanoma.
- It is an experimental medicine in this study as it is not approved for treating cytokine-release syndrome due to RO7293583.

What did researchers want to find out?

- Researchers did this study to find out what dose of RO7293583 to give to people living with melanoma when given with or without the pre-treatment medicine, obinutuzumab, and how the body processed RO7293583 (see Section 4 "What were the results of the study?").
- They also wanted to find out what type of side effects participants had (see Section 5 "What were the side effects?").

The main questions that researchers wanted to answer were:

1. What was the highest dose of RO7293583 that could safely be given, and the safest way to give it?
2. How many participants have side effects when RO7293583 is given with or without the pre-treatment medicine?
3. How does the body break down and process RO7293583?

What kind of study was this?

This study was a 'Phase 1' study. This was the first study of RO7293583 in people. A small number of people with different types of melanoma that had spread in the body took RO7293583.

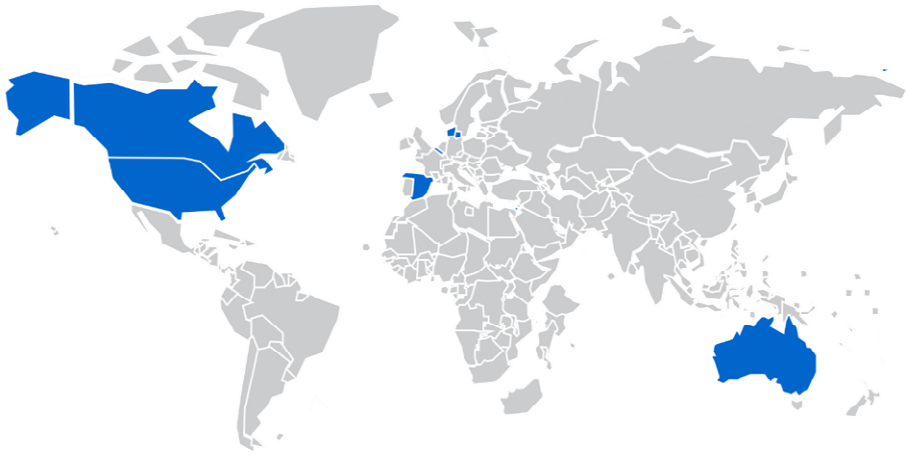
This was an ‘open label’ study. This means that both the people taking part in the study and the study doctors knew what treatments were being given.

When and where did the study take place?

The study started in October 2020 and stopped early. This summary presents the results of the study up until it was stopped in July 2022.

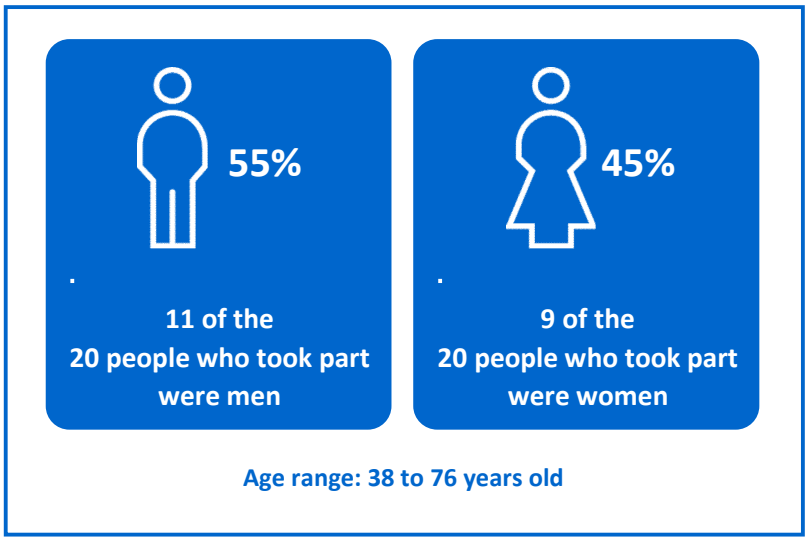
The study took place at nine study centres – across 6 countries in Europe, Australia, and North America. The following map shows the countries where this study took place.

- Australia
- Belgium
- Canada
- Denmark
- Spain
- USA



2. Who took part in this study?

In this study, 20 people with melanoma that had spread in the body took part.



People had to meet certain medical criteria to take part in the study. This was to make sure that the study medicine was given to people as safe as possible and that researchers could see how well the study medicine had worked in people with a similar medical condition. The main criteria that people had to meet are listed below.

People could take part in the study if they had either:

- Skin cancer that had spread in the body (Stage III or IV cutaneous melanoma) and could not be removed with surgery
  or
- Skin cancer affecting the inner lining of the body (such as the mouth, throat, nose and genitals, known as 'mucosal melanoma') or eye (known as 'uveal melanoma') that had spread in the body and could not be removed with surgery or treated with standard therapy.

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

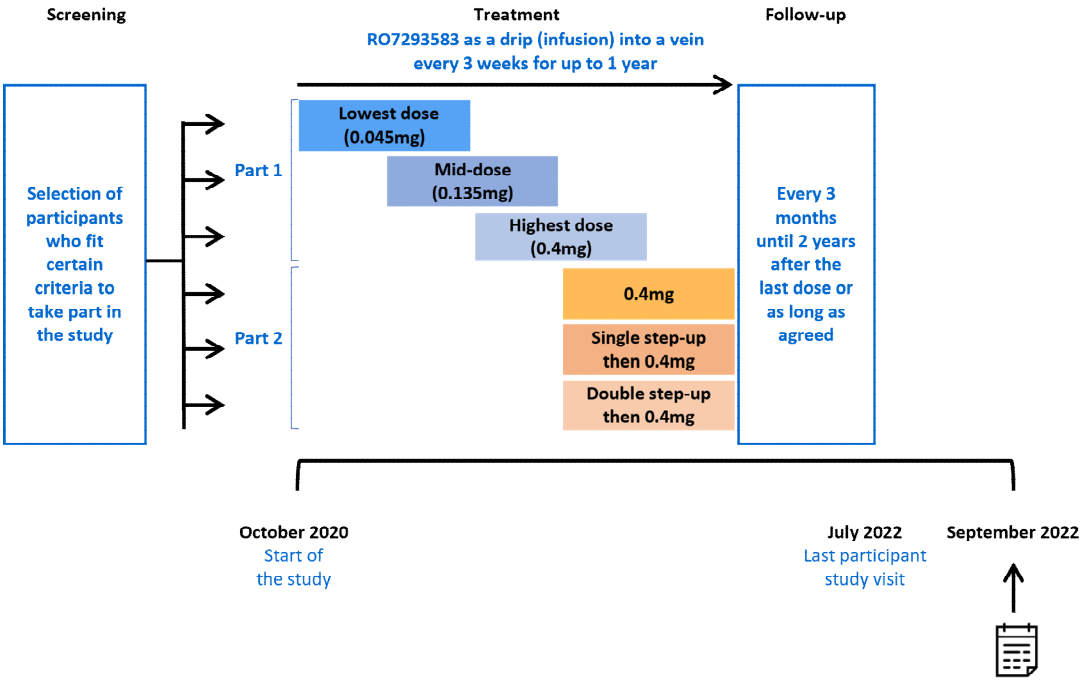
- Skin cancer that had spread to the brain or spinal cord unless it had been treated and did not cause symptoms
- Certain medical conditions such as problems affecting the skin, eyes, ears, or heart, another type of cancer, infections, uncontrolled high blood pressure, pregnancy or if they were breastfeeding.

3. What happened during the study?

There were 2 parts to the study. The treatment groups in each part were:

- **Part 1: RO7293583 –** given as a drip (slow infusion) into a vein every 3 weeks with the full dose given at once. Four people were given one of three doses (0.045mg, 0.135mg or 0.4mg).
- **Part 2: RO7293583 –** given as a drip (slow infusion) into a vein every 3 weeks with the dose given one of three ways:
    - Seven participants were given 0.4mg with the full dose given every 3 weeks
    - Five participants were first given a lower dose, then 0.4mg 3 weeks later, then every 3 weeks (known as 'single step-up dosing')
    - Five participants were first given a low part-dose on Day 1, a higher part-dose on Day 8, then a full dose (0.4mg) given all at once 2 weeks later, then every 3 weeks (known as 'double step-up dosing').
- The study was to include up to 310 participants – however, only a small number joined the study before it stopped.
- Some participants were planned to be given RO7293583 as an injection under the skin – the study stopped before this happened.
- Researchers predicted that RO7293583 would work best at a dose of around 40mg when given as an infusion (into a vein). The highest dose that participants were given before the study stopped was 0.4mg.

After participants finished taking their medicine for this study, they were asked to go back to their study centre for two more visits – to check their overall health. The study flowchart shows all stages planned for the study.



This study stopped early, so the symbol on the timeline ( ) shows when the information shown in this summary was collected – after nearly 2 years (September 2022).

4. What were the results of the study?

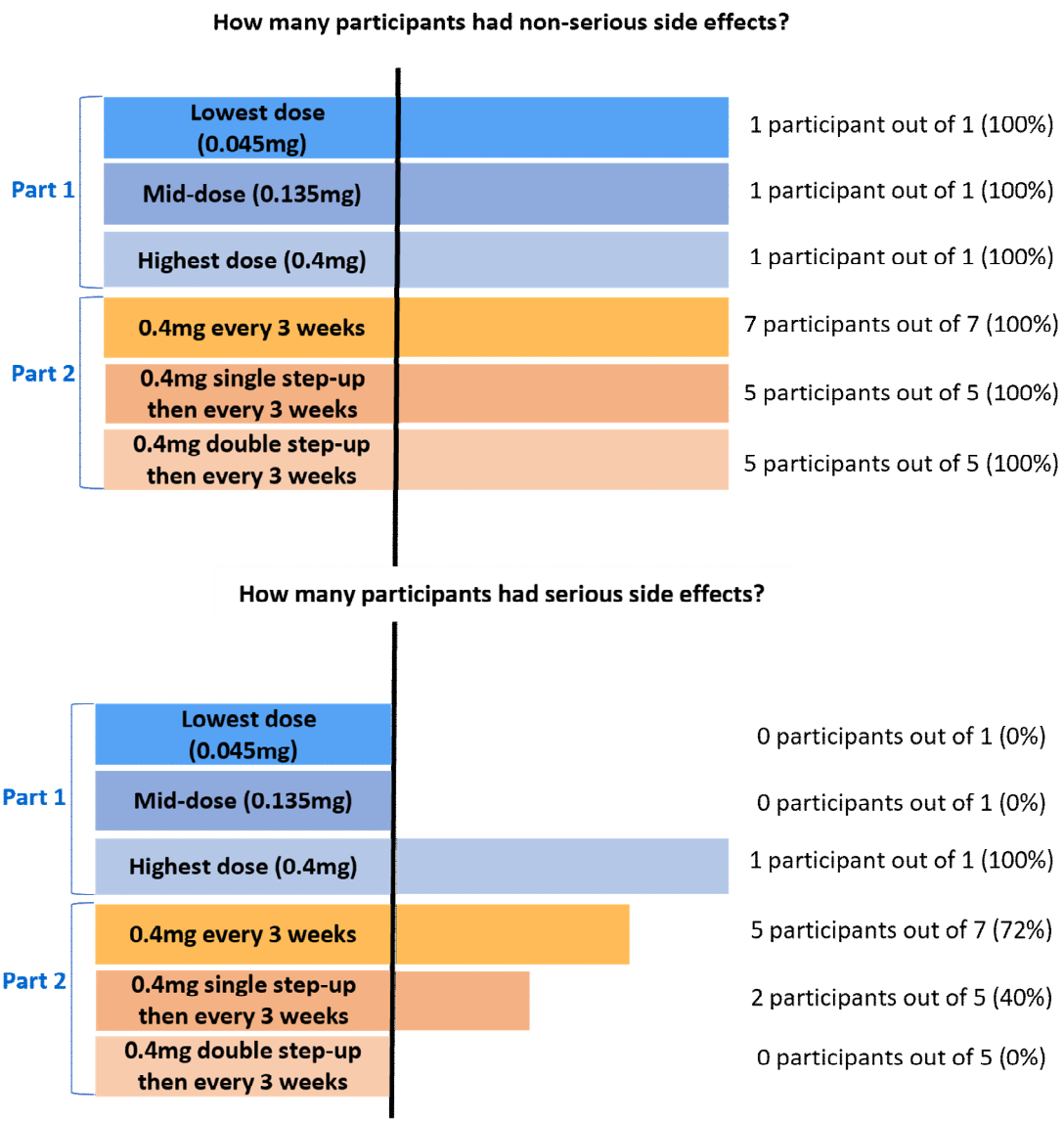
Question 1: What was the highest dose of RO7293583 that could safely be given, and the safest way to give it?

Side effects are medical problems (such as feeling dizzy) during the study. Serious side effects are those that cause unplanned hospitalisation (or hospitalisation for longer than planned) or are life-threatening, cause long-term disability or loss of life. Only side effects doctors' thought were related to the study medicine are shown.

The highest dose of RO7293583 that was given before the study was stopped was 0.4mg. Because the study stopped early, researchers did not give participants high doses of RO7293583 as planned. This means that they did not find out the highest maximum dose of RO7293583 that could be given before unmanageable or intolerable side effects happened. All participants in Part 1 and 2 had at least one side effect that was not considered serious after being given RO7293583.

Most of the participants (1 out of 1 person in Part 1, and 5 out of 7 people in Part 2) who were given the highest dose (0.4mg) in full (with the first dosing) had serious side effects. The number of participants who had serious side effects was smaller when a lower dose of RO7293583 was given before the planned dose of 0.4mg every 3 weeks (in Part 2).

The picture below shows the percentage of participants in each group who had side effects. The types of side effects are described in Section 5 ('What were the side effects?').



Question 2: How many participants have side effects when RO7293583 is given with or without a pre-treatment medicine?

Some participants were to be given the pre-treatment medicine, obinutuzumab, if their body's made antibodies against RO7293583 which could stop RO7293583 from working properly. Because the study was stopped early, no participants were given RO7293583 with obinutuzumab pre-treatment.

The number of participants who had side effects when RO7293583 was given without obinutuzumab is described above.

Question 3: How does the body process RO7293583?

- RO7293583 could be detected in the blood immediately after it had been given, and levels had reduced by half in 3 to 5 days.

- Almost half of all participants (9 out of 20) made antibodies that removed RO7293583 from the blood, which would likely stop it from working properly as a treatment for melanoma.

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 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.
- 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, causes a stay (or a longer stay) in hospital or lasting problems.

During this study, 1 in every 4 participants (8 out of 20 participants) had one side effect that was considered serious (see also Section 4). In all 8 participants, this was 'cytokine release syndrome' – an overreaction of the immune system to infusion of the study medicine. One participant required a single treatment with tocilizumab (as a drip [slow infusion] into a vein) due to cytokine-release syndrome.

Of the 20 participants, 12 had died from cancer by the time the study stopped. None of the participants died due to side effects that may have been related to one of the study medicines.

During the study, none of the participants decided to stop taking their medicine because of side effects.

Most common side effects

During this study, all 20 participants had a side effect that was not considered serious.

The most common side effects are shown in the following table – these side effects affected at least 1 in 5 participants (20%) across all treatment groups. Some participants 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	Participants **taking RO7293583** (20 participants total)
Overreaction of the immune system to infusion of the study medicine (cytokine release syndrome)	60% (12 out of 20)
Rash	35% (7 out of 20)
Extreme tiredness (fatigue)	25% (5 out of 20)
Fever	20% (4 out of 20)
Itchiness	20% (4 out of 20)
Rash with flat and raised areas	20% (4 out of 20)

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 20 participants with different types of skin cancer (melanoma) that has spread in the body. These results helped researchers learn more about melanoma and RO7293583.

- RO7293583 (up to 0.4mg) given every 3 weeks as an infusion (into a vein) was well-tolerated and side effects were manageable.
- It took 3 to 5 days for levels of RO7293583 in the blood to reduce by half and almost half of all participants made antibodies that removed RO7293583 from the blood.
- 8 out of 20 participants taking RO7293583 without pre-treatment medicine had a serious side effect of cytokine release syndrome - only one of these participants required treatment with tocilizumab.

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 RO7293583 are planned at the current time.

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/NCT04551352
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-000793-18/results
- https://forpatients.roche.com/en/trials/cancer/skin-cancer/a-study-of-ro7293583-in-participants-with-unresectable--00455.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/skin-cancer/a-study-of-ro7293583-in-participants-with-unresectable--00455.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 1 study to evaluate safety, tolerability, pharmacokinetics, and pharmacodynamics of RO7293583, a TYRP1-targeting CD3 T-cell engager, in participants with metastatic melanoma”.

- The protocol number for this study is: BP42169.
- The ClinicalTrials.gov identifier for this study is: NCT04551352.
- The EudraCT number for this study is: 2020-000793-18.