Summary of Clinical Trial Results

A study to find out if a new medicine (RO7297089) is safe and effective for people with cancer (multiple myeloma)

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 July 2020 and stopped early – in July 2021 – because the medicine being studied did not work as well as expected.

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.**

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Thank you to the people who took part in this study

The people who took part have helped researchers answer important questions about a certain type of cancer called "multiple myeloma", and the study medicine, "RO7297089".

Key information about this study

- This study was done to find out how safe was it to give people a new medicine, whether the medicine was effective, and how the medicine behaved in the body.
- People who had cancer (multiple myeloma) were given the study medicine, called "RO7297089".
- This study included 27 people in 4 countries.
- The main finding was that the medicine was not as effective as researchers had expected. Side effects were generally tolerable for the people in this study.
- Six of the 27 people (22%) in this study had serious side effects thought to be caused by the study medicine.
- This study stopped early because the medicine being studied did not work as well as expected.

1. General information about this study

Why was this study done?

Multiple myeloma (**MM**) is a type of cancer that affects the bone marrow in various parts of the body. The cancer is caused by the growth and buildup of unhealthy (**defective**) plasma cells. Healthy plasma cells are mainly found in the bone marrow where they make antibodies to kill germs.

About 160,000 people around the world are diagnosed with MM every year. Plasma cells in people with MM become overcrowded and interfere with the function of other blood cells. The diseased plasma cells also produce proteins that cause problems in different parts of the body.

MM cannot be cured. Several medicines can help prolong the life of someone with MM. People with "standard risk" MM live for about 8-10 years and those with "high risk" MM live for about 2-3 years after diagnosis.

For most patients with MM, the disease comes back – the patient "**relapses**". The disease can also become unresponsive to available medicines – the disease becomes "**refractory**".

New medicines are needed for people with MM. This study was done to find out if a new medicine for MM, called "RO7297089" was safe and effective for patients with MM.

What was the medicine being studied?

The study medicine was called "**RO7297089**".

- RO7297089 is a type of medicine called an "**immunotherapy**" - it encourages the body's immune cells to attack cancer cells.
- RO7297089 is a "**bispecific antibody**" – it is a protein that binds to two different protein targets in the body.
- One target is a protein called "**BCMA**". BCMA is present on plasma cells. It is overexpressed on defective plasma cells in patients with MM. BCMA allows the plasma cells to live for long periods.
- Another target is a protein called "**CD16a**". CD16a is found on different immune cells in the blood (macrophages, natural killer cells, and monocytes).
- When RO7297089 binds to BCMA and CD16a, the medicine catches immune cells and plasma cells. This allows the immune cells to kill the cancer-causing plasma cells.

What did researchers want to find out?

This was the first time that the study medicine was given to people.

The main questions that researchers wanted to answer were:

1. How safe was it to give people different doses of the study medicine?
2. How much study medicine was available in the body at different time points with different doses?
3. Was there any response to the study medicine – by the cancer?

What kind of study was this?

This was a "**Phase 1 study**", which means that this was one of the early studies for RO7297089. A small number of people with MM were given the study medicine. Researchers did medical tests and observed the people to find out more about the effects of the medicine.

This was an "**open-label study**". That means the researchers and people who took part in the study knew which medicine and what dose was given to the people.

This was a "**dose-escalation**" study. Each new group of people received a higher dose of the study medicine. Giving out the next higher dose of the study medicine was called "dose-escalation". The decision for dose escalation was made after reviewing results from all previously dosed people at the lower dose levels.

When and where did the study take place?

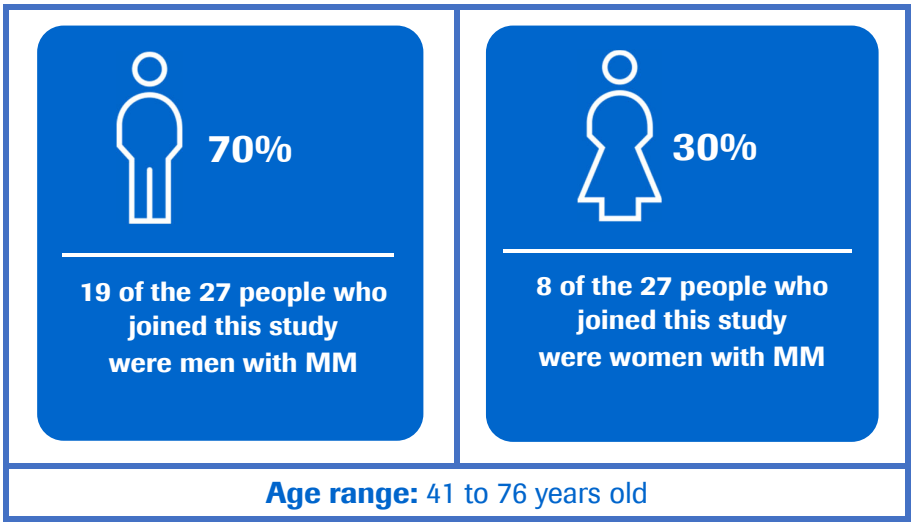
The study started in July 2020 and stopped early because RO7297089 did not work as well as expected. This summary presents the results of the study up until it was stopped in July 2021.

The study took place at 10 study centers – in 4 countries:

Australia (5 centers)
Belgium (2 centers)
Denmark (2 centers)
Norway (1 center)

2. Who took part in this study?

Twenty-seven people who had MM – took part in this study.



People could take part in the study if:

- They were at least 18 years old and had relapsed/refractory MM for which there was no treatment available.
- They signed an informed consent form and were able to do what was required during the study.
- They were able to perform physical activities at a level expected for this study.
- They had a life expectancy of at least 12 weeks.
- Their MM disease could be measured by doing lab tests on serum and urine samples.
- Tests showed they had normal blood calcium levels and sufficient organ function (liver, blood, and kidney).

People could not take part in the study if:

- They were pregnant, breastfeeding, or planned a pregnancy while on the study.
- They had previously received certain cancer medicines or medicines that slowed down the immune system.
- They had recently received stem cell transplantation.
- The MM disease level (plasma cell count) was too high or the disease had progressed to the brain.
- They had certain heart or lung diseases, or certain other cancers.
- They had certain infections.
- They received a vaccine that contained live virus – anytime during the 4 weeks before the study.
- They had a history of drug or alcohol abuse in the last 12 months.
- They had major surgery within 4 weeks of the study, or intended to have surgery during the course of the study.
- They had uncontrolled pain caused by the cancer.

3. What happened during the study?

Doctors examined (**screened**) the people who wanted to join the study. If the people met the conditions for joining the study, they started the study within 28 days of screening.

People received RO7297089 by drip – also called "intravenous (**IV)** infusion". People in the lowest dose group received the study medicine first.

Doctors observed people in every new dose group for 14 days before allowing people in the next higher dose group to receive the study medicine – if the doctors thought it was safe to give people the higher dose.

Dose groups	How was the study medicine given?
Group 1A Dose = 60 mg Number of people = 3	People got their dose by IV once a week. They got a "**flat dose**". That means the medicine was given in one sitting and everyone in the same group got the same dose – regardless of how much people weighed.
Group 2A Dose = 180 mg Number of people = 5	
Group 3A Dose = 360 mg Number of people = 4	
Group 4A Dose = 1080 mg Number of people = 6	
Group 4B Dose = 1080 mg Number of people = 6	People got their dose by IV once a week. They got their first dose as a "**split-dose**" - the full dose was split and given in two sittings, over two days. Starting with the second dose, each dose was given in one sitting.
Group 5B Dose = 1850 mg Number of people = 3	

People had to stop the study medicine treatment if their MM disease became worse. In addition, they could get off the study at any time.

After people stopped getting the study medicine, they were asked to go back to their study center for more visits. Researchers checked their overall health for at least 90 days after stopping the study medicine.

4. What were the results of the study?

Question 1: How safe was it to give people different doses of the study medicine?

Among 27 people who were treated, 14 people (52%) got a side effect that researchers thought was caused by the study medicine.

Researchers looked at all the data from the study and decided that this study showed RO7297089 to be well-tolerated by the people in this study – up to the highest dose tested in this study – 1850 mg.

Results may be different in other studies – it will take many people in many studies to learn more about the study medicine.

Question 2: How much study medicine was available in the body at different time points with different doses?

The highest amount of RO7297089 was found in the body – in serum – after the IV transfusion was completed and up to 4 hours afterwards.

For different doses, it took different amounts of time for the level of RO7297089 to fall to half of the peak level. This "time to half peak level" varied from over a day to under 7 days – for the different doses.

Question 3: Was there any response to the study medicine – by the cancer?

Researchers looked at 25 of the 27 people to find out if the study medicine was useful for MM when used alone (as a single therapy).

Two of the 25 people (7%) with MM responded to treatment. Another two (7%) showed a little bit of response (minimal).

Researchers stopped the study early because the response results were not what they had expected to see with this study medicine.

Section 4 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 happened during the study.

- They are described in this summary because the study doctor believes the side effects were related to the treatment 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.

During this study, 6 of the 27 people (22%) had at least one serious side effect.

The serious side effects are shown in the following table. Some people had more than one side effect – this means that they are included in more than one row in the table.

Number (and percentage) of people	Serious side effect
6 people (22%)	A reaction to the drip (infusion) of the study medicine (infusion-related reactions)
2 people (7%)	Strong immune response in the body (cytokine release syndrome)
1 person (4%)	Fever (pyrexia)

There were 12 people in the study who died. None of the deaths were thought to be caused by the study medicine.

- Ten people died because the MM disease got worse (disease progression).
- One person died because of kidney failure.
- One person died because of other reasons.

During the study, 2 people (7%) stopped the study medicine because of side effects caused by the medicine.

Most common side effects

During this study, 14 of the 27 people (52%) had a side effect that was not considered serious – but was thought to be caused by the study medicine.

The most common side effects – those that happened in 2 or more people – are shown in the following table. Some people had more than one side effect – this means that they are included in more than one row in the table.

Number (and percentage) of people	Most common side effect
10 people (37%)	A reaction to the drip (infusion) of the study medicine (infusion-related reactions)
4 people (14%)	Abnormal liver tests (alanine aminotransferase and aspartate aminotransferase increased)
3 people (11%)	Inflammation in the body (C reactive protein increased)
2 people (7%)	Abnormal liver tests (Gamma glutamyltransferase increased)
2 people (7%)	Strong immune response in the body (cytokine release syndrome)

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 27 people with MM. These results helped researchers learn more about MM and RO7297089.

The response to treatment with RO7297089 used alone (single therapy) in people with MM was not as expected. Researchers stopped the study early and did not enroll (add) more people to the study.

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 RO7297089 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/NCT04434469

https://forpatients.roche.com/en/trials/cancer/multiple-myeloma/a-study-evaluating-the-safety-and-pharmacokinetics-of-e-39731.html

Who can I contact if I have questions about this study?

If you have 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:

An open-label, multicenter, phase 1 trial evaluating the safety and pharmacokinetics of escalating doses of RO7297089 in patients with relapsed or refractory multiple myeloma.

- The protocol number for this study is GO41582.
- The ClinicalTrials.gov identifier for this study is NCT04434469.
- The EudraCT number for this study is 2019-003540-76.