Summary of Clinical Trial Results

A study to look at how safe RO7283420 was and how well it worked in the body to remove signs of disease in people with acute myeloid leukaemia

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 November 2020 and stopped early – in August 2023 – 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.

- **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

- AML = acute myeloid leukaemia

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about acute myeloid leukaemia (AML) and the medicine studied – 'RO7283420'.

Key information about this study

Why was this study done?
- This study was done to look at how safe RO7283420 was for people with AML and how well it worked in the body to remove signs of AML that can be measured in the blood

What medicine was being studied and who took part?
- In this study, people were given the medicine being studied (called 'RO7283420')
- This study included 62 people in 8 countries

What were the results?
- The main findings were that the safety of RO7283420 was in line with similar types of medicines, and that 6% of people with AML had a response to treatment
- Around 40% of people (25 out of 62 people) taking RO7283420 had serious unwanted effects
- This study stopped early because the medicine being studied did not work well at lowering levels of AML cells. Higher doses could not be given due to unwanted effects

1. General information about this study

Why was this study done?

Acute myeloid leukaemia (AML) is a blood cancer that affects the bone marrow and blood cells. In AML, the bone marrow produces too many immature and abnormal white blood cells, red blood cells, and platelets, which can crowd out the healthy blood cells. This can lead to symptoms like fatigue, infections and bleeding problems.

Standard treatment for AML includes chemotherapy and bone marrow or stem cell transplants. But chemotherapy can stop working, and some people, especially the elderly or those with other health conditions, cannot be given standard treatment. Therefore, new therapies are needed to treat people with AML.

Immunotherapy is a type of medicine that helps a person's own immune system attack cancer cells. The immune system is the body's natural defence, protecting the body from foreign or harmful substances such as bacteria and viruses. In this study, researchers looked at an immunotherapy targeting a part of AML cells called Wilms' tumour 1 (WT1).

WT1 is a promising target because it is often found on AML cells. WT1 is not found, or is only at very low levels, on healthy bone marrow cells or other cells in the body. This means healthy cells may not be affected by treatment.

The immune system's cells scan the body for signs of disease by checking the surface of cells, which allows it to detect cancerous, infected or diseased cells. Immune cells do not usually recognise WT1 as a target on cancer cells.

What was the medicine being studied?

A medicine called ‘RO7283420’ was the focus of this study.

- RO7283420 targets WT1 on cancer cells and links them to cancer-killing cells of the immune system
- This may mean that RO7283420 could work as a treatment for AML
- RO7283420 was tested at different doses

What did researchers want to find out?

- Researchers did this study to find out how safe RO7283420 was – by checking how many people had unwanted effects and seeing how serious they were (see Section 4 ‘What were the results of the study?’ and Section 5 ‘What were the unwanted effects?’)
- They also wanted to see how well RO7283420 may work, by looking at the effects it had in the body (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 RO7283420 that could be given safely?

Another question that researchers wanted to answer was:

3. How well did RO7283420 work as a treatment for AML?

What kind of study was this?

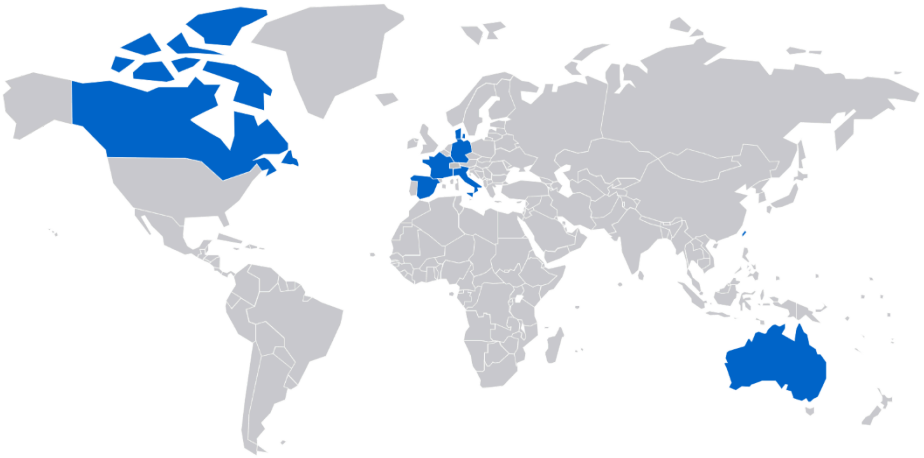
This study was a ‘Phase 1’ study. This was the first time RO7283420 was given to people. A small number of people with AML took RO7283420, and the researchers did medical tests on the people who took part to find out more about RO7283420.

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 November 2020 and stopped early because RO7283420 did not work as well as expected at lowering levels of AML cells. Higher doses could not be given due to unwanted effects. This summary presents the results of the study up until it was stopped in August 2023.

The study took place at 17 study centres – across 8 countries in Asia, Australia, Europe and North America. The following map shows the countries where this study took place.



- Australia
- Canada
- Denmark
- France
- Germany
- Italy
- Spain
- Taiwan

2. Who took part in this study?

In this study, 62 people with AML took part.

People who took part in the study were between 35 and 84 years of age. 34 of the 62 people (55%) were male and 28 of the 62 people (45%) were female.

People could take part in the study if they:

- Had been given standard treatment before, but had no other standard treatment options available
- Agreed to have samples of bone marrow taken during the study

People could not take part in the study if they:

- Had certain health conditions, such as uncontrolled infection, another type of cancer, or current or past disease of the liver, brain or spinal cord
- Were pregnant or breastfeeding

3. What happened during the study?

The study was in 3 parts (A, B and C).

Researchers began by looking at the safety of RO7283420 in Part A. Very small amounts, or doses, were given, which were not expected to affect a person's cancer.

- 2 people were given RO7283420 as a drip into the vein, every 3 weeks for up to 7 months:
  - 1 person received the lowest dose (0.15mg), then
  - the other person received a very low dose (0.5mg)

Once these doses were deemed safe, Part B began.

Part B tested higher doses of RO7283420. Participants received either the full (target) dose each time – known as 'fixed doses'. Or, they were given 'step-up' doses. Step-up doses started with a lower dose that was increased weekly until the target dose was reached. Using
step-up doses can be a safer way to give the first doses of a medicine than fixed doses.

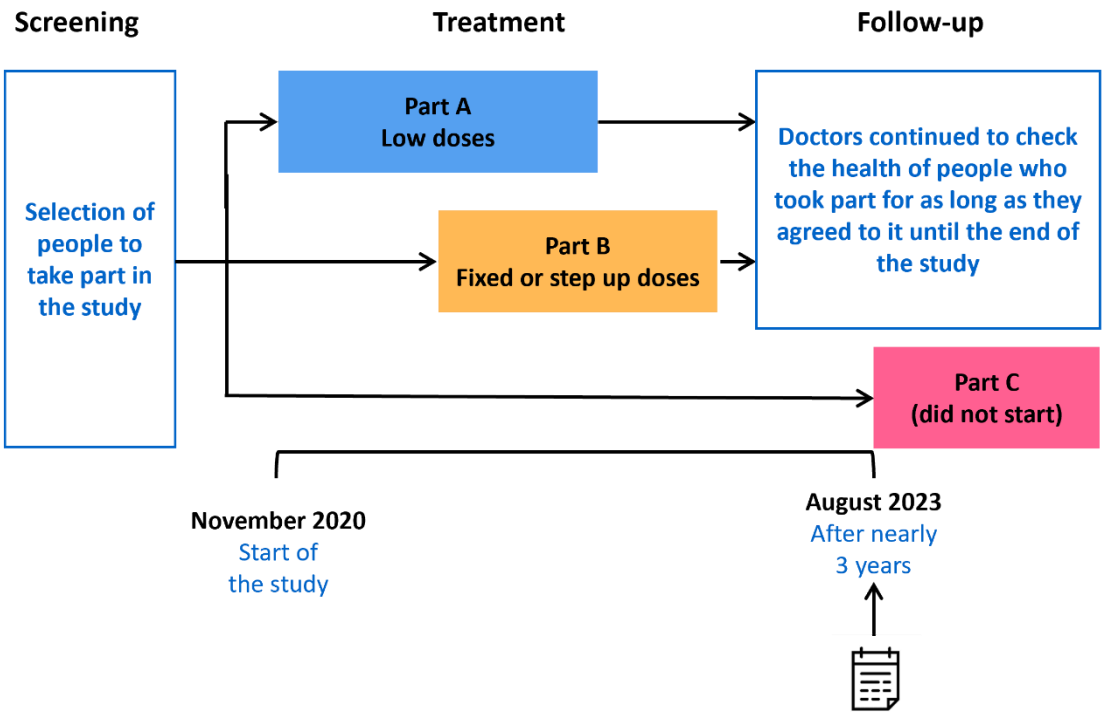
The target doses ranged from 1mg to 18mg. Researchers studied the effects of different dose levels on the body to find the most effective dose for treating AML.

- 60 people were given RO7283420 for up to 7 months. This was given as a drip into the vein, except for 6 people who were given RO7283420 as an injection under the skin. These were given as:
  - fixed doses every 3 weeks
  - 1 step-up dose, then the target dose every 3 weeks
  - 2 step-up doses, then the target dose every week
  - 2 step-up doses, then the target dose every 3 weeks

The study stopped early because RO7283420 did not work as well as expected at lowering levels of AML cells. Higher doses could not be given due to unwanted effects.

Part C planned to look at how safe the best dose of RO7283420 was and how well it worked in a larger number of people with AML. The study was stopped before Part C began.

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

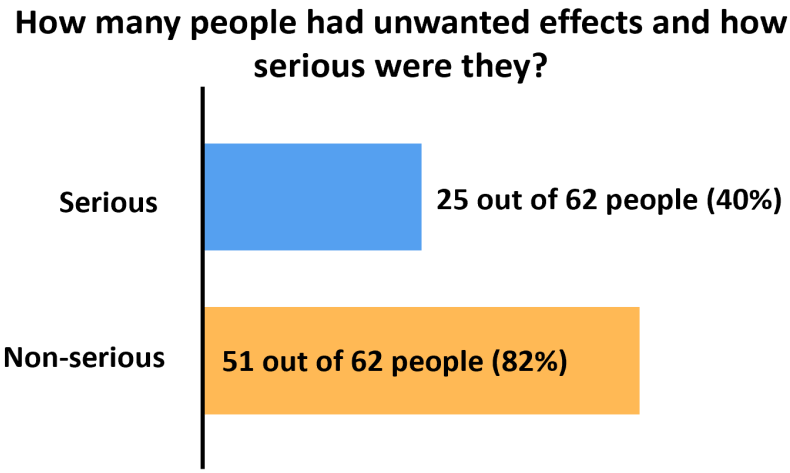
Serious and common unwanted effects are listed in the following sections.

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

During this study, 4 in every 10 people (40%) had at least 1 serious unwanted effect.

Around 8 in every 10 people (82%) had an unwanted effect that was not considered serious.

The safety of RO7283420 was similar to other immunotherapies in people with AML



More information on the type of unwanted effects that people had is in Section 5 'What were the unwanted effects?'.

Question 2: What was the maximum dose of RO7283420 that could be given safely?

The maximum dose of RO7283420 that could be safely given was 12mg. This was given after 2 step-up doses (1mg then 3mg) then the 12mg target dose.

The most common unwanted effect that stopped people being given higher doses of RO7283420, was 'cytokine release syndrome'. Cytokine release syndrome happens when the immune system reacts in an unusual way to an infection or cancer immunotherapy. During this reaction, substances called cytokines are released into the body. This can cause a variety of symptoms, such as a fever, nausea, headache and rash. The person can also have a fast heartbeat, low blood pressure and trouble breathing.

Question 3: How well did RO7283420 work as a treatment for AML?

Information on how well RO7283420 worked was available from 47 people in the study.

Researchers looked at how many people had a positive response to the treatment.

- 3 out of 47 people (6%) had no cancer on tests or scans after treatment
  - 1 person was given 1 step-up dose (2mg), then 12mg target doses
  - 1 person was given 2 step-up doses (1mg, then 3mg), then 6mg target doses
  - 1 person was given 2 step-up doses (1mg, then 6mg), then 12mg target doses

They also looked at how much lower the number of AML cells in blood or bone marrow were after treatment in the best responders.

- 8 out of 47 people (17%) had more than 50% fewer AML cells in their blood or bone marrow after treatment compared with the start of the study

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?

Serious unwanted effects

The most common serious unwanted effects related to the study medicine are shown in the following table – these happened in 2 or more people in the study. Some people had more than 1 unwanted effect – this means that they are included in more than 1 row in the table.

Serious unwanted effects reported in this study	**People taking RO7283420** (62 people total)
Cytokine release syndrome	29% (18 out of 62 people)
A reaction on the skin where it has been pricked with a needle to give a treatment*	3% (2 out of 62 people)
A reaction to the drip into the vein**	3% (2 out of 62 people)

*Symptoms include redness, swelling or rash on the skin.
**Symptoms include throwing up, wanting to throw up, a feeling of coldness that makes the body shiver, low
or high blood pressure, fever, pain or discomfort in the head, frequent watery stools, shortness of breath and cough.

1 person died due to an unwanted effect that may have been related to the study medicine. This unwanted effect was an extreme overreaction of the immune system (known as haemophagocytic lymphohistiocytosis, or HLH). HLH is similar to cytokine release syndrome, but much more serious.

During the study, some people decided to stop taking their medicine because of unwanted effects:

- 9 out of 62 people (15%) stopped taking their medicine

Most common unwanted effects

The most common unwanted effects are shown in the following table – these happened in 3 or more people in the study. Some people had more than 1 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 RO7283420** (62 people total)
Cytokine release syndrome	61% (38 out of 62 people)
Higher than usual levels of 'ALT' in the blood, which can indicate potential liver damage	11% (7 out of 62 people)
Higher than usual levels of 'AST' in the blood, which can indicate potential liver, heart or kidney damage	10% (6 out of 62 people)
Rash	8% (5 out of 62 people)
Higher than usual levels of 'GGT' in the blood, which can indicate potential liver or bile duct damage	5% (3 out of 62 people)
Not having energy or strength	5% (3 out of 62 people)
Fever	5% (3 out of 62 people)
Throwing up	5% (3 out of 62 people)
Higher than usual levels of protein in the urine, which can indicate potential kidney damage	5% (3 out of 62 people)

Other unwanted effects

You can find information about other unwanted 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 62 people with AML. These results helped researchers learn more about AML and RO7283420.

- RO7283420 did not lower levels of AML cells as much as it needed to, in order for it to work well as a treatment for AML
- Overall, high doses of RO7283420 did not have a greater effect at lowering the level of AML cells than lower doses
- Even higher doses of RO7284320 could not be given due to unwanted effects

7. Are there plans for other studies?

At the time of writing this summary, no more studies looking at RO7283420 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/NCT04580121
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-000216-30/results
- https://forpatients.roche.com/en/trials/cancer/leukemia/a-dose-escalation-and-expansion-study-evaluating-the-sa-65126.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/leukemia/a-dose-escalation-and-expansion-study-evaluating-the-sa-65126.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, multi-center, phase I study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of RO7283420 as a single agent in hematologic and molecular relapsed/refractory acute myeloid leukemia'.

- The protocol number for this study is: WP42004
- The ClinicalTrials.gov identifier for this study is: NCT04580121
- The EudraCT number for this study is: 2020-000216-30