Summary of Clinical Trial Results

A study to look at whether RO7300490 worked in people with solid tumours that had spread – and how safe this medicine was

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 May 2021 and stopped early – in January 2024 – because the drug company (Roche) made the decision to no longer develop the study medicine. This was to prioritise the development of other medicines.

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

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about solid tumours that have spread and the medicine studied – 'RO7300490'.

Key information about this study

- This study was done to look at how safe a potential new medicine (called 'RO7300490') is for solid tumours and how well it works on its own or when given with an existing medicine.
- The study stopped early, so people were not given RO7300490 with the existing medicine (called 'atezolizumab').
- This study included 80 people in 5 countries.
- The main findings were that:
    - Around 6% of people (5 out of 80 people) taking RO7300490 on its own had serious unwanted effects
    - At the highest doses given, no-one in the study had unwanted effects that prevented them from being given their intended dose of RO7300490
    - Around 43% of people (31 out of 73 people) had tumours that did not grow as a 'best response', however cancer worsened in 60 out of 80 people (75%) by the end of the study
    - No-one in the study had cancer that shrank after treatment.
- This study stopped early because the drug company (Roche) made the decision to no longer develop the study medicine. This was to prioritise the development of other medicines.

1. General information about this study

Why was this study done?

Solid tumours are cancer cells that grow in organ systems throughout the body. This includes, for example, cancers of the lung, skin and breast.

Standard treatment includes chemotherapy and immunotherapy. Immunotherapy is a type of medicine that helps a person's own immune system (the body's natural defence) to attack cancer cells. Immunotherapy is often given on its own or with other treatments (such as chemotherapy) to treat solid tumours that have spread to nearby tissue surrounding the tumour or to other parts of the body.

In this study, researchers tested a new possible immunotherapy medicine (RO7300490) for solid tumours. They aimed to see how safe and how well it worked, either on its own or with an existing immunotherapy medicine called atezolizumab.

What were the study medicines?

This study looked at 2 immunotherapy medicines:

- **Atezolizumab** – existing medicine
- **RO7300490** – the medicine that was studied.

'Atezolizumab' is an existing medicine given to people with some types of solid tumours.

- You say this as 'ah-tezz-oh-LIZ-yoo-mab'.
- Atezolizumab works by blocking a protein called 'PD-L1' that is often found on some types of cancer cells.
  - PD-L1 'hides' the cancer from the immune system
  - Blocking PD-L1 allows the immune system to attack the cancer cells.
- This may mean that atezolizumab could stop solid tumours from growing.
- Atezolizumab is approved for treating some types of bladder, lung, liver and breast cancer.

'**RO7300490**' is the medicine that was studied here – it works in a different way to atezolizumab.

- RO7300490 works by activating a protein called 'CD40' found on a type of cell of the immune system.
- This may mean that RO7300490 could help the immune system attack cancer cells.

What did researchers want to find out?

- Researchers did this study to find out how safe the medicine was – by checking how many people had unwanted effects and 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 the medicine worked (see Section 4 'What were the results of the study?').

The main questions that researchers wanted to answer were:

1. How many people had unwanted effects and how serious were they?
2. What types of unwanted effects prevented people from being given their intended dose of study medicine, and how many people had them?
3. How many people had a reduction of their cancer after treatment, or tumours that didn't grow?

Another question that researchers wanted to answer was:

4. How long did people live without their cancer getting worse?

What kind of study was this?

This study was a 'Phase 1' study. This was the first study for RO7300490. A small number of people with solid tumours that had spread took RO7300490 and the researchers did medical tests on the people who took part to find out more about RO7300490.

This study was 'open-label'. An open-label study 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?

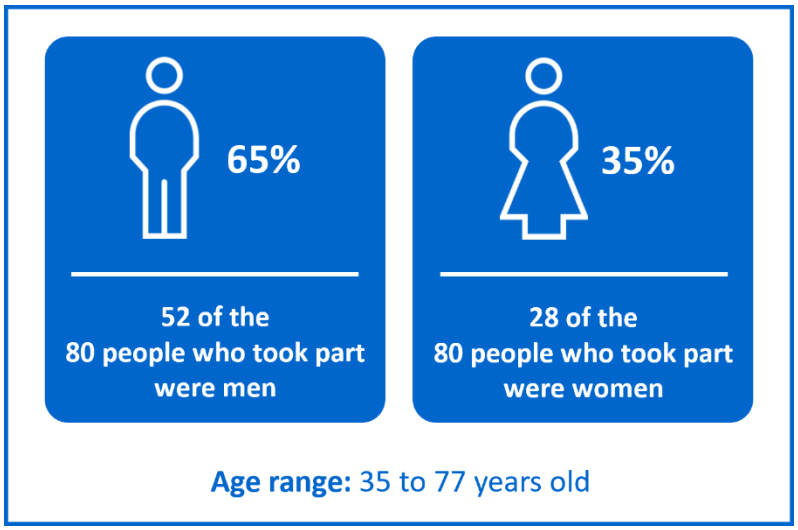
The study started in May 2021 and stopped early because the drug company (Roche) made the decision to no longer develop the study medicine. This was to prioritise the development of other medicines. This summary presents the results of the study up until it was stopped in January 2024.

The study took place at 10 study centres – across 5 countries in Europe and Asia. The countries were: Denmark, France, South Korea, Spain and the United Kingdom.

2. Who took part in this study?

In this study, 80 people with solid tumours that had spread took part.

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 a solid tumour that had spread to nearby tissue or to other parts of the body
- Had no standard treatments available for their solid tumour

People could not take part in the study if they:

- Had cancer that had spread to the brain or spinal cord
- Had other medical conditions, such as heart, liver or lung disease
- Were pregnant or breastfeeding

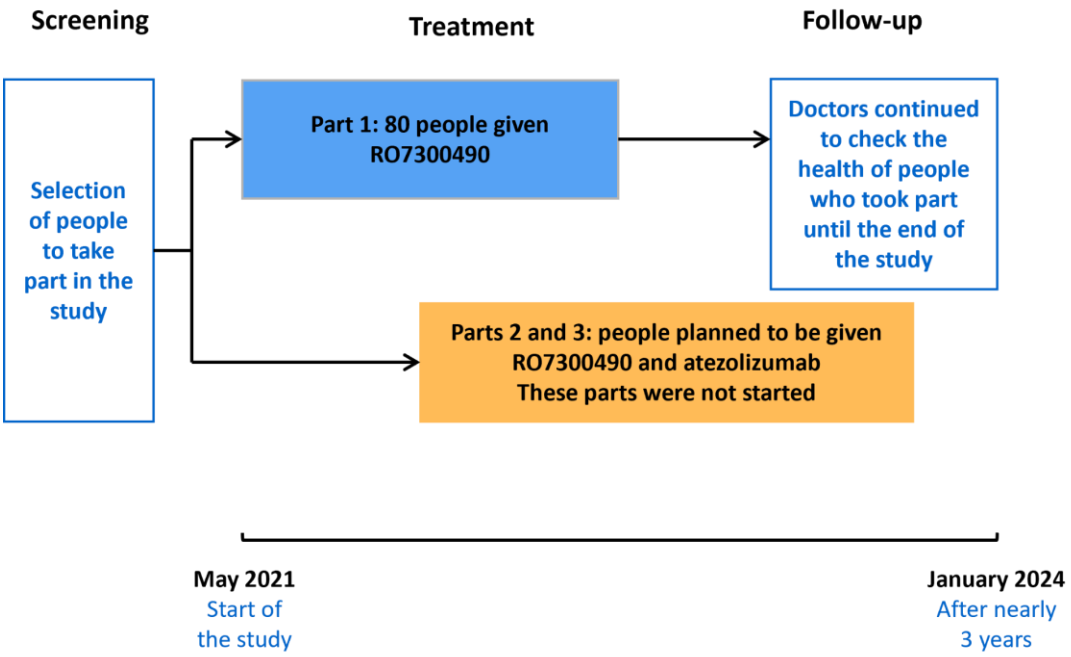
3. What happened during the study?

The study was in 3 parts.

Part 1 aimed to find out the safest and most effective dose of RO7300490 when given alone. Different groups of people were given varying doses, starting with low doses. This was because it was the first time RO7300490 was given to people.

Parts 2 and **3** planned to find the best dose of RO7300490 when combined with atezolizumab, and how well it worked as a treatment for solid tumours. However, the study stopped before these parts of the study 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.



4. What were the results of the study?

Question 1: How many people had unwanted effects and how serious were they?

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 treatment in the study.
- Not all of the people in this study had all of the unwanted effects.
- It is important to be aware that the unwanted effects reported here are from this single study.
- Unwanted effects can vary from mild to very serious and may vary from person to person.

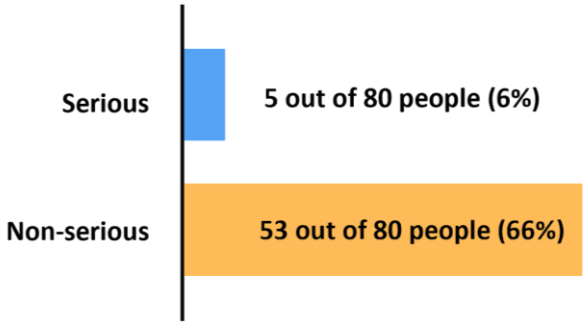
Overall, people tolerated RO7300490 at all doses given in this study, and unwanted effects improved with or without needing medical treatment.

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

During this study:

- Around 6 in every 100 people (6%) had at least one serious unwanted effect that was considered related to the study medicine.
- Around 7 in every 10 people (66%) had an unwanted effect that was not considered serious and was considered related to the study medicine.

How many people had unwanted effects and how serious were they?



More information on the types of unwanted effects is given in Section 5.

Question 2: What types of unwanted effects prevented people from being given their intended dose of study medicine, and how many people had them?

Another piece of information that researchers collected was the highest amount of RO7300490 that could be given to a person safely – before they had unacceptable or unmanageable unwanted effects.

- At the highest doses given in the study, no one had unwanted effects that stopped them from receiving their intended dose of RO7300490.
- As a result, the study did not determine the highest safe dose of RO7300490.

Question 3: How many people had a reduction of their cancer after treatment, or tumours that didn't grow?

How well RO7300490 worked was looked at in 73 of the 80 people in the study.

The 'best responses' people had between starting treatment and their disease getting worse were:

- Tumours did not grow in 31 out of 73 people (43%). This outcome did not depend on the dose of RO7300490 that people were given.
- Cancer worsened in 39 out of 73 people (53%).
- No-one had cancer that shrank after treatment; information on responses at certain timepoints during the study was missing from the remaining 3 people (4%).

By the end of the study, 60 out of 80 people (75%) had stopped taking the study treatment because their cancer had worsened.

Question 4. How long did people live without their cancer getting worse?

On average, people had study treatment for 50 days before their cancer worsened. This outcome did not depend on the dose of RO7300490 that people were given.

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 unwanted effects?

Serious and common unwanted effects that were related to RO7300490 are listed in the following sections.

Serious unwanted effects

Serious unwanted effects are shown in the following table. These were the serious unwanted effects that were related to RO7300490 and in any dose group. Some people had more than one unwanted effect – this means that they are included in more than one row in the table.

Serious unwanted effects reported in this study	**People taking RO7300490** (80 people total)
Difficulty breathing	1% (1 out of 80)
Inflammation of the lung tissue	1% (1 out of 80)
Heart attack	1% (1 out of 80)
Frequent, watery stools	1% (1 out of 80)
Higher than usual levels of 'ALT' in the blood, which indicates potential liver damage	1% (1 out of 80)
Higher than usual levels of 'AST' in the blood, which indicates potential liver, heart or kidney damage	1% (1 out of 80)

No-one in the study died due to unwanted effects that may have been related to the study medicine.

During the study, 2 out of 80 people (3%) stopped taking the study medicine because of unwanted effects thought to be caused by it. These people were given low doses of the study medicine.

Most common unwanted effects

The most common unwanted effects related to RO7300490 are shown in the following table – these were seen in at least 1 in every 10 people. 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 RO7300490** (80 people total)
Pain in joints	31% (25 out of 80)
Not having energy or strength	14% (11 out of 80)

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.

6. How has this study helped research?

The information presented here is from a single study of 80 people with solid tumours that had spread. These results helped researchers learn more about solid tumours and RO7300490.

7. Are there plans for other studies?

At the time of writing this summary, no more studies looking at RO7300490 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/NCT04857138
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-004489-21/results
- https://forpatients.roche.com/en/trials/cancer/solid-tumors/a-study-to-evaluate-safety--pharmacokinetics-and-anti-t-88927.html

If you would like to find out more about the results of this study, the full title of the relevant scientific conference presentation is: “A Phase I study of a tumor-targeted, fibroblast activation protein (FAP)-CD40 agonist (RO7300490) in patients with advanced solid tumors”. The authors are: Melero I, Bardaji ML, Spanggaard I , Lee D, Spicer J and others. The abstract is published in the journal ‘Journal for Immunotherapy of Cancer’, volume number 11, issue Supplement 1.

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-anti-t-88927.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: “A Phase I Open-Label, Multicenter, Dose-Escalation and Expansion Study to Evaluate Safety, Pharmacokinetics, and Anti-Tumor Activity of RO7300490 a fibroblast activation protein-alpha (FAP) targeted CD40 agonist, as Single Agent or in Combination with Atezolizumab in Participants with Advanced and/or Metastatic Solid Tumors”.

- The protocol number for this study is: WP42627.
- The ClinicalTrials.gov identifier for this study is: NCT04857138.
- The EudraCT number for this study is: 2020-004489-21.