Clinical Trial Results – Layperson Summary

A study to look at whether RO6874281 plus atezolizumab worked in people with solid tumours that are advanced or have spread and how safe this experimental drug combination 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 (August-2022). More information may now be known.

The study started in February 2018 and was discontinued in December 2021 because the drug company, Roche, decided to prioritise the development of other, potentially more impactful medicines, and not because too many people had concerning side effects or because the experimental drug was not effective.

No single study can tell us everything about the risks and benefits of an experimental drug. 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 experimental drug.

- 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 to answer important questions about solid tumours that are advanced or have spread in the body and the experimental drug.

Key information about this study

- This study was done to assess whether RO6874281 works when given with atezolizumab in people with solid tumours that are not treatable with surgery or have spread in the body.
- RO6874281 and atezolizumab are drugs that help the patients' immune system seek out and fight cancer cells (known as 'immunotherapies').
- In this study, people were given RO6874281 and atezolizumab or standard chemotherapy treatment.
- This study included 256 people in 15 countries.
- The main findings were that the number of people with cancer that had reduced or disappeared after treatment (response rate) was dependent on the type of cancer and previous treatment that a person had been given. No new safety concerns were seen. The response rate was highest in people with cervical cancer, with approximately 1 in 4 people (27%) responding to treatment with RO6874281 and atezolizumab.
- Around 37% of people (95 out of 254 people taking only RO6874281 and atezolizumab and not chemotherapy) had serious side effects that were considered related to RO6874281 and atezolizumab.
- Around 7% of people (19 out of 254) stopped taking RO6874281 and atezolizumab due to side effects.
- This study did not include as many patients as planned because the drug company (Roche) decided to discontinue the study. This was to prioritise the development of other, potentially more impactful medicines, and not because too many people had concerning side effects or because the experimental drug was not effective.

1. General information about this study

Why was this study done?

Solid tumours can start in the lung, in the head and neck, the lower part of the womb (the cervix), the food pipe that connects the throat to the stomach (the oesophagus) or in another organ. Current medicines can be very effective against solid tumours, but they do not work very well for everyone, and some people have concerning side effects.

New medicines are needed for advanced solid tumours that cannot be removed with surgery (also known as 'unresectable tumours') or tumours that have spread further to other parts of the body (also known as 'metastasis).

What were the study medicines?

An experimental drug called **RO6874281** was the focus of this study.

- RO6874281 is called an experimental drug because health authorities have not approved it for the treatment of advanced and/or metastatic solid tumours.
- The study was developed to see how well RO6874281 worked for the possible treatment of cancers (such as lung cancer, cancers of the head and neck, oesophageal cancer, and cervical cancer).
- RO6874281 is similar to a type of molecule that the body naturally produces called a cytokine (you say this as 'sye-tow-kine') that stimulates the immune system. This type of drug is known as an 'immunotherapy'.
- RO6874281 recognizes a structure on tumours called FAP, which is short for fibroblast activation protein-alpha. FAP is part of the connective tissue that is needed for solid tumours to grow. RO6874281 delivers the immunotherapy to immune cells that filter into the solid tumours.
- RO6874281 was designed to be given in combination with other medicines, such as atezolizumab, to make them more effective by boosting the body's immune response to fight cancer cells.

Atezolizumab (Tecentriq™) is an existing standard medicine which is approved by the Food and Drug Administration (FDA) in the United States and by the European Medicines Agency (EMA) for the treatment of some types of bladder, liver, skin and lung cancers.

- You say this as 'a-teh-zoh-LIZ-yoo-mab'.
- Atezolizumab is a type of immunotherapy medicine. It blocks a protein called PD-L1, which can be found in some cancers. PD-L1 'hides' the cancer from the immune system. Blocking it gives a signal to the body's immune system to attack the cancer cells.
- RO6874281 was tested with atezolizumab in this study.

In one part of this study, people were to be given either RO6874281 with atezolizumab, or existing standard chemotherapy medicines for people with advanced or metastatic lung cancer (**gemcitabine** [Gemzar®] or **vinorelbine** [Navelbine™]).

- You say gemcitabine as 'jem-she-TUH-been'.
- You say vinorelbine as 'vin-nor-REL-been'.
- Gemcitabine and vinorelbine work by attacking growing tumour cells.

What did researchers want to find out?

Researchers did this study to see whether RO6874281 in combination with atezolizumab worked, and the initial plan was also to see how well it worked compared with standard chemotherapy medicines in patients with lung cancer (see section 4 “What were the results of the study?”).

They also wanted to find out how safe the combination of RO6874281 and atezolizumab was – by checking how many people had side effects and what these were when taking the experimental drug combination during this study (see section 5 “What were the side effects?”).

The main question that researchers wanted to answer was:
Does RO6874281 given in combination with atezolizumab reduce the size of cancer in people with advanced solid tumours?

Other questions that researchers wanted to answer included:
How long does RO6874281 given in combination with atezolizumab prevent cancer getting worse in people with advanced solid tumours?

What kind of study was this?

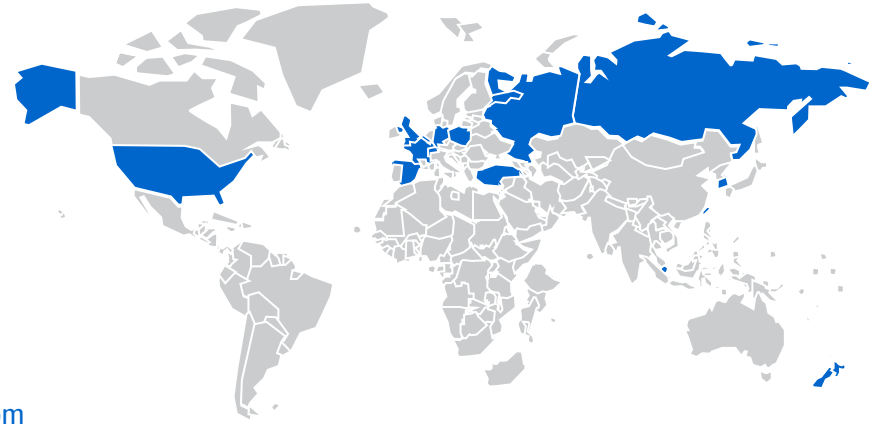
This study was a ‘Phase 2’ study. This means that both RO6874281 and atezolizumab have been tested in a number of people with solid tumours before this study.

When and where did the study take place?

The study ran from February 2018 to December 2021.

The study took place at 42 study centres across 15 countries in Asia, Europe, Oceania, and North America. The following map shows the countries where this study took place.

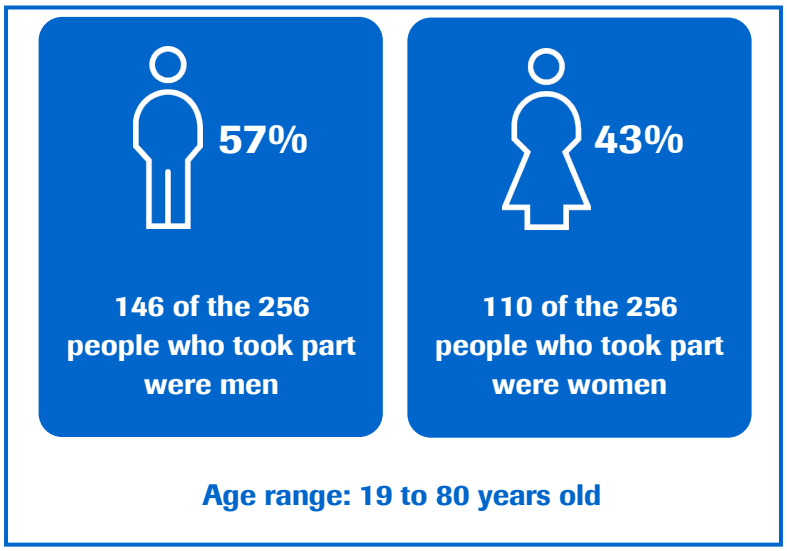
Belgium
France
Germany
Israel
South Korea
New Zealand
Poland
Russia
Singapore
Spain
Switzerland
Taiwan
Turkey
United Kingdom
USA



2. Who took part in this study?

In this study, 256 people with advanced solid tumours took part. Of these 256 people, 95 people had lung cancer, 78 people had head and neck cancer, 35 people had oesophageal cancer and 48 people had cervical cancer.

People who took part in the study were between 19 and 80 years of age. 146 of the 256 people (57%) were men and 110 of the 256 people (43%) were women.



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

People could take part in the study if they:

- Were over 18 years old
- Had been diagnosed with an advanced or metastatic solid tumour according to certain criteria
- Had received certain medicines previously, and their cancer has not responded to it, or had returned

People could not take part in the study if they:

- Had cancer that had spread to the brain or spinal cord and was untreated or caused symptoms
- Had received certain medicines or treatments previously
- Had certain other medical conditions
- Were pregnant or breastfeeding

3. What happened during the study?

During the study, people were placed into treatment groups (Groups A to N) depending on the type of cancer they had, and, in some cases, the type of treatment that they had received in the past for their tumour.

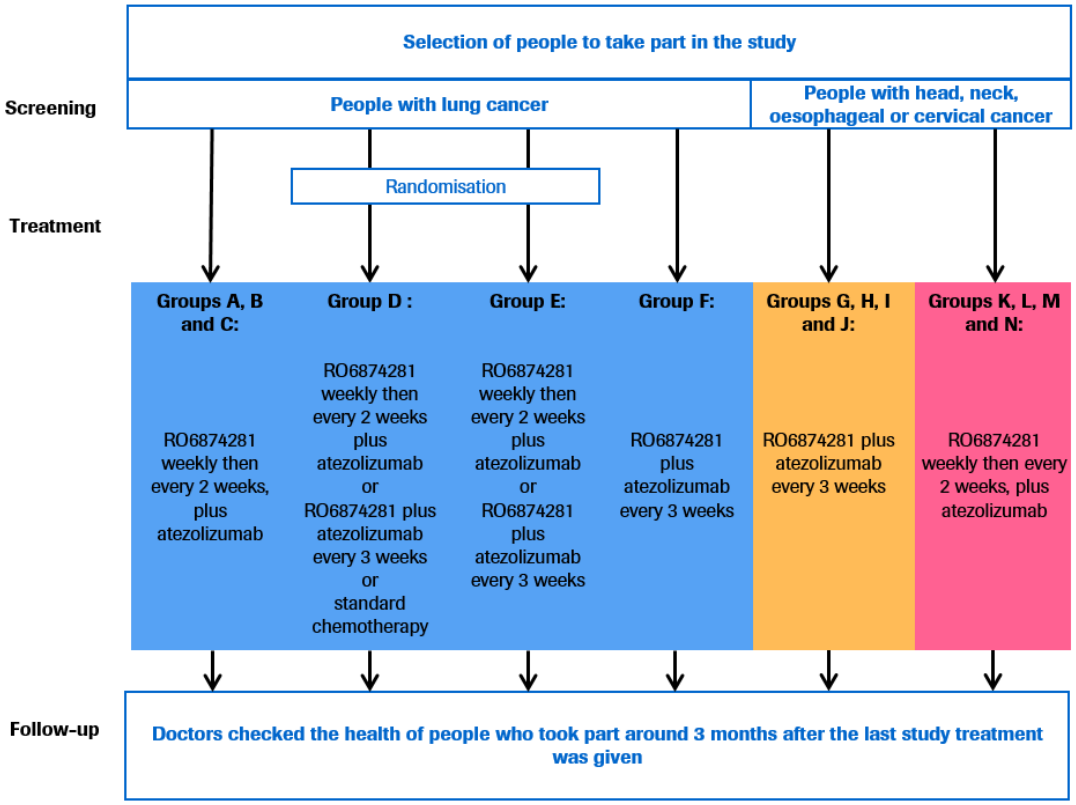
People in this study were given RO6874281 with atezolizumab in two different treatment schedules, as follows:

- RO6874281 every week plus atezolizumab every 2 weeks for 4 weeks, then RO6874281 plus atezolizumab every 2 weeks, all given as an infusion (into a vein)
  OR
- RO6874281 with atezolizumab given as an infusion every 3 weeks.

Some people in Group D were planned to be given gemcitabine or vinorelbine (standard chemotherapy) as an infusion according to local medical guidelines.

People in Groups D and E were selected randomly to be given treatment (known as "randomisation"). This means that it was decided by chance which of the study medicines people in the study would have – like tossing a coin.

The study flowchart shows all planned stages and treatment groups of the study.



People were given study medicine until their cancer started to get worse, or they stopped treatment due to side effects or for other reasons.

Some people had a good response to treatment and continued to be given RO6874281 plus atezolizumab (after they had completed the planned course of treatment in the study) for as long as the treatment benefitted them.

After people finished taking their study medicine, they were asked to go back to their study centre for a follow up visit – to check their overall health.

The study was discontinued and did not include as many people as planned because the drug company (Roche) decided to prioritise the development of other, potentially more impactful medicines, and not because too many people had concerning side effects or because the experimental drug was not effective.

4. What were the results of the study?

The number of people who were given treatment in each group before the study was stopped was smaller than planned – so researchers were only able to look at whether the study medicines had worked in some of the treatment groups.

No people were given treatment in Groups C and L by the time the study was discontinued, and the number of people in Group D was too small to see if RO6874281 plus atezolizumab had worked, or to see how well it worked compared to standard chemotherapy medicines.

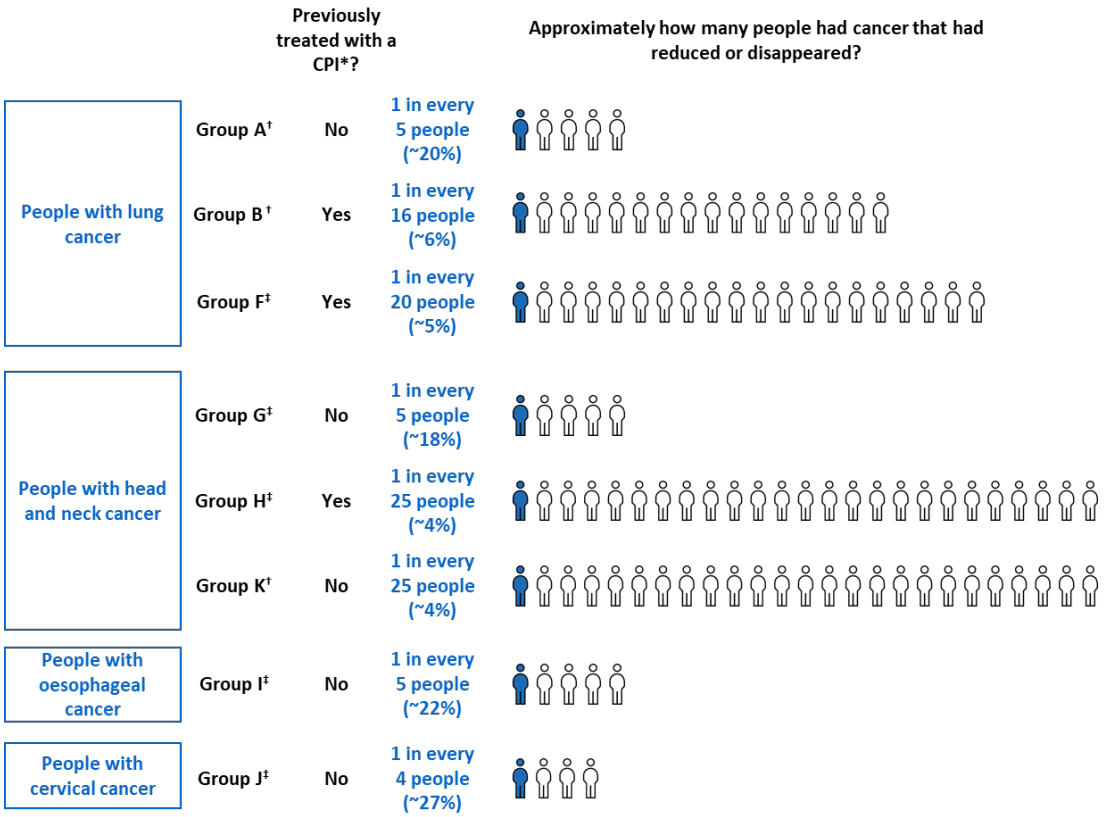
The table below shows how many people were given treatment in each group, the type of cancer people had, and if they were allowed to have previously received a certain treatment (called a 'checkpoint inhibitor') to be in each group.

Group Name	Cancer type	Previous treatment with a medicine called a CPI (a 'checkpoint inhibitor')	RO6874281 plus atezolizumab treatment schedule	Number of people treated
A	Lung cancer	No	Weekly then every 2 weeks	26
B		Yes		32
C		No		0
D		Yes	Weekly then every 2 weeks	3
			OR Every 3 weeks OR	5
			Standard chemotherapy*	2
E		No	Weekly then every 2 weeks OR	3
			Every 3 weeks	2
F		Yes	Every 3 weeks	22
G	Head and neck cancer	No		23
H		Yes		30
I	Oesophageal cancer	No		33
J	Cervical cancer			47
K	Head and neck cancer		Weekly then every 2 weeks	25
L		Yes		0
M	Oesophageal cancer	Either yes or no		2
N	Cervical cancer			1

* Gemcitabine or vinorelbine; these two people were given RO6874281 and atezolizumab after they had finished taking chemotherapy

Question 1: Does RO6874281 given in combination with atezolizumab reduce the size of cancer in people with advanced solid tumours?

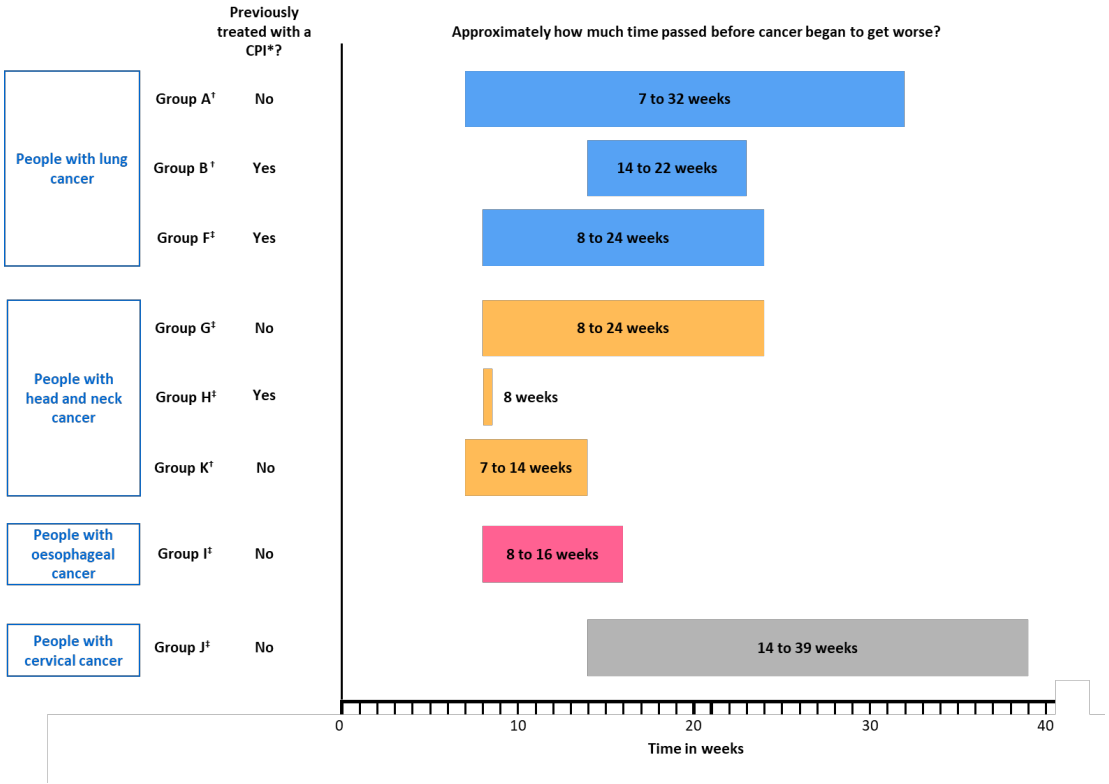
Researchers looked at how many people had cancer that had reduced or disappeared after treatment (known as the 'objective response rate'). The results are shown in the picture below. Overall, between around 1 in 4 and around 1 in 25 people responded to treatment, depending on the type of cancer they had, and what previous treatment they had received.



* CPI = checkpoint inhibitor (a type of medicine)
† RO6874281 plus atezolizumab treatment weekly then every 2 weeks
‡ RO6874281 plus atezolizumab treatment every 3 weeks

Question 2: How long does RO6874281 given in combination with atezolizumab prevent cancer getting worse in people with advanced solid tumours?

Researchers looked at how much time passed from the start of the study until cancer began to get worse (known as 'progression-free survival'). The results are shown in the picture below. The number of weeks shown is the shortest and longest amount of progression-free survival time that was seen for most of the people (95%) in each group. Across all of the groups in this study, the shortest amount of time that passed before cancer began to get worse was 7 to 14 weeks. The longest amount of time that passed before cancer began to get worse was 14 to 39 weeks across all of the groups.



The shortest and longest survival time in Group H was 8 weeks
* CPI = checkpoint inhibitor (a type of medicine)
† RO6874281 plus atezolizumab treatment weekly then every 2 weeks
‡ RO6874281 plus atezolizumab treatment every 3 weeks

This section only shows the key results from the 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 (also known as 'adverse reactions') are unwanted medical problems (such as a headache) that happen during the study.

- They are described in this summary because the study doctor believes the side effects were related to the experimental drug.
- Not all of the people in this study had all of the side effects.

Serious and common side effects that were reported by any of the 254 people who were given RO6874281 in combination with atezolizumab in this study are listed in the following sections. The two people in Group D who were treated initially with chemotherapy and then with RO6874281 plus atezolizumab, were not included in this safety assessment.

Serious side effects

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

During this study, around 1 in every 3 people (37%; 95 out of 254 people) had at least one serious side effect that was related to the RO6874281 given in combination with atezolizumab.

148 people (58%) died during the study. Of these, 87% (128 out of 148 people) died due to cancer, and 12% (18 out of 148 people) died due to health problems that were not considered related to the study medicine or were due to other, non-health related causes. In 2 of the 148 patients who died (around 1%), the study doctor thought their death may have been related to RO6874281 and atezolizumab treatment.

During the study, around 7% (19 out of 254 people) decided to stop taking the study medicine because of side effects.

Most common side effects

During this study, 98% of people (248 out of 254 people) had a side effect that was not considered serious and was considered related to study treatment.

The most common side effects that were reported by at least 1 in every 3 people (33%) in this study, are shown in the following table – these are the most common side effects across all treatment groups.

Most common side effects reported in this study	Percentage of people in the study who had the side effect
Fever	80% (204 out of 254)
Liver, heart or kidney damage – shown by higher levels of something called 'AST' in the blood	39% (99 out of 254)
Chills	35% (90 out of 254)
Low level of red blood cells (anaemia)	35% (89 out of 254)
Feeling sick (nausea)	35% (89 out of 254)
Liver damage – shown by higher levels of something called 'ALT' in the blood	34% (87 out of 254)
Low energy levels	32% (81 out of 254)
Feeling tired (fatigue)	30% (77 out of 254)

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 256 people with advanced solid tumours. These results helped researchers learn more about the safety of RO6874281 given in combination with atezolizumab for people with advanced solid tumours. RO6874281 plus atezolizumab showed an acceptable safety profile that was similar to the known safety profiles of each individual drug. Because the study was discontinued and the number of people in each group was smaller than planned, no conclusions could be drawn about how effective RO6874281 and atezolizumab treatment is for people with advanced solid tumours.

No single study can tell us everything about the risks and benefits of a medicine or drug. 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 the combination of RO6874281 and atezolizumab 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/NCT03386721
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2017-003182-94/results
- https://forpatients.roche.com/en/trials/cancer/study-to-evaluate-the-therapeutic-activity-of-ro6874281-as-a-com.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/study-to-evaluate-the-therapeutic-activity-of-ro6874281-as-a-com.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 organized 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 II Study To Evaluate The Therapeutic Activity Of Ro6874281, an Immunocytokine, Consisting of Interleukin-2 Variant (IL-2V) Targeting Fibroblast Activation Protein-A (FAP), In Combination With Atezolizumab (Anti-PD-L1), Administered Intravenously, In Participants With Advanced and/or Metastatic Solid Tumours”

- The protocol number for this study is: BP40234.
- The ClinicalTrials.gov identifier for this study is: NCT03386721
- The EudraCT number for this study is: 2017-003182-94.