

Summary of Clinical Trial Results

A study to look at how safe different doses of vopikitung (RO7296682 or RG6292) were in combination with atezolizumab for people with solid tumours that have spread

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 January 2021 and stopped early – in January 2024 – because researchers found the medicine being studied was unlikely to work as well as expected, and because it was difficult to find the right people to join the next parts of 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.**

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Glossary

- Tregs = a type of immune cell (regulatory T cells) which act as the 'brakes' of the immune system

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 and the medicines studied – ‘vopikitug’ (also known as ‘RO7296682’ or ‘RG6292’), and ‘atezolizumab’.

Key information about this study

Why was the study done?

- This study was done to look at how safe different doses of a potential new treatment combination is for people with solid tumours that have spread and who have no standard treatment available.
- The study also looked at how well the treatments worked.

What was the medicine being studied and who was involved?

- In this study, people were given the medicine being studied (called ‘vopikitug’) with an existing medicine (called ‘atezolizumab’).
- This study included 49 people in 6 countries.

What were the results?

- The main findings were:
 - Vopikitug was well-tolerated at all doses (0.3mg to 160mg) when given with atezolizumab
 - 2 people had unwanted effects that prevented them from being given their intended dose.
 - 1 person had a problem with their immune system after being given 20mg of vopikitug. This was considered a serious unwanted effect.
 - 1 person had a rash with raised and flat areas after being given 80mg of vopikitug. This was not considered serious.
 - 3 out of 48 people (6%) had a positive response to treatment.
 - 2 of these people had been given 40mg of vopikitug
 - 1 person had been given 80mg of vopikitug
- Around 16% of people (8 out of 49 people) taking the study medicines had serious unwanted effects.
- This study stopped early because the medicine being studied looked like it would not work as well as expected, and because it was difficult to find the right people to join the next parts of the study.

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 cancers of the lung, skin and breast.

Solid tumours that have spread to nearby tissue are known as 'advanced' cancer. Solid tumours that have spread to other parts of the body are known as 'metastatic' cancer. Standard treatment includes chemotherapy and can include immunotherapy. Immunotherapy is a type of medicine that helps a person's own immune system attack cancer cells. Immunotherapy is often given on its own to treat advanced solid tumours. Cancers can become 'resistant' – which means treatment stops working.

One type of immune cell – known as 'regulatory T-cells' (or Tregs – you say this as 'tee-regs') – is responsible for dampening down (or 'putting the brakes on') an immune response to protect the body from over-reacting and harming itself. Tregs may slow down the effect of immunotherapies against cancer – so researchers designed an experimental drug called vopikitug that should temporarily lower the number of Tregs in a person's body.

This study looked at how safe different doses of a potential new immunotherapy were when given in combination with an existing, standard immunotherapy.

What were the study medicines?

'Atezolizumab' is an existing medicine given to certain people with advanced solid tumours.

- You say this as 'ah-tezz-oh-LIZ-yoo-mab'
- Atezolizumab works by blocking a protein called 'PD-L1' that can be found on 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

A medicine called 'vopikitug' was the focus of this study.

- You say this as 'voe-PI-kee-tug'.
- Vopikitug sticks to a marker called CD25 on the surface of Treg cells – the 'brakes' of the immune system – and signals to other cells of the immune system to destroy them.
- This may allow the immune system to better fight cancer cells, particularly when vopikitug is given with other immunotherapies that have an immune-boosting effect.
- Vopikitug was tested at different doses.

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 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 the combination of study medicines 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 well did they tolerate different doses of vopikitug when given with atezolizumab?
2. How well did vopikitug work against advanced solid tumours when given with atezolizumab?

What kind of study was this?

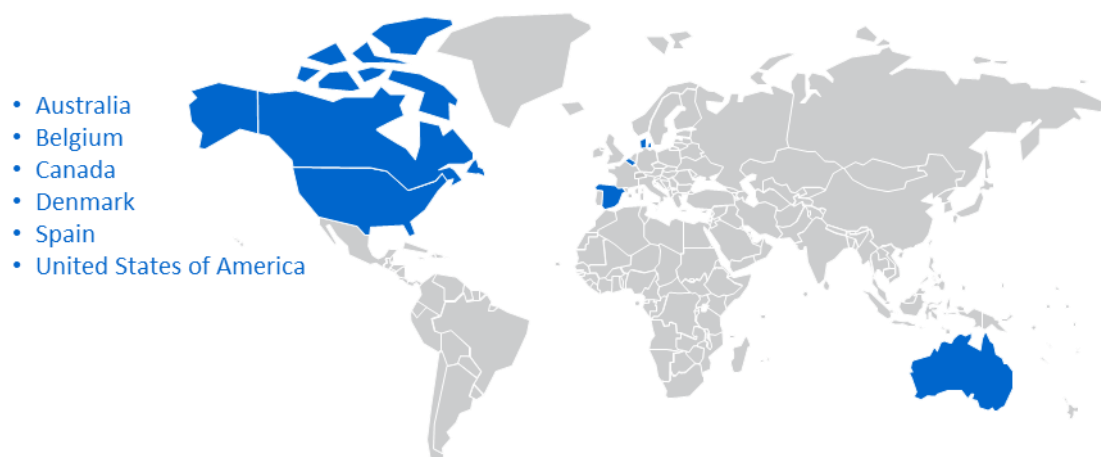
This study was a ‘Phase 1’ study. This was the first study for vopikitug in combination with atezolizumab. A small number of people with advanced solid tumours took vopikitug with atezolizumab and the researchers did medical tests on the people who took part to find out more about the study medicines.

This was an ‘open label’ study. This means that both the people taking part in the study and the study doctors knew people were taking vopikitug with atezolizumab.

When and where did the study take place?

The study started in January 2021 and stopped early because the medicine being studied was found to be unlikely to work as well as expected, and because it was difficult to find the right people to join the next parts of the study. This summary presents the results of the study up until it was stopped in January 2024.

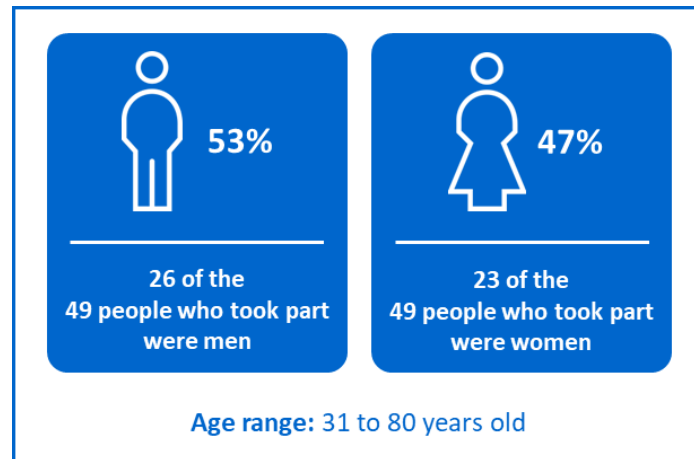
The study took place at 10 study centres – across 6 countries in Australia, Europe and North America. The following map shows the countries where this study took place.



2. Who took part in this study?

In this study, 49 people with advanced solid tumours 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
- They had an advanced solid tumour that had not responded to standard treatment
- They had no standard treatments available for their cancer

People could not take part in the study if:

- They had cancer of the brain or spinal cord
- They had cancer that had spread to the brain or spinal cord that was not under control

3. What happened during the study?

During the study, everyone was given:

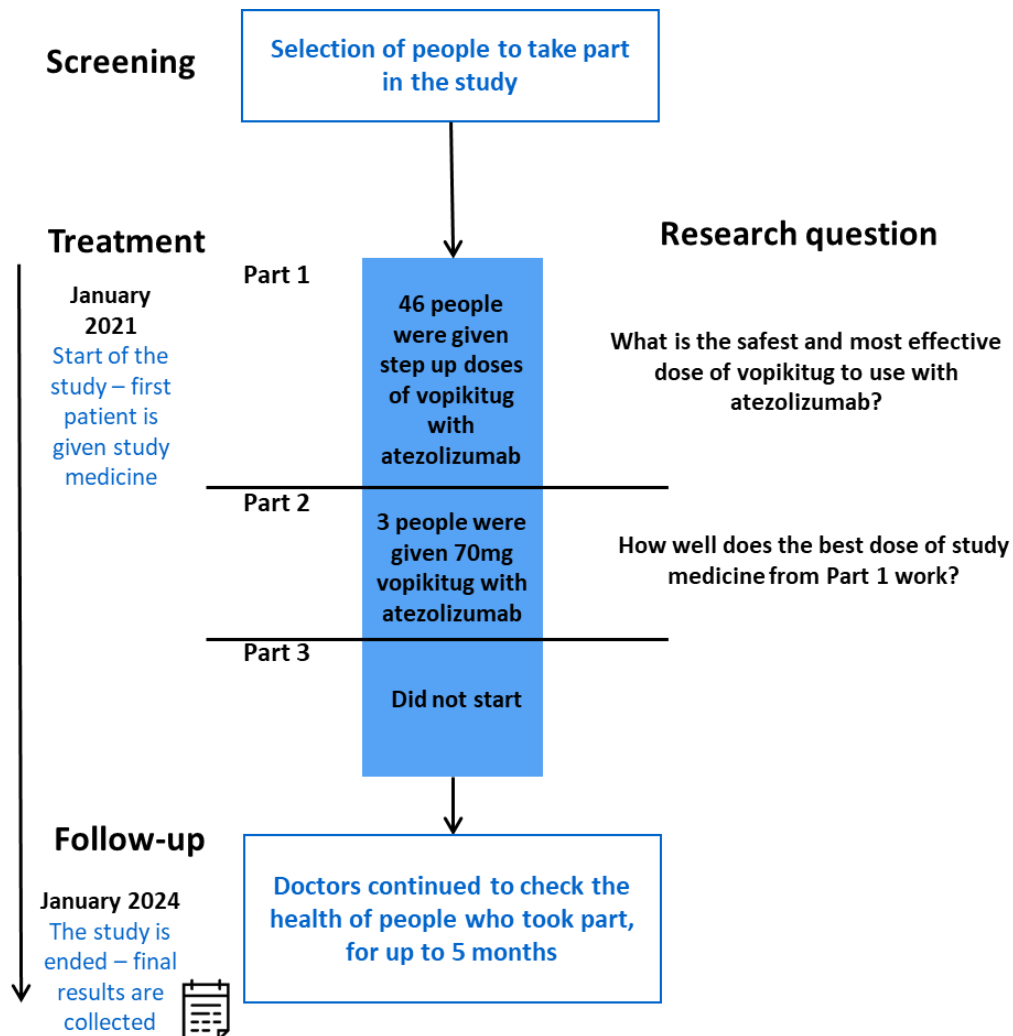
- **Vopikitug** and **atezolizumab** every 3 weeks for up to 2 years. Both were given as drips into the vein (infusions)
- This was the first time that people had been given vopikitug with atezolizumab, so very small doses of vopikitug were first given to a smaller number of people, to check safety. This dosage was then increased gradually in the next groups of participants

The study was in 3 parts.

- Part 1 looked at the effects of increasing doses of vopikitug with a standard dose of atezolizumab
- Part 2 involved people who had previously been given anti-PD-L1 medicines, such as atezolizumab, that stopped working for them

- The dose of vopikitug was chosen based on the results of Part 1
 - This Part was to check how safe and how well the study medicines worked
- Part 3 was to look at how well vopikitug and atezolizumab with other treatments worked for treating advanced solid tumours. The treatment combinations were to be selected depending on the results of other vopikitug studies and to match changes in how standard treatment was given (for example, atezolizumab on its own, or with chemotherapy)
 - Part 3 was not started due to the results of Parts 1 and 2

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. This study stopped early, so the symbol on the timeline (📅) shows when the information shown in this summary was collected – after 3 years (January 2024).



4. What were the results of the study?

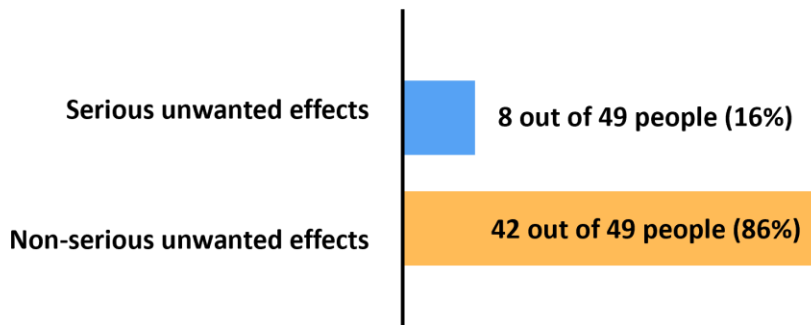
Question 1: How many people had unwanted effects, and how well did they tolerate different doses of vopikitug when given in combination with atezolizumab?

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.
- It is important to be aware that the unwanted effects reported here are from this single study. Therefore, the unwanted effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflet.
- Unwanted effects can vary from mild to very serious and may vary from person to person.

Researchers looked at the number of people who had serious or non-serious unwanted effects related to the study treatment.

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



Overall, all doses of vopikitug were well-tolerated by people in the study, including the highest dose of 160mg.

2 people had unwanted effects that prevented them from being given their intended dose.

- 1 person had a problem with their immune system after being given 20mg of vopikitug. This was considered a serious unwanted effect.
- 1 person had a rash with raised and flat areas after being given 80mg of vopikitug. This was not considered serious.

The highest dose of vopikitug was 160mg when given with atezolizumab.

Question 2: How well did vopikitug work against advanced solid tumours when given in combination with atezolizumab?

Another piece of information that researchers collected was the number of people who had a reduction of their cancer after treatment.

Information on how well treatment had worked was available for 48 of the 49 people in the study.

- 3 out of 48 people (6%) had a reduction of their cancer after treatment.
 - 2 of these people had been given 40mg of vopikitug
 - 1 person had been given 80mg of vopikitug

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 are listed in the following sections.

Serious unwanted effects

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

All serious unwanted effects that were considered related to the study medicines are shown in the following table. 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 vopikitug and atezolizumab (49 people total)
Confusion and difficulty understanding what's happening	2% (1 out of 49 people)
Immune system problems	2% (1 out of 49 people)
Frequent, watery stools	2% (1 out of 49 people)
Inflammation of muscles	2% (1 out of 49 people)
Inflammation of the liver	2% (1 out of 49 people)
Fever	2% (1 out of 49 people)
Inflammation of the lung tissue	2% (1 out of 49 people)
Collapsed lung	2% (1 out of 49 people)
Inflammation of the large bowel	2% (1 out of 49 people)
Pain in the belly	2% (1 out of 49 people)

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

During the study, 5 people decided to stop taking their medicine because of unwanted effects.

Most common unwanted effects

The most common unwanted effects are shown in the following table – these were seen in 4 or more people in the study. 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 vopikitug and atezolizumab (49 people total)
Itching	41% (20 out of 49 people)
Rash	35% (17 out of 49 people)
Rash with flat and raised areas	22% (11 out of 49 people)
Not having energy or strength	20% (10 out of 49 people)
Feeling tired or weak	12% (6 out of 49 people)
Dry skin	8% (4 out of 49 people)
Fever	
Frequent, watery stools	
Wanting to throw up	
Throwing up	

Less thyroid hormone than usual (that helps control cells in the body influencing how quickly or slowly they produce energy).	
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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 49 people with advanced solid tumours. These results helped researchers learn more about these types of cancer and vopikitung given with atezolizumab.

7. Are there plans for other studies?

At the time of writing this summary, no more studies looking at vopikitung 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/NCT04642365>
- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-003164-82/results>
- <https://forpatients.roche.com/en/trials/cancer/solid-tumors/a-study-to-evaluate-the-safety-and-tolerability-of-ro72-03496.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: “Safety and anti-tumor activity of a novel Treg depleter RG6292, as a single agent and in combination with atezolizumab in patients with solid tumors”. The authors of the presentation are: Valentina Gambardella, Michael Ong, Maria Esperanza Rodriguez Ruiz, Jean-Pascal Machiels, Miguel Fernandez de Sanmamed and others. The presentation is published in the journal ‘Cancer Research’, volume number 83, 8_Supplement, abstract number CT110

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-the-safety-and-tolerability-of-ro72-03496.html>

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- 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 Ib study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary anti-tumor activity of RO7296682 in combination with atezolizumab in participants with advanced and/or metastatic solid tumors”.

- The protocol number for this study is: BP42595.
- The ClinicalTrials.gov identifier for this study is: NCT04642365.
- The EudraCT number for this study is: 2020-003164-82.