Summary of Clinical Trial Results

A study of atezolizumab combined with interferon alpha with or without bevacizumab in people with a type of kidney cancer called 'renal cell carcinoma' and in people with other types of cancer

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
- People who took part in the study

This summary is based on information known at the time of writing (February 2022).

The study **started in August 2014 and ended in December 2019**. This summary was written after the study ended.

- **You should not make decisions based on this one summary – always talk to your doctor before making any decisions about your treatment.**

Contents of the summary

Glossary

- **Checkpoint inhibitor (CPI):** a type of 'immunotherapy' medicine used in cancer treatment to help the body's immune system attack tumours
- **Colorectal cancer (CRC):** a type of colon cancer
- **Non-small cell lung cancer (NSCLC):** a type of lung cancer
- **Renal cell carcinoma (RCC):** a type of kidney cancer

Thank you to the people who took part in this study

The people who took part in this study helped researchers answer important questions about 4 types of cancers:

- A type of kidney cancer called 'renal cell carcinoma' or '**RCC**'.
- A type of skin cancer called '**melanoma**'.
- A type of colon cancer called colorectal cancer or '**CRC**'.
- A type of lung cancer called 'non-small cell lung cancer' or '**NSCLC**'.

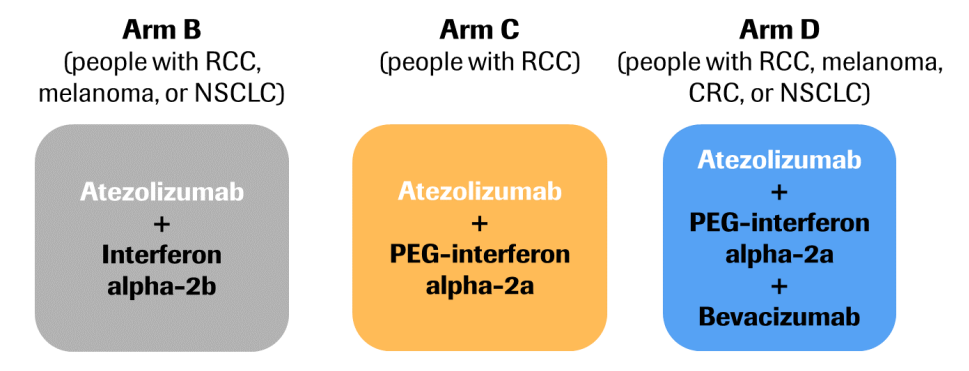
Researcher also learned more about the 3 different medicines being studied:

- 'Atezolizumab'

- ‘Interferon alpha’
- ‘Bevacizumab’

Key information about this study

- This study was done to compare 3 treatments in people with **RCC, melanoma, CRC, or NSCLC** that had spread to nearby cells or other parts of the body.
- People were split into 3 ‘Arms’ and each arm was given a different combination of the medicines as shown in the picture:
- The medicine being studied, called ‘**atezolizumab**’ taken together with an existing medicine called ‘**interferon alpha-2b**’.
- Atezolizumab taken together with another existing medicine called ‘**PEG-interferon alpha-2a**’.
- Atezolizumab taken together with PEG-interferon alpha-2a and another existing medicine called ‘**bevacizumab**’.



- The study also included 2 other arms (Arm A and Arm E) which are not included in this summary.
- The study was done at 8 centres in North America and 1 centre in Europe.
- A total of 116 people took part in the study: 77 people had RCC, 17 people had melanoma, 14 people had CRC, and 8 people had NSCLC.

The main findings were:

- Overall, about 36% of the people (42 out of 116 people) had serious side effects.
- The most common side effects that were thought to be caused by the medicine(s) were feeling tired, chills, and fever.
- During this study, researchers looked to see if the tumours got smaller after treatment with the different combinations of medicines
    - In **Arm B**, 20% of people (13 out of 65) had their tumours get smaller after taking atezolizumab plus interferon alpha-2b.
    - In **Arm C**, none of the 6 people had their tumours get smaller after taking atezolizumab plus PEG-interferon alpha-2a.
    - In **Arm D**, 24% of people (11 out 45) had their tumours get smaller after taking atezolizumab plus PEG-interferon alpha-2a plus bevacizumab.

1. General information about this study

Why was this study done?

People with cancers that spread to nearby cells or to other parts of the body are very sick and have poor chances of surviving because there is no treatment that can cure all patients. These people are sometimes given a treatment called 'immunotherapy' – a medicine that helps a person's own immune system attack tumours (cancer). This study looked at people who had RCC, melanoma, CRC, or NSCLC. In these people, the cancer had spread to nearby cells or other parts of the body.

Some immunotherapy medicines are man-made versions of natural substances called '**interferons**'. In the body, interferons are made by the immune system to help fight infections and cancer. One man-made interferon called '**interferon alpha**' is sometimes given to people with cancer.

Other types of immunotherapy medicines called '**checkpoint inhibitors**' (**CPIs**) work by blocking substances called checkpoint proteins. Everyone has checkpoint proteins in their body. These proteins stop the immune system from attacking healthy cells. Cancer cells can use these proteins to stop the immune system from killing the tumour. CPIs block these proteins and allow the immune system to attack the cancer cells. One checkpoint protein that CPIs can block is called 'programmed death-ligand 1' or '**PD-L1**'.

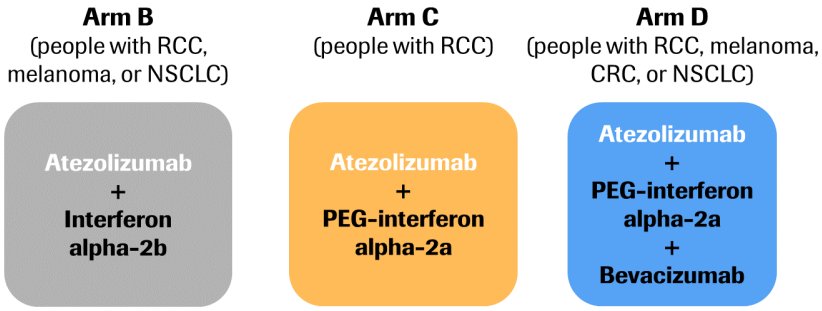
Immunotherapy medicines are sometimes given with a type of medicine called an '**anti-angiogenic**' treatment. Anti-angiogenic medicines stop the cancer cells from forming the new blood vessels that they need to grow and spread. Anti-angiogenic medicines can also help immunotherapy medicines kill cancer cells.

In this study, researchers wanted to see if adding a CPI that blocks PD-L1 (**atezolizumab**) to **interferon alpha** with or without an anti-angiogenic medicine (**bevacizumab**) will be safe for people with different types of solid tumours. Researchers also wanted to find out how well the medicines worked.

What were the medicines being studied?

This study looked at different combinations of 2 immunotherapy medicines and an anti-angiogenic medicine in people who had different types of cancer. The people in the study were separated into three 'arms':

- **Arm B: atezolizumab** (study medicine) plus **interferon alpha-2b** (existing interferon medicine).
- **Arm C: atezolizumab** (study medicine) plus **PEG-interferon alpha-2a** (another existing interferon medicine).
- **Arm D: atezolizumab** (study medicine) plus **PEG-interferon alpha-2a** (existing interferon medicine) plus **bevacizumab** (existing anti-angiogenic medicine).



Atezolizumab (known by its brand name, Tecentriq®) is the medicine being studied here, in combination with other medicines.

- The body's immune system fights diseases like cancer. However, cancer cells containing PD-L1 can block (stop) the immune system from attacking the cancer. Atezolizumab releases this blockage – meaning that the immune system is able to fight the cancer cells.
- Atezolizumab is a type of immunotherapy medicine.
- When people take atezolizumab, their tumour (cancer) may get smaller.

Interferon alpha-2b and **PEG-interferon alpha-2a** are 2 existing interferon medicines used in the study.

- Both medicines are man-made versions of substances called interferons that are made by the immune system. Interferons alert the body when a virus enters the body. Man-made interferons help the immune system to fight cancer. They can also prevent cancer cells from growing and spreading quickly.
- Man-made interferons are a type of immunotherapy medicine.

Bevacizumab (known by its brand name, Avastin®) is an existing anti-angiogenic medicine used in the study.

- Cancers grow their own blood vessels so they can get food and oxygen from the blood. To do this, the cancer needs a protein called vascular endothelial growth factor (VEGF). Bevacizumab blocks VEGF and stops the cancer from growing blood vessels, so the cancer starves and can't grow.

What did researchers want to find out?

- Researchers did this study to look at whether adding atezolizumab to interferon alpha with or without bevacizumab led to any side effects (an unwanted effect of a medicine or medical treatment) and how serious these side effects were (see section 4 "What were the side effects?").
- They also wanted to find out how well the different medicines worked when taken together (see section 5 "How well did the medicines work?").

The main questions that researchers wanted to answer were:

1. How many people had side effects or serious side effects during the study?

Other questions that researchers wanted to answer included:

2. How many people had smaller tumours after taking the study medicines?

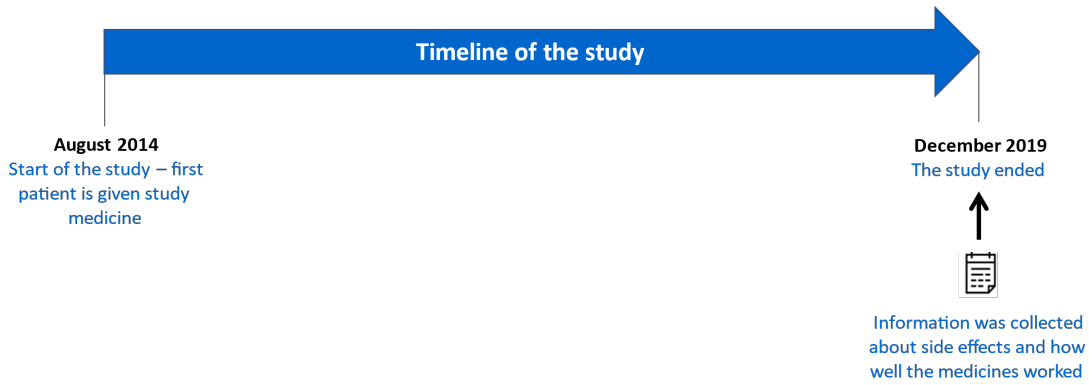
3. How long did it take for people's cancer to get worse after the start of the study?

What kind of study was this?

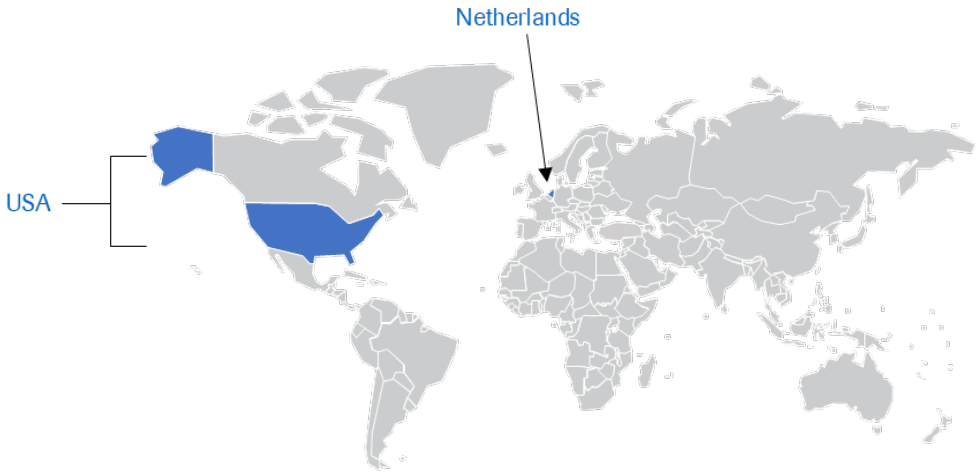
This was a 'Phase 1' study, which means that this was one of the first studies of atezolizumab plus interferon alpha with or without bevacizumab in people with these types of cancers. A small number of people with RCC, melanoma, CRC, or NSCLC took the study medicines, and researchers did medical tests to find out if the drugs were safe. Researchers also wanted to find out how well the medicines worked together.

When and where did the study take place?

The study is part of a larger study that started in August 2014 and ended in December 2019. This summary was written after the study ended.

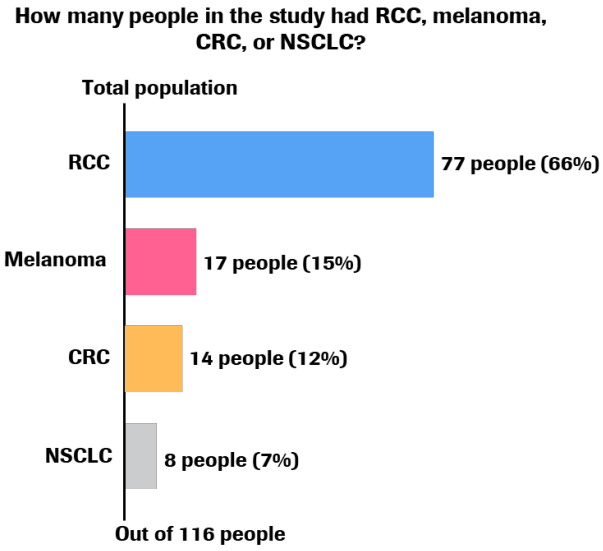


The study took place at 8 study centres in North America and 1 centre in Europe (the Netherlands). This map shows the countries where this study took place.

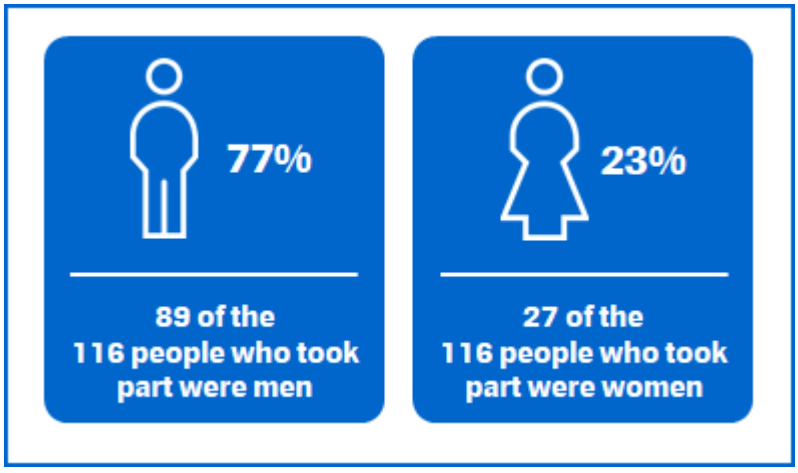


2. Who took part in this study?

In this study, 116 people with either RCC, melanoma, CRC or NSCLC took part. Most of the people (66%) in the study had RCC. Here is more information about how many people had each type of cancer:



Here is more information on the people who took part in the study:



People could take part in the study if they:

- Were at least 18 years old.
- Had RCC, melanoma, CRC or NSCLC that had spread to nearby cells or other parts of the body.
- Had already been treated for their cancer with other medicines such as CPIs before they joined the study and started taking the study medicines.
    - People with RCC who had not been treated with any medicines before the study started were also allowed to join the study.
- Were able to perform activities as well or almost as well as they could before they got cancer.

People could not take part in the study if they:

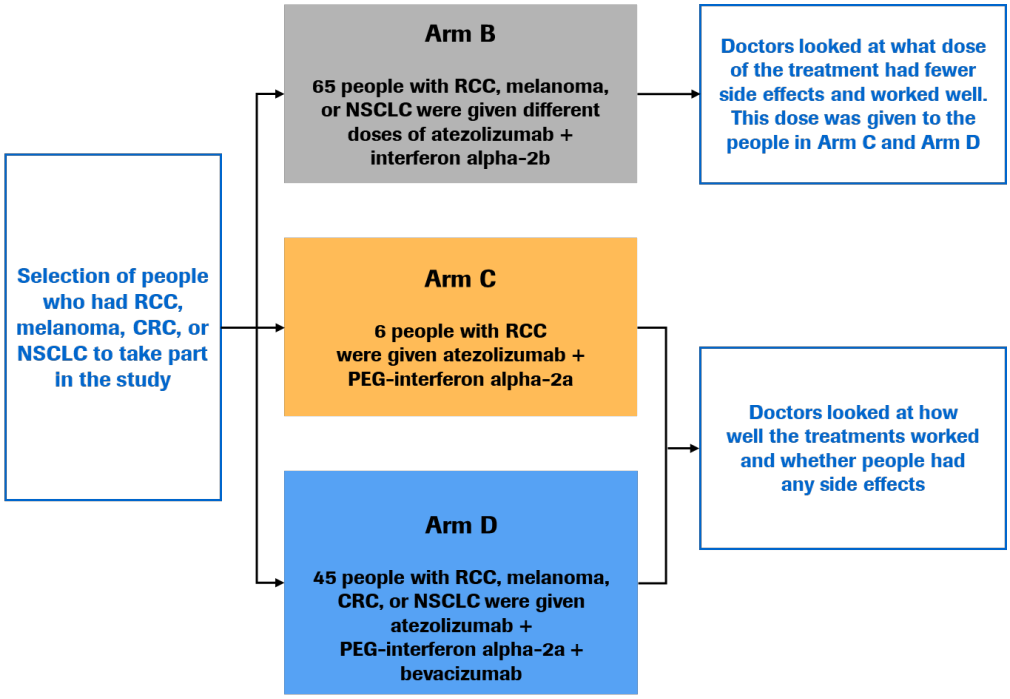
- Had cancer that had spread to the brain or spinal cord.
- Had NSCLC that had changes (mutations) in genes called *EGFR* or *ALK* or had melanoma that had changes (mutations) in genes called *BRAF*.

3. What happened during the study?

People in the study were separated into 3 '**Arms**'. In each arm, people were given a combination of the study medicines. At the start of the study, people in Arm B were given increasing doses of the study medicines (atezolizumab plus interferon alpha-2b) to find the highest dose that did not cause side effects. This dose was then given to the people in Arm C and Arm D to see how well the medicines worked and whether people had any side effects. All the study medicines were injected into a vein:

- Atezolizumab, PEG-interferon alpha-2a, and bevacizumab were given every 3 weeks.
- Interferon alpha-2b was given 3 times every week.

This picture gives more information about what happened in the study.



When the study ended, the people who took part were asked to go back to their study centre for more visits to check their overall health.

The people in **Arm D** were also separated into these 3 groups:

- '**No previous treatment'** group – people with RCC who had not been given any medicines for their cancer before joining the study. This group had 15 people in it.
- '**Previously treated**' group – people with CRC or NSCLC who had been treated with other medicines for their cancers before joining the study. This group had 15 people in it.
- '**Previous CPI treatment**' group – people with RCC, melanoma, or NSCLC who had been treated with CPIs for their cancers before joining the study. This group had 15 people in it.

To look at how well the study medicines worked, researchers also put the people in **Arm B** who had never received any CPI treatment before joining the study into a group. This was called the '**No previous CPI treatment**' group and it had 45 people in it.

This table gives more information about the different arms and groups in the study.

	Arm B: atezolizumab + interferon alpha-2b		**Arm C:** atezolizumab + PEG-interferon alpha-2a	**Arm D:** atezolizumab + PEG-interferon alpha-2a + bevacizumab			
	All people	**No previous CPI treatment**	**All people**	**All people**	**No previous treatment**	**Previously treated**	**Previous CPI treatment**

Number of people	65	45	6	45	15	15	15
Number of people who had RCC	50	45	6	21	15	0	6
Number of people who had melanoma	14	0	0	3	0	0	3
Number of people who had CRC	0	0	0	14	0	14	0
Number of people who had NSCLC	1	0	0	7	0	1	6

4. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happen during the study.

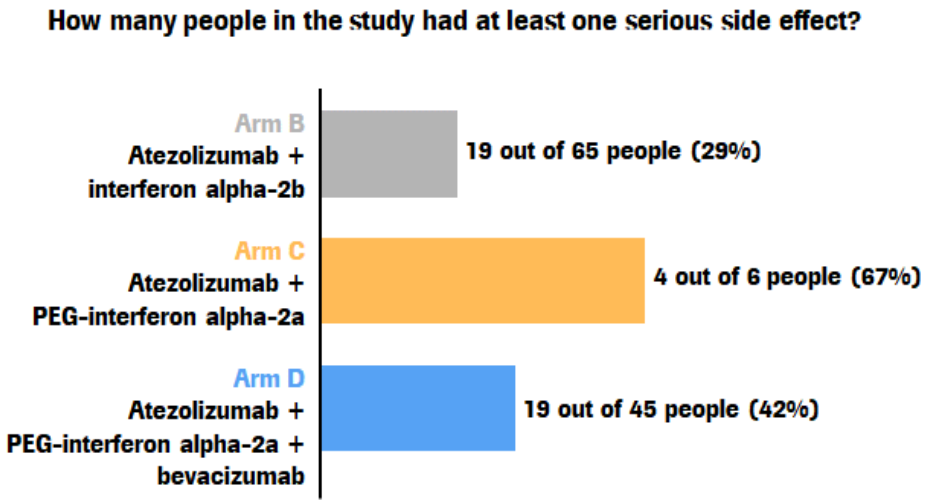
- Some side effects were caused by the medicines given in the study.
- Not all of the people in this study had all of the side effects.
- Side effects may be mild to very serious.
- The side effects were different from person to person.
- It is important to know that the side effects reported here are from this one study. Therefore, the side effects shown here may be different from those seen in other studies or those that appear in the medicine leaflets.
- 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, 42 out of the 116 people who took part (36%) had at least one serious side effect.

This picture shows the number of people who had at least one serious side effect in each arm:



Researchers looked at how many people died from side effects that may have been related to one of the study medicines:

- None of the 65 people in **Arm B** died.
- None of the 6 people in **Arm C** died.
- 1 out of 45 people (2%) in **Arm D** died.

During this study, some people stopped taking one of the study medicines because of side effects:

- **Arm B**
  - 3 out of 65 people (5%) stopped taking atezolizumab.
  - 3 out of 65 people (5%) stopped taking interferon alpha-2b.
- **Arm C**
  - 1 out of 6 people (17%) stopped taking both atezolizumab and PEG-interferon alpha-2a.
- **Arm D**
  - 1 out of 45 people (2%) stopped taking atezolizumab.
  - 2 out of 45 people (4%) stopped taking PEG-interferon alpha-2a.
  - 8 out of 45 people (18%) stopped taking bevacizumab.

Most common side effects

During this study, all patients (100%) had at least one side effect of any severity due to any cause.

This table shows the most common side effects related to either **atezolizumab or interferon alpha-2b** that happened in at least 10 out of 100 people (10%) in **Arm B** are shown in this table.

Most common side effects related to either atezolizumab or interferon alpha-2b that happened in at least 10 out of 100 people (10%) in Arm B (*medical term*)	**Related to atezolizumab** (65 patients)	**Related to interferon alpha-2b** (65 patients)
Feeling tired (*fatigue*)	28% (6 out of 65)	39% (25 out of 65)
Chills	18% (12 out of 65)	42% (27 out of 65)
Fever (*pyrexia*)	12% (8 out of 65)	35% (23 out of 65)
Joint pain (*arthralgia*)	17% (11 out of 65)	14% (9 out of 65)
Muscle pain (*myalgia*)	11% (7 out of 65)	22% (14 out of 65)
Feeling sick (*nausea*)	8% (5 out of 65)	11% (7 out of 65)
Influenza-like illness	5% (3 out of 65)	12% (8 out of 65)
Low thyroid activity (*hypothyroidism*)	12% (8 out of 65)	3% (2 out of 65)

The most common side effects related to either **atezolizumab or PEG-interferon -2a** that happened in at least 10 out of 100 people (10%) in **Arm C** are shown in this table.

Most common side effects related to either atezolizumab or PEG-interferon alpha-2a that happened in at least 10 out of 100 people (10%) in Arm B (*medical term*)	**Related to atezolizumab** (6 patients)	**Related to PEG-interferon alpha-2a** (6 patients)
Feeling tired (*fatigue*)	33% (2 out of 6)	33% (2 out of 6)
Fever (*pyrexia*)	0	17% (1 out of 6)
Headache	17% (1 out of 6)	17% (1 out of 6)
Feeling sick (*nausea*)	0	17% (1 out of 6)
Low thyroid activity (*hypothyroidism*)	17% (1 out of 6)	0
Cough	17% (1 out of 6)	17% (1 out of 6)
Drooping eyes (*eyelid ptosis*)	17% (1 out of 6)	17% (1 out of 6)

High levels of substances in the blood called 'creatinine phosphokinases' that are needed for muscle cells to work	17% (1 out of 6)	17% (1 out of 6)
High levels of substances in the blood called 'transaminases' that are needed for the liver to work	17% (1 out of 6)	17% (1 out of 6)
Decreased appetite	17% (1 out of 6)	17% (1 out of 6)
Weakness in the joints (*myasthenia gravis*)	17% (1 out of 6)	17% (1 out of 6)
Acute respiratory failure	17% (1 out of 6)	17% (1 out of 6)
High thyroid activity (*hyperthyroidism*)	17% (1 out of 6)	17% (1 out of 6)
Vomiting	17% (1 out of 6)	17% (1 out of 6)
Muscular weakness	17% (1 out of 6)	17% (1 out of 6)
Pneumonia	17% (1 out of 6)	17% (1 out of 6)
Low oxygen in the blood (*hypoxia*)	17% (1 out of 6)	0
High levels of acid in the blood due to problems breathing (*respiratory acidosis*)	17% (1 out of 6)	0
Fever related to the tumour	17% (1 out of 6)	0
Low level of red blood cells (*anaemia*)	0	17% (1 out of 6)
Reactions related to how the drug was given (*infusion-related reactions*)	0	17% (1 out of 6)

The most common side effects related to **atezolizumab or PEG-interferon alpha-2a or bevacizumab** that happened in at least 10 out of 100 people (10%) in **Arm D** are shown in this table.

Most common side effects related to atezolizumab or PEG-interferon alpha-2a or bevacizumab that happened in at least 10 out of 100 people (10%) in Arm D	**Related to atezolizumab** (45 patients)	**Related to PEG-interferon alpha-2a** (45 patients)	**Related to bevacizumab** (45 patients)
Feeling tired (*fatigue*)	51% (23 out of 45)	56% (25 out of 45)	36% (16 out of 45)
Chills	13% (6 out of 45)	13% (6 out of 45)	11% (5 out of 45)
Fever (*pyrexia*)	16% (7 out of 45)	18% (8 out of 45)	11% (5 out of 45)
Joint pain (*arthralgia*)	9% (4 out of 45)	18% (8 out of 45)	2% (1 out of 45)
Muscle pain (*myalgia*)	13% (6 out of 45)	9% (4 out of 45)	4% (2 out of 45)
Feeling sick (*nausea*)	13% (6 out of 45)	16% (7 out of 45)	13% (6 out of 45)
Influenza-like illness	11% (5 out of 45)	20% (9 out of 45)	9% (4 out of 45)
High levels of protein in the urine (*proteinuria*)	2% (1 out of 45)	2% (1 out of 45)	27% (12 out of 45)
High blood pressure (*hypertension*)	0	2% (1 out of 45)	22% (10 out of 45)
Low thyroid activity (*hypothyroidism*)	11% (5 out of 45)	2% (1 out of 45)	0
Nose bleed (*epistaxis*)	0	0	11% (5 out of 45)

Other side effects

You can learn about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see section 8.

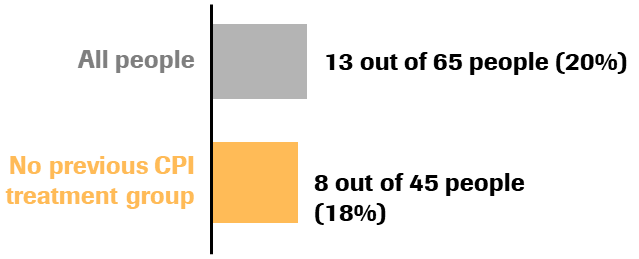
5. How well did the medicines work?

Question 1: How many people had smaller tumours after taking the study medicine?

Researchers looked at how many people had smaller tumours after they started taking the study medicines.

- In **Arm B**, 20% of all people and 18% of people in the **No previous CPI treatment** group had their tumours get smaller after taking atezolizumab plus interferon alpha-2b.

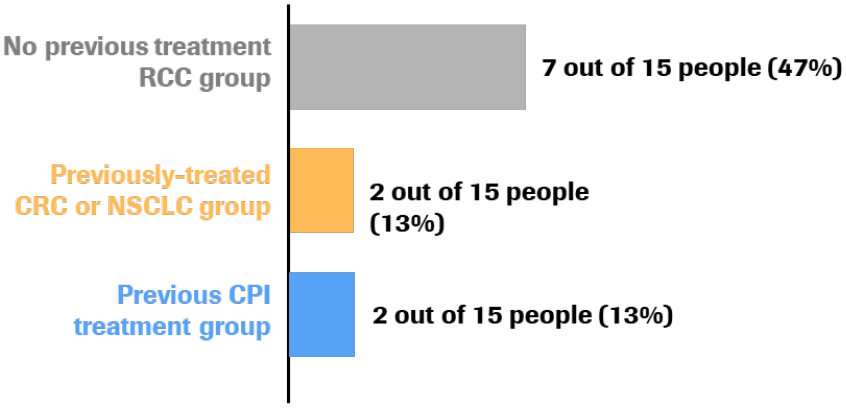
How many people in Arm B of the study had smaller tumours after taking the study medicines?



- In **Arm C**, none of the 6 people with **RCC** had their tumours get smaller after taking atezolizumab plus PEG-interferon alpha-2a.

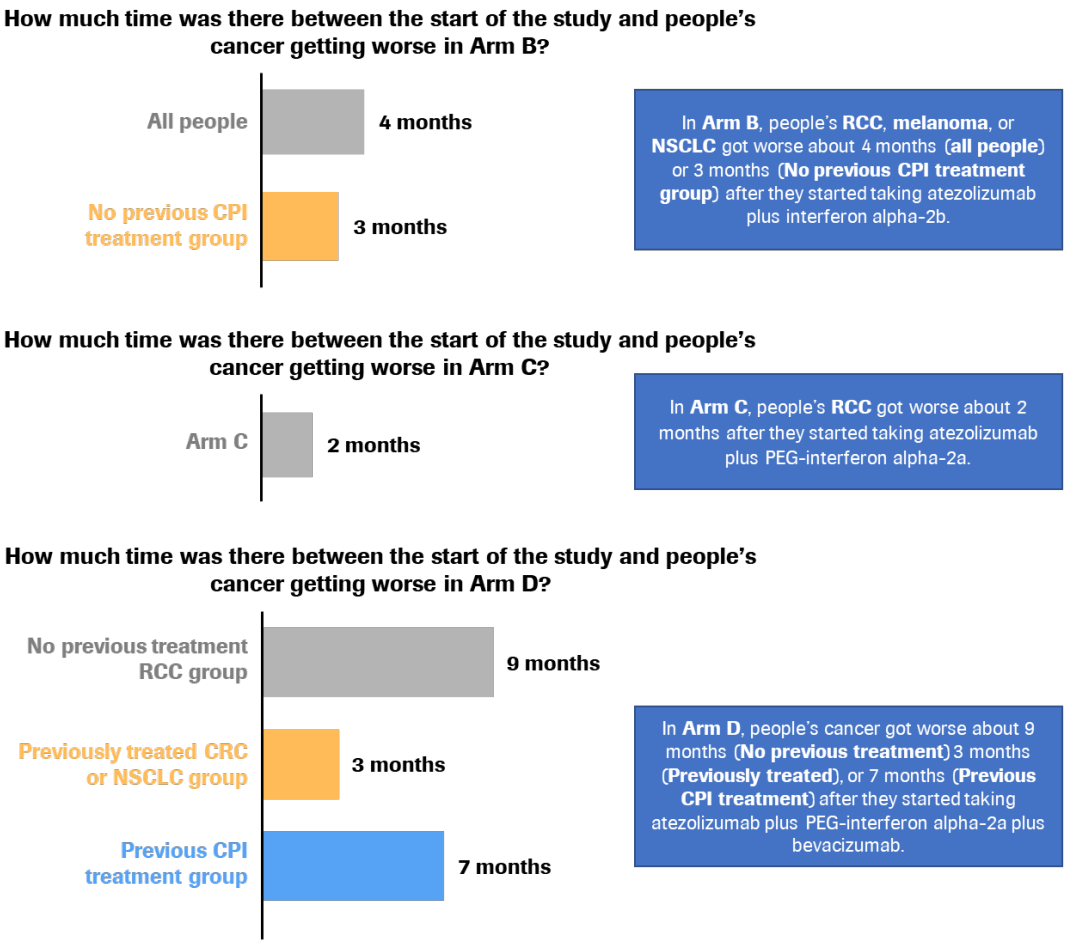
- In **Arm D**, 47% of people in the **'No previous treatment'** group (RCC), 13% of people in the '**Previously treated'** group (CRC or NSCLC), and 13% of people in the '**Previous CPI treatment'** group had their tumours get smaller after taking atezolizumab plus PEG-interferon alpha-2a plus bevacizumab.

How many people in Arm D of the study had smaller tumours after taking the study medicines?



Question 2: How long did it take for people's cancer to get worse after the start of the study?

Researchers looked at how much time it took for people's cancer to get worse.



These numbers are averages – that means some people's cancer got worse sooner than this, and some people's cancer got worse after a longer time than this.

6. How has this study helped research?

The information in this summary is from one study of 116 people with different types of cancer. These results helped researchers learn more about RCC, melanoma, CRC, and NSCLC that has spread to nearby cells or other parts of the body:

Researchers also learned more about 3 medicines and how well these worked together:

- Atezolizumab
- Interferon alpha
- Bevacizumab

All the medicines used in this study were found to be safe. Side effects seen in people in this study were similar to the side effects seen in other studies that looked at atezolizumab, interferon alpha, or bevacizumab. Overall, this study found that atezolizumab plus interferon alpha-2b was effective in people who had not had previous CPI treatment for RCC. Atezolizumab plus PEG-interferon alpha-2a, and bevacizumab was also found to be effective

in people with previously untreated RCC. Generally, most people did not see additional benefit adding atezolizumab to interferon-alpha.

You should not make decisions based on this one summary – always speak with your doctor before making any decisions about your treatment.

7. Are there plans for other studies?

Other studies looking at how safe atezolizumab is and how well the medicine works in combination with other medicines are still happening, and more studies are planned.

8. Where can I find more information?

You can learn more about this study on the websites listed below:

- https://clinicaltrials.gov/ct2/show/NCT02174172
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2014-000812-33/results
- https://forpatients.roche.com/en/trials/cancer/solid-tumors/a-study-to-assess-the-safety-and-tolerability-of-atezol-62655.html

If you want to learn more about the results of this study, the full title of the relevant scientific paper is: "Phase Ib study of atezolizumab plus interferon alpha with or without bevacizumab in patients with metastatic renal cell carcinoma and other solid tumors". The authors of the scientific paper are: Christian U. Blank, Deborah J. Wong, Thai H. Ho, Todd M. Bauer, Carrie B. Lee, Mario Sznol, and others. The paper is published in the journal *Current Oncology*, volume number 28, pages 5466-5479.

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

If you have any 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-assess-the-safety-and-tolerability-of-atezol-62655.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, which has its headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: "A Phase Ib Study of The Safety and Pharmacology of Atezolizumab (Anti-Pd-L1 Antibody) Administered With Ipilimumab, Interferon-Alpha, or Other Immune-Modulating Therapies in Patients With Locally Advanced or Metastatic Solid Tumors".

- The protocol number for this study is: GO29322.
- The ClinicalTrials.gov identifier for this study is: NCT02174172.
- The EudraCT number for this study is: 2014-000812-33.