

Summary of Clinical Trial Results

A study of atezolizumab plus radium-223 in men with prostate cancer that has spread to other parts of the body and in which male hormone-reducing medicines no longer work

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) and was written for:

- Members of the public and
- People who took part in the study.

The study started in September 2016 and finished in July 2019. This summary is based on information known at the time it was written (August 2021).

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

- 'Metastatic castration-resistant prostate cancer' – defined as prostate cancer that has spread to other parts of the body and in which male hormone-reducing medicines no longer work.

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about prostate cancer and about treatment with atezolizumab taken with radium-223.

Key information about this study

- This study was done to:
 - See whether the medicines being studied (a type of immunotherapy called ‘atezolizumab’ plus a type of radioactive drug called ‘radium-223’) are safe in men with metastatic castration-resistant prostate cancer (how many men had side effects?).
 - See whether the combination of atezolizumab and radium-223 can stop cancer from getting worse and in what order they work best in men with metastatic castration-resistant prostate cancer.
- The men in this study were given the medicines 1 of 3 ways: **Group A** was given atezolizumab and radium-223 on the same day, **Group B** was given radium-223 for 1 month before starting atezolizumab and **Group C** was given atezolizumab for 1 month before starting radium-223. **Group A** was made up of 3 smaller groups. Groups **B** and **C** each were made up of 2 smaller groups.
 - **Group A1** was given treatment first. After that, it was decided by a computer by chance which men were put into either **Group A2** or **B2** or **C2**. This was done so doctors could better learn how the different orders of giving the medicines were handled by these men and to see how well these orders worked.
 - To further study how these medicines were handled, more men were put into **groups A3, B3** and **C3**.

Treatment Groups



- **Groups A, B, and C** included different men.
- This study included 44 men in the United States.
- Of all men, 20 out of 44 (45%) who were given atezolizumab plus radium-223 for up to 2 year and 10 months had at least one serious side effect (a serious side effect is any side effect that results in death, is life-threatening, needs a hospital stay or causes longer hospital stays).
- The study also showed that:
 - Tumours got smaller in 3 out of 44 men (7%).
 - Tumours stayed about the same size in 14 out of 44 men (32%).
 - Tumours got larger in 25 out of 44 men (56%).
 - Tumours could not be measured at in 2 out of 44 men (5%).
- At the time of writing this summary (August 2021), the study has finished.

1. General information about this study

Why was this study done?

Men with metastatic castration-resistant prostate cancer are often treated with medicines that lower the amount of male hormones in the body. Male hormones may help the tumours grow, so taking medicines that reduce these might stop the tumours from getting bigger or even make them shrink. After time, these medicines often stop working and the tumours start to grow again and may even spread to different parts of the body (like the bone). Doctors may then use combinations of medicines that act in different ways to help prevent tumours from growing for a longer period of time.

New medicines or combinations of medicines are needed to stop prostate cancer from coming back or getting worse – to help men live longer.

Immunotherapy is a type of medicine that helps a person's own immune system attack cancer cells, and atezolizumab is an immunotherapy medicine that is already used in other kinds of cancers.

Radium-223 is a radiopharmaceutical that uses radiation (waves of energy) to kill tumour cells that go into your bone.

In this study, researchers wanted to see if combining an immunotherapy medicine with a radiopharmaceutical would be safe for men to take. They also wanted to see if combining these two medicines would shrink tumours in men with metastatic castration-resistant prostate cancer that has also spread to other areas of the body like the bone.

What are the study medicines?

This study looked at a medicine called 'atezolizumab' (known by its brand name, Tecentriq®).

- You say this as 'a – teh – zo – liz – oo – mab'.
- The body's immune system fights diseases like cancer. However, cancer cells 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.
- When people take atezolizumab, their tumour (cancer) may get smaller.
- This medicine is a type of immunotherapy.

In this study, atezolizumab was taken together with a medicine called radium-223 (known by its brand name Xofigo®).

- You say this as 'RAY – dee – uhm – 2 – twenti– thrEE'.
- As cancers get worse, some cancers will spread to the bone and cause bones to become weak and more likely to break. This is why the body will try to add calcium, a mineral that helps build bones, back into the bones where the cancer has spread.
- Radium-223 looks like calcium, so after it is injected into a vein, it goes directly into the bones where there are tumours and emits radiation that can stop cancer from growing.
- This medicine is a type of radioactive drug.

What did researchers want to find out?

- Researchers wanted to find out how safe the combination of medicines is – by seeing what the side effects were and counting how many men had side effects (plus seeing how severe these side effects were) when taking both medicines together during this study.
 - See section 4 ‘What were the side effects?’
- They also wanted to know whether the order of atezolizumab plus radium-223 would affect how much tumours shrink in people with prostate cancer that has spread.
 - See section 5 ‘What were the results of the study?’

The main questions that researchers wanted to answer were:

1. How many men had serious side effects related to atezolizumab + radium-223?
2. How many men had smaller tumours that could be measured after taking their medicine?

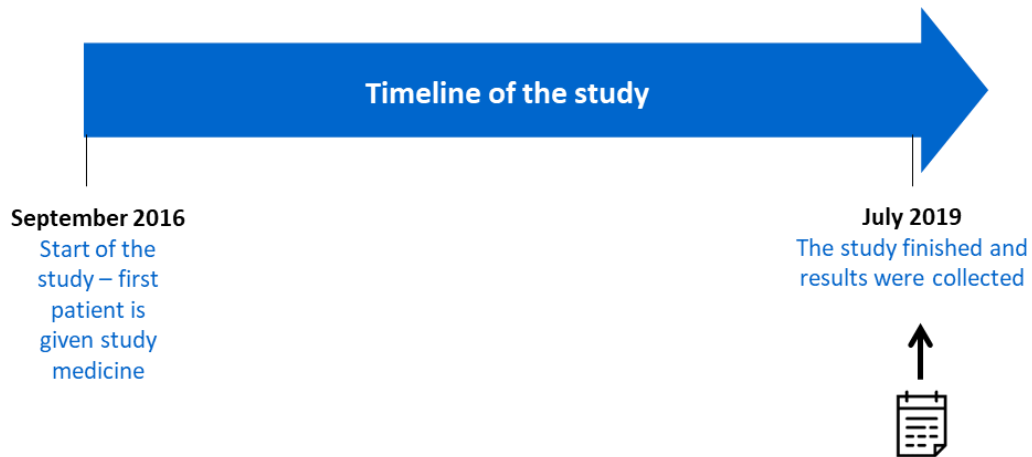
What kind of study was this?

This was a **‘Phase 1’** study, which means that this was the first study of atezolizumab taken together with radium-223. A small number of men with prostate cancer took atezolizumab plus radium-223, and the researchers did medical tests on the men who took part to find out more about the two-medicine combination.

This was an ‘open label’ study. This means that both the men taking part in the study and the study doctors or nurses knew which study medicines the men were taking.

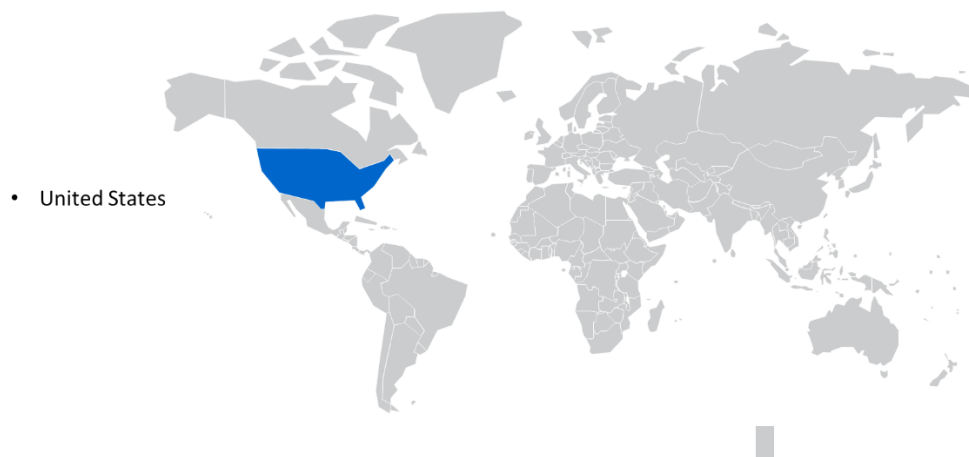
When and where did the study take place?

The study started in September 2016 and finished in July 2019. This summary includes the results up to July 2019.



This study has finished. The symbol on the timeline (📅) shows when the information shown in this summary was collected – at the time the study was finished in July 2019.

The study took place at 11 study centres in the United States. This map shows where this study took place.



2. Who took part in this study?

In this study, 44 men with metastatic castration-resistant prostate cancer took part. The men in this study were between 41 and 85 years old.

Men could take part in the study if they:

- Were 18 years of age or older.
- Had a type of prostate cancer that has spread to other parts of the body and has also spread to at least two different places on the bones.
- Had already been treated for their cancer with male hormone-reducing medicine and for whom these medicines no longer work.
- Had already been treated or could not be treated for their cancer with medicine that stops cancer from growing larger by dividing into new cells.

3. What happened during the study?

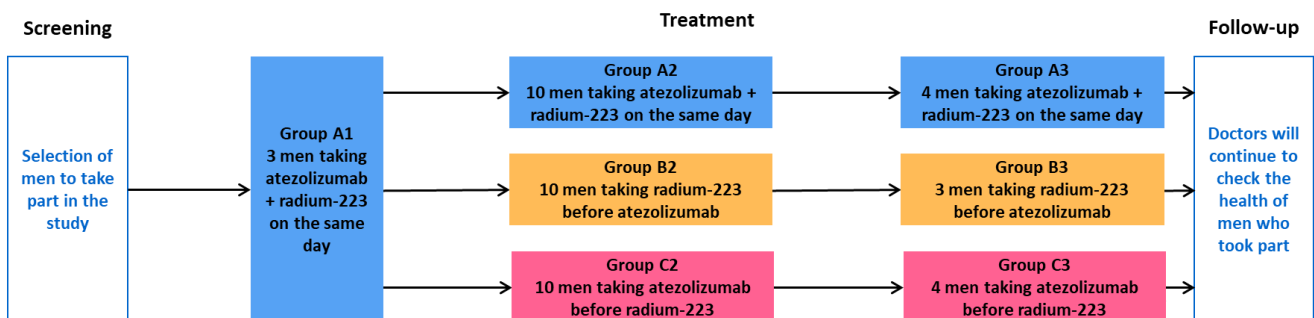
The treatment groups were:

- **Groups A:** atezolizumab (study medicine) plus radium-223 (existing medicine) on the same day
- **Groups B:** Radium-223 (existing medicine) for 1 month before starting atezolizumab (study medicine)
- **Groups C:** Atezolizumab (study medicine) for 1 month before starting radium-223 (existing medicine)

This table shows the groups in each study and the order of the drugs they were taking.

	Group A Atezolizumab + Radium-223 on the same day			Group B Radium-223 before Atezolizumab		Group C Atezolizumab before Radium-223	
	Group A1	Group A2	Group A3	Group B2	Group B3	Group C2	Group C3
When and how the drugs were taken	Atezolizumab and radium-223 given by injection on the same day			Radium-223 given by injection 1 month before starting atezolizumab		Atezolizumab given by injection 1 month before starting radium-223	

This picture shows what happened in the study.



5. 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 medicines in the study.
- Not all of the men in this study had all of the side effects.
- Side effects were mild to serious.
- The side effects were different from person to person.
- It is important to be aware 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 on 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, results in death or causes lasting problems.

Question 1: How many men had serious side effects related to the study medicines?

During this study, 20 out of 44 men in the study (45%) had at least one serious side effect.

- Serious side effects that were considered by the study doctor to be related to atezolizumab were seen in 8 out of 44 men in the study (18%).
- Serious side effects that were considered by the study doctor to be related to radium-223 were seen in 2 out of 44 men in the study (5%).

Some men in the study died due to side effects that may have been related to one of the study medicines.

- 3 out of 44 men (7%) died from a side effect considered by the study doctor to be related to atezolizumab.
- No one died from a side effect related to radium-223.

During the study, some men decided or were directed by their doctor to stop taking their medicine because of side effects:

- 3 out of 44 men (7%) stopped taking atezolizumab.
- 1 out of 44 men (2%) stopped taking radium-223.

This information was collected from men in this study whose health had been followed by doctors for up to 2 year and 10 months.

Most common side effects

During this study, all men (100%) had a side effect of any kind (not serious or serious).

This table shows the most common side effects – these are the side effects that happened in one-fifth (20%) or more of the men in in this study. These side effects could have been serious or not serious (meaning an undesirable effect, but one that was not life-threatening and did not require hospitalisation or have lasting effects). Some men had more than one side effect – this means that they are included in more than one row in the table.

Most common side effects reported in this study	Groups A-C (44 men total)
Feeling tired	57%
Not wanting to eat (less appetite)	50%
Diarrhoea	45%
Feeling sick (nausea)	43%
Throwing up (vomiting)	34%
Low level of red blood cells	32%
Joint pain	30%
Back pain	25%
Constipation	25%
Low level of white blood cells	20%
Weight loss	20%

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.

5. What were the results of the study?

Question 2: How many men in Groups A-C had smaller tumours that could be measured after taking their medicine?

Researchers collected information on how many men had smaller tumours for over a year (14 months), on average, after they started taking atezolizumab plus radium-223 in the study.

- Tumours got smaller in 3 out of 44 men (7%).
- Tumours stayed about the same size and did not grow bigger in 14 out of 44 men (32%).
- Tumours got larger in 25 out of 44 men (57%).
- Tumours could not be measured in 2 out of 44 men (5%).
- None of the men had tumours that went away after treatment.

This information was collected from September 2016 until July 2019.

This section only shows the key results from this study. You can find information about all other results 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 study of 44 men with metastatic castration-resistant prostate cancer. These results are helping researchers learn more about prostate cancer and treatment with atezolizumab plus radium-223.

- During the study, the side effects that men had while taking atezolizumab plus radium-223 were similar to those felt by people taking the individual medicines in other studies.
- The results showed that, for most of the 44 men with prostate cancer in this study, taking atezolizumab plus radium-223 did not appear to shrink their tumours.

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?

At the time of writing this summary, there are no plans for studies looking at the combination of atezolizumab plus radium-223 in people with prostate cancer.

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/NCT02814669>
- <https://forpatients.roche.com/en/trials/cancer/prostate-cancer/safety-and-tolerability-of-atezolizumab--atz--in-combin-41710.html>

If you want to find out more about the results of this study, the full title of the relevant scientific paper is: “A Phase Ib Study of Atezolizumab with Radium-223 Dichloride in Men with Metastatic Castration-Resistant Prostate Cancer”. The authors of the scientific paper are Lawrence Fong, Michael J. Morris, Oliver Sartor, Celestia S. Higano, Lance Pagliaro and others. The paper is published in the journal *Clinical Cancer Research*, volume number 27, on pages 4746-4756.

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

If you have any more questions after reading this summary:

- Visit the For Patients platform and fill out the contact form – <https://forpatients.roche.com/en/trials/cancer/prostate-cancer/safety-and-tolerability-of-atezolizumab--atz--in-combin-41710.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: "Safety and Tolerability of Atezolizumab (ATZ) in Combination With Radium-223 Dichloride (R-223-D) in Metastatic Castrate-Resistant Prostate Cancer (CRPC) Progressed Following Treatment With an Androgen Pathway Inhibitor."

- The protocol number for this study is: BO30013.
- The ClinicalTrials.gov identifier for this study is: NCT02814669.
- The EudraCT number for this study is: 2015-003606-17.