

Summary of Clinical Trial Results

A study to look at whether atezolizumab with or without Bacille Calmette-Guérin worked in people with high-risk bladder cancer that has not spread to the muscle – and how safe these medicines were

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 it was written (June 2022).

The study started in June 2016 and this summary was written after the study ended in September 2020.

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

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Glossary

- **Non-muscle-invasive bladder cancer (NMIBC):** a type of bladder cancer that has not spread to the muscle
- **Immunotherapy (for cancer):** medicine used in cancer treatment to help the body's immune system attack tumours
- **Programmed death-ligand 1 (PD-L1):** a protein that normally stops the immune system from attacking good cells. In cancer, tumour cells can use PD-L1 to hide from the immune system

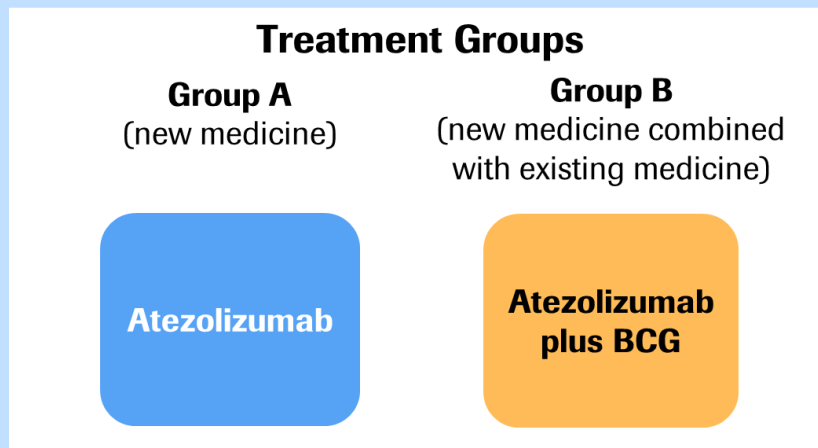
Thank you to the people who took part in this study

The people who took part have helped researchers answer important questions about a type of bladder cancer that has not spread to the muscle called 'non-muscle-invasive bladder cancer' or 'NMIBC'. Researchers also learnt more about the medicines being studied – 'atezolizumab' and 'Bacille Calmette-Guérin' or 'BCG'.

Key information about this study

Why was this study done?

- This study was done to see if atezolizumab, given with or without Bacille Calmette–Guérin (or BCG), was safe and if these medicines could help to make the cancer disappear (after 6 months) in people with high-risk NMIBC whose cancers had either worsened or came back after treatment with BCG.
- Currently, there are few treatment options for people who are not able to undergo, or do not want to undergo, the surgical removal of all or part of the bladder.
- People were given atezolizumab alone or a combination of atezolizumab and BCG – both the people taking part in the study and the study doctors knew which of the treatment groups people were in.



- This study was done at 8 centres in the United States.
- There were 24 people in the study.

What were the results?

- The main findings were that:
 - In both **Group A** and **Group B**, no new side effects were found and no deaths due to their treatments occurred.
 - The treatments appeared to have made cancer disappear in some people.

How many people had side effects?

- About 50% of people (6 out of 12 people) in **Group A** had side effects related to their treatment, compared with 58% of people (7 out of 12 people) in **Group B**.
- Serious side effects were experienced by 33% of people (4 out of 12 people) in **Group A** and 25% of people (3 out of 12 people) in **Group B**.

1. General information about this study

Why was this study done?

People who have bladder cancer that has not spread into muscles of the bladder are generally considered as having ‘non-muscle-invasive bladder cancer’ or ‘NMIBC’. For people with high-risk NMIBC (high-grade bladder tumors that affect the outermost lining of the bladder wall), the recommended treatment is surgery (called ‘transurethral resection of bladder tumour’ or ‘TURBT’), which removes any cancer that can be seen, followed by a medicine called ‘Bacille Calmette-Guérin’, or ‘BCG’, delivered into the bladder.

However, after BCG treatment, the cancer may worsen or come back. People who do not get better after being given BCG often have a type of surgery called ‘cystectomy’ to remove the cancer from in and around the bladder. Sometimes the whole bladder or nearby organs may need to be removed. There are currently few treatment options for people who are not able to undergo or do not want to undergo cystectomy.

New medicines are needed in addition to surgery to stop the cancer from coming back or getting worse – to help people to live longer. Immunotherapy is a type of medicine that helps a person’s own immune system attack cancer cells, and atezolizumab is a new immunotherapy drug that is already used in other kinds of cancers.

In this study, researchers wanted to see if giving an immunotherapy drug called ‘atezolizumab’ alone or in combination with BCG, an existing immunotherapy drug, was safe and if these medicines would make the cancer disappear after 6 months. The people who took part in this study already had TURBT for NMIBC and their cancer either did not get better or came back after BCG treatment.

What was the medicine being studied?

This study looked at a medicine called atezolizumab and a combination of atezolizumab and another medicine, called Bacille Calmette-Guérin or BCG, in two groups of people who had bladder cancer that has not spread to the muscles of the bladder – ‘non-muscle-invasive bladder cancer’:

- **Group A: atezolizumab** (new medicine).
- **Group B: atezolizumab plus BCG** (new medicine combined with existing medicine).

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

- The body’s immune system fights diseases like cancer. However, cancer cells can block 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 medicine called “immunotherapy”.
- When people are given atezolizumab, their tumour (cancer) may get smaller.
- In this study, this medicine was given to people who did not get better or whose cancer came back after BCG treatment in order to make the cancer disappear.

Bacille Calmette-Guérin (available in different forms; the type used in this study is known by its brand name, OncoTICE®) or BCG is an existing medicine used in this study:

- BCG is a type of immunotherapy medicine that is delivered into the bladder (or intravesical) to treat early-stage bladder cancer
- BCG treatment is usually given after bladder surgery (called ‘transurethral resection of bladder tumour’ or ‘TURBT’), during which any cancer that can be seen is removed

What did researchers want to find out?

- Researchers did this study to see how safe ‘atezolizumab’ alone or in combination with ‘Bacille Calmette-Guérin’ or ‘BCG’ was – by checking how many people in each treatment group had side effects and how serious these side effects were (see section 4 “What were the side effects?”).
 - People in **Group A** were given atezolizumab after their cancer either did not get better or came back after BCG treatment.
 - People in **Group B** were given atezolizumab plus BCG after their cancer either did not get better or came back after BCG treatment.
- Researchers also looked at whether atezolizumab alone or in combination with BCG would make the cancer disappear after 6 months – to see how well atezolizumab worked in people with non-muscle-invasive bladder cancer (see section 5 “What were the results of the study?”).

The main questions that researchers wanted to answer were:

1. How safe is atezolizumab? How many people in **Group A** and **Group B** had side effects and how severe were they?
2. In **Group A** and **Group B**, how many people’s cancer disappeared after 6 months of treatment?

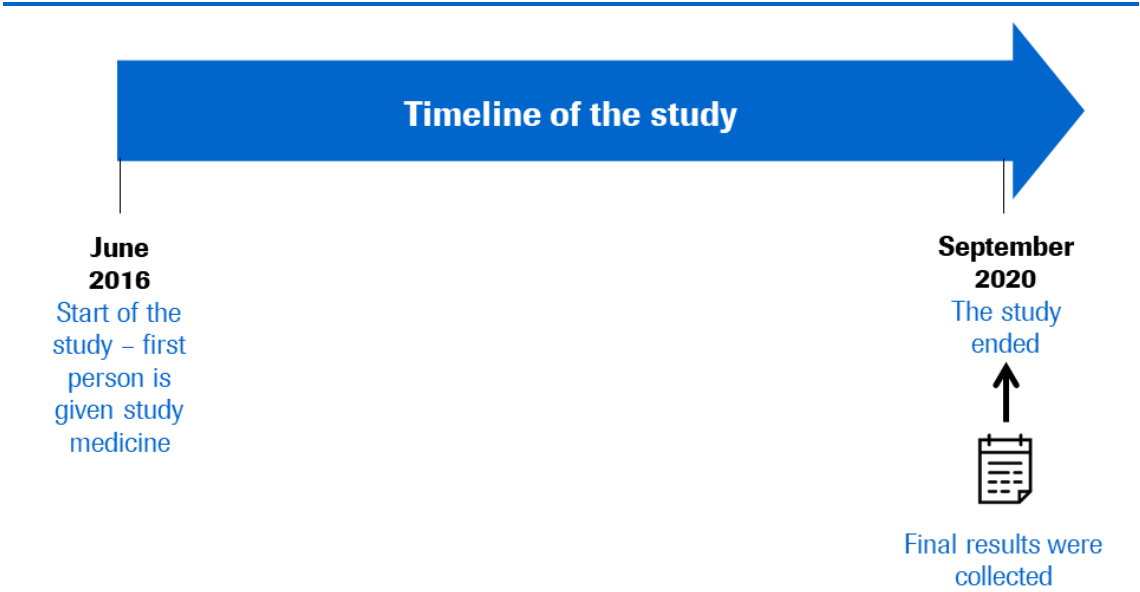
What kind of study was this?

This study was a ‘**Phase 1b/2**’ study. This means that before this study, atezolizumab with and without BCG had not been tested in healthy people or people with NMIBC. Phase 1b/2 studies are done in a small number of healthy people or people with NMIBC to see if a drug is safe before testing in a larger number of people to test if it works better than the usual treatment and is safe enough for it to be ‘approved’ by the health authorities as a treatment that can be prescribed by your doctor.

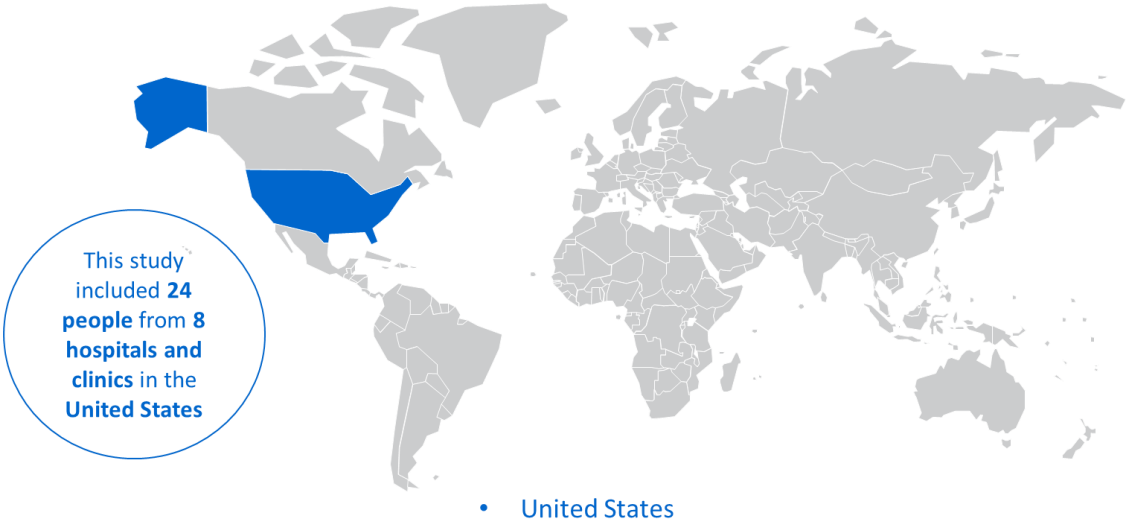
The study was ‘**open label**’. This means that both the people taking part in the study and the study doctors knew which of the treatment groups people were in. Other than the different study treatments given to people in each group, all other care was the same.

When and where did the study take place?

The study started in June 2016 and ended in September 2020.

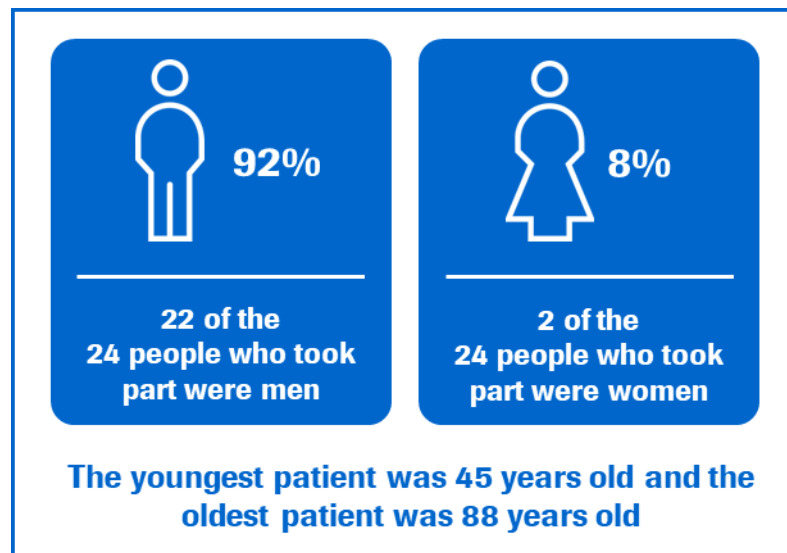


The study took place at 8 hospitals and clinics in the United States. This map shows where this study took place.



2. Who took part in this study?

In this study, 24 people with NMIBC took part.



People could take part in the study if they:

- Were at least 18 years old.
- Had bladder cancer that had not spread into the muscles of the bladder.
- Had bladder cancer that did not get better or came back after BCG treatment.
- Did not have radiation to the bladder or pelvic region to treat bladder cancer.
- Were able to perform activities >50% as well as they could before they got cancer.

People could not take part in the study if they:

- Had bladder cancer that had spread to other parts of the body, including the muscles of the bladder and outside of the bladder.
- Had received any approved anti-cancer therapy, including chemotherapy, radiation or hormonal therapy (a medicine that changes the level of hormones in the body) within 3 weeks before the first dose of the study medicine.

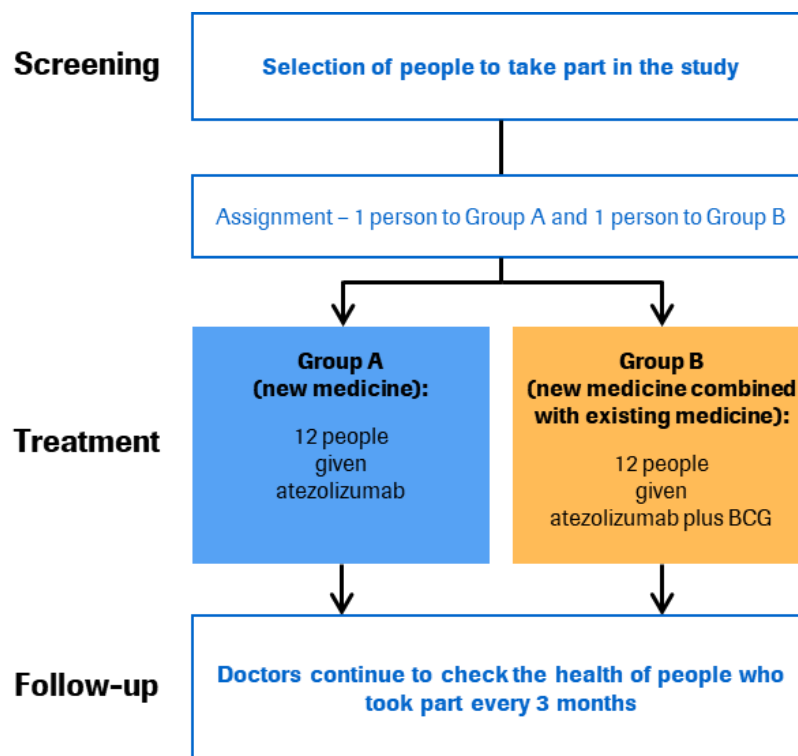
These are just some of the requirements that people needed to meet to be able to take part in this study. There were also other requirements that are not listed above.

3. What happened during the study?

During the study, people were selected by their doctor to be in one of two treatment groups. For every person that was selected for Group A, another person was selected for Group B.

The treatment groups were:

- **Group A:** atezolizumab – these people were given atezolizumab injected into a vein every 3 weeks.
- **Group B:** atezolizumab plus BCG – these people were given atezolizumab injected into a vein every 3 weeks plus BCG instilled into the bladder every week for 6 weeks and from the third month onwards, every week for 3 weeks.



This table shows the number of people who were given each study treatment, and how often the drugs were given.

	Group A Atezolizumab	Group B Atezolizumab plus BCG
Number of enrolled people randomly chosen to be included in each group	12	12
Number of people given this medicine or being observed	12	12
How and when the drug was given in each 21-day treatment cycle	Atezolizumab given by injection once every 21 days	Atezolizumab given by injection once every 21 days BCG delivered into the bladder every 7 days for 6 times for the first 84 days and from the third month onwards, every 7 days for 3 times within each 84-day period

4. What were the side effects?

- Side effects are medical problems (such as feeling dizzy) that may happen during the study.
- Not all the people in this study had all of the side effects.
- Side effects may be mild to very serious and can be different in each 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.

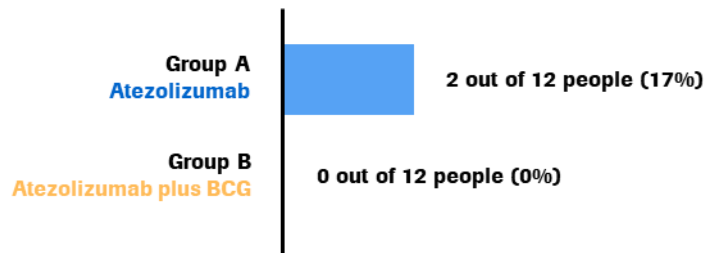
The side effects shown in this section are thought to be caused by the treatment being studied – atezolizumab with or without BCG.

Serious side effects

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

- During this study, 2 out of the 24 people who took part (8%) had at least one serious side effect that may have been related to one of the study medicines.

How many people in the study had at least one serious side effect that may have been related to one of the study medicines?



None of the patients in Group A or Group B died due to study medicines.

During this study, some people decided to stop taking their medicine because of side effects:

- **Group A:** 1 out of 12 people (8%) stopped taking atezolizumab.
- **Group B:** None of the patients stopped taking either atezolizumab or BCG.

Most common side effects

During this study, all patients had a side effect. These are all the side effects – including those that could have happened for reasons other than the treatments.

The most common side effects are shown in this table – these are the most common side effects seen in patients taking the new medicine (atezolizumab) and patients taking the new medicine in combination with the existing medicine (atezolizumab plus BCG), and could have happened for reasons other than the treatments. These side effects happened in at least 20 out of 100 people (20%) in either the atezolizumab or atezolizumab plus BCG group. Some people 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 (<i>medical terms</i>)	People taking atezolizumab (12 people total)	People taking atezolizumab plus BCG (12 people total)
Feeling tired (<i>fatigue</i>)	58% (7 out of 12)	17% (2 out of 12)
Rash	42% (5 out of 12)	17% (2 out of 12)
Pain or burning sensation during urination (<i>dysuria</i>)	17% (2 out of 12)	33% (4 out of 12)
Rash with both flat and raised parts (<i>maculopapular rash</i>)	17% (2 out of 12)	25% (3 out of 12)
Bladder muscles squeezes suddenly (<i>bladder spasm</i>)	8% (1 out of 12)	42% (5 out of 12)
Pain in the stomach area (<i>abdominal pain</i>)	8% (1 out of 12)	25% (3 out of 12)
Constipation	8% (1 out of 12)	25% (3 out of 12)
Blood in urine (<i>haematuria</i>)	0% (0 out of 12)	50% (6 out of 12)
Frequent urination (<i>pollakiuria</i>)	0% (0 out of 12)	50% (6 out of 12)
Low thyroid activity (<i>hypothyroidism</i>)	0% (0 out of 12)	25% (3 out of 12)

- The most common side effects caused by the medicine (atezolizumab) in **Group A and Group B** were feeling tired (*fatigue*), rash with both flat and raised parts (*maculopapular rash*), and rash.
- The most common side effects caused by the medicine (BCG) in **Group B** were frequent urination (*pollakiuria*), bladder muscles squeezes suddenly (*bladder spasm*), and blood in urine (*haematuria*).

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.

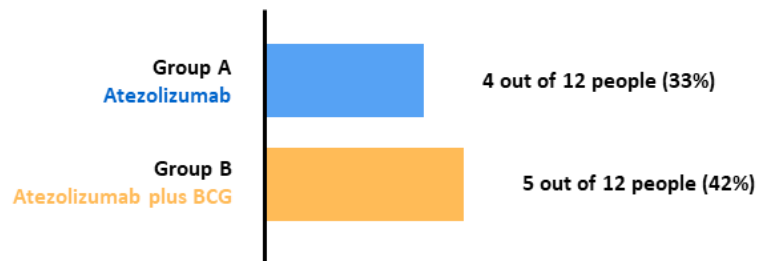
5. What were the results of the study?

How many people's cancer disappeared after 6 months in **Group A** and **Group B**?

Researchers looked at how many people's cancer disappeared after 6 months in **Group A** and **Group B**. This information was collected from all the people in both groups from June 2016 until September 2020.

- In **Group A**, the cancer disappeared after 6 months in 4 people (33%). This is shown in the graph below.
- In **Group B**, the cancer disappeared after 6 months in 5 people (42%). This is shown in the graph below.
- The difference between **Group A** and **Group B** was not big enough to show researchers that being given atezolizumab plus BCG helped more people have their cancer disappear than being given atezolizumab alone.

How many people's cancer disappeared after 6 months?



This information was collected from June 2016 until September 2020.

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 one study of 24 people with bladder cancer that has not spread into the muscle of the bladder – ‘non-muscle-invasive bladder cancer’. These results helped researchers learn more about this type of bladder cancer and treatment with atezolizumab with or without BCG after cancer had either worsened or came back after BCG treatment.

Overall, people in this study did not have any new side effects and no deaths due to treatment occurred. The treatments appeared to make cancer disappear in some people after 6 months. However, the difference between Group A and Group B was not big enough to show researchers that being given atezolizumab plus BCG helped more people have their cancer disappear than being given atezolizumab alone. More research is needed to know whether atezolizumab plus BCG can help bladder cancer disappear in more people than atezolizumab alone.

One study cannot tell us everything about how safe a medicine is and how well it works. 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 with your doctor before making any decisions about your treatment.**

7. Are there plans for other studies?

Other studies looking at the safety and effects of atezolizumab are happening. These studies are looking at the use of atezolizumab in different situations, for example:

- In combination with other medicines, including chemotherapy.
- In people with bladder cancer that has spread to other parts of the body.
- In people with bladder cancer that has not spread to the muscle, called ‘non-muscle invasive bladder cancer’, who were never given Bacille Calmette-Guérin

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/NCT02792192>
- <https://forpatients.roche.com/en/trials/cancer/bladder-cancer/safety-and-pharmacology-study-of-atezolizumab-alone-and-in-combi.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/II Study of Atezolizumab with or without Bacille Calmette-Guérin in Patients with High-Risk Non-Muscle-Invasive Bladder Cancer”. The authors of the scientific paper are Brant A. Inman, Noah M. Hahn, Kelly Stratton, Ryan Kopp, Alex Sankin and others. The paper is published in the journal ‘European Urology Oncology’ (DOI: <https://doi.org/10.1016/j.euo.2023.01.013>).

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

If you have any more questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – <https://forpatients.roche.com/en/trials/cancer/bladder-cancer/safety-and-pharmacology-study-of-atezolizumab-alone-and-in-combi.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, and Genentech, Inc, a member of the Roche group who are based in San Francisco, United States of America.

Full title of the study and other identifying information

The full title of this study is: “Safety and Pharmacology Study of Atezolizumab Alone and in Combination With Bacille Calmette-Guérin (BCG) in High-Risk Non-Muscle-Invasive Bladder Cancer (NMIBC) Participants”.

- The protocol number for this study is: WO29635.
- The ClinicalTrials.gov identifier for this study is: NCT02792192.