

Clinical Trial Results – Layperson Summary

A study to compare three drug treatments – atezolizumab with chemotherapy, atezolizumab alone, and placebo with chemotherapy – in people with advanced or metastatic bladder cancer who have not had any chemotherapy

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 (November 2019).

The study started in June 2016 and is expected to end at the end of 2020. This summary includes the results until 31 May 2019. The study is still happening – Some patients are still being treated and study doctors are still collecting information. This summary will be updated when the study will end.

One study can't tell us everything about the possible side effects of a medicine and how well the medicine works. It takes lots of people in many studies to learn as much as we can about a medicine. The results from this study may be different from results from other studies of the same medicine. **This means that you should not make medical decisions based on this one summary. Always talk to your doctor before making any decisions about your treatment.**

Contents of the summary

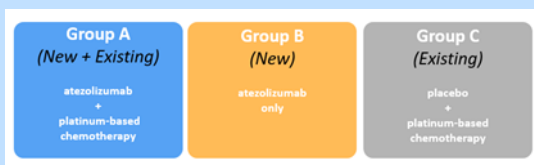
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Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about advanced or metastatic bladder cancer (metastatic means that the cancer has spread to other parts of the body), and about treatment with a drug called atezolizumab (the study medicine).

Key information about this study

- This study is being done to compare three treatments:
 - A new medicine (the 'study medicine') used alone called atezolizumab.
 - The study medicine combined with a medicine typically used to treat this disease that kills cancer cells using platinum – called 'platinum-based chemotherapy'.
 - The existing platinum-based chemotherapy medicine. This is the current treatment that the new treatments are being compared with.
- In this study, people are taking either (1) the study medicine (atezolizumab) with an existing platinum-based chemotherapy (gemcitabine and carboplatin or gemcitabine and cisplatin) (Group A – New + Existing) or (2) atezolizumab alone (Group B – New) or (3) a placebo (a dummy drug which looks the same as the study medicine but doesn't contain any real medicine and doesn't have any medicine-related effect on the body) with an existing platinum-based chemotherapy (gemcitabine and carboplatin or gemcitabine and cisplatin) (Group C – Existing). Patients in Group C won't be able to know whether they are having the new medicine or not.



- It was decided by chance which treatment each person would take.
- This study included 1213 people in 35 countries.
- The first analysis for this study that included data through 31 May 2019 has shown that for people taking atezolizumab plus platinum-based chemotherapy, their cancer did not get worse until about 8.2 months from the start of the study, compared with about 6.3 months for those taking placebo plus platinum-based chemotherapy alone.
- Early results for survival showed that people taking atezolizumab plus platinum-based chemotherapy lived for about 16.0 months from the start of the study (some died earlier, some lived longer), compared to about 15.7 months for those taking atezolizumab alone and about 13.4 months for those taking placebo plus platinum-based chemotherapy alone. These are still early results and final results about survival will be disclosed at the time of study closure.
- The study showed that adding atezolizumab to platinum-based chemotherapy extended the amount of time patients had before their cancer got worse compared with chemotherapy alone.
- Serious side effects were experienced by about half of patients in Groups A and C and by a bit less than half in Group B. The numbers are as follows: 52% (234 out of 453 people) taking atezolizumab plus platinum-based chemotherapy, 49% (191 out of 390 people) taking the placebo plus platinum-based chemotherapy, and 43% (152 out of 354 people) taking atezolizumab alone.
- At time of writing (November 2019), the study is still going on. It is expected to end at the end of 2020.

1. General information about this study

Why was this study done?

People with bladder cancer that has spread to other parts of the body are very ill with poor chances of survival, and there is no current treatment that can cure all patients. Patients usually take medicines that kill cancer cells called 'platinum-based chemotherapy'. It is preferred for patients to get a platinum-based chemotherapy called cisplatin, unless their health doesn't allow them to receive it. If they are not healthy enough or if patients have too many side effects while taking cisplatin, they will take a different platinum-based chemotherapy called carboplatin. Doctors can also choose to give a treatment called immunotherapy, which is a medicine that helps the body's immune system to attack tumours.

In this study, researchers wanted to see if giving patients both chemotherapy and immunotherapy at the same time would work better to shrink the tumour.

What are the study medicines?

This study looked at a new immunotherapy 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. But cancer cells can block (stop) the immune system from attacking the cancer. Atezolizumab releases this blockage - meaning that the immune system again becomes able to fight the cancer cells.
- When people take atezolizumab, their tumour (cancer) may get smaller.

In this study, atezolizumab was used by itself (Group B - New) or with platinum-based chemotherapy (Group A - New + Existing).

- The platinum-based chemotherapy used in this study was a drug called gemcitabine plus another drug - the doctor could choose either carboplatin or cisplatin
- Gemcitabine: You say this as 'jem-SYE-ta-been'
- Carboplatin: You say this as 'KAR-boe-PLA-tin'
- Cisplatin: You say this as 'sis-PLA-tin'

Atezolizumab alone (Group B) or with platinum-based chemotherapy (Group A) was compared to platinum-based chemotherapy plus a 'placebo' (Group C - Existing).

- You say this as 'plah - see - bo'
- The placebo looked the same as atezolizumab but did not contain any real medicine. This means it had no medicine-related effect on the body. A placebo is used so that the patient and the doctor does not know whether they are receiving the real medicine or not, as knowing can sometimes affect the results of the study.
- Researchers gave some people the medicine and some people the placebo plus platinum-based chemotherapy so they could see which benefits or side effects are actually caused by the medicine. The use of a placebo in a study is called a "blinded" study.

What did researchers want to find out?

Researchers did this study to compare the study medicine (atezolizumab) with or without platinum-based chemotherapy – to see how well the study medicine worked (see section 4 “What were the results of the study?”).

The main questions that researchers wanted to answer were:

1. How much time was there between the start of the study treatment and people’s cancer getting worse and was this time longer for patients receiving the study medicine (atezolizumab) with platinum-based chemotherapy?
2. How long did people in this study live and did the people treated with the study medicine (atezolizumab) plus platinum-based chemotherapy live longer than patients treated with only platinum-based chemotherapy?

Other questions that researchers wanted to answer were:

- Were there changes in the size of people’s tumours? Researchers looked at this several times during the study.
- For people whose tumours got smaller during the study, how much time was there until their cancer got worse again? Cancer getting worse means that the cancer is growing again either in the same area of the body as before and/or in a new body area. This means that the treatment is not working anymore and need to be changed.
- How safe are these medicines? How many people had side effects when taking each of the medicines during this study?

What kind of study was this?

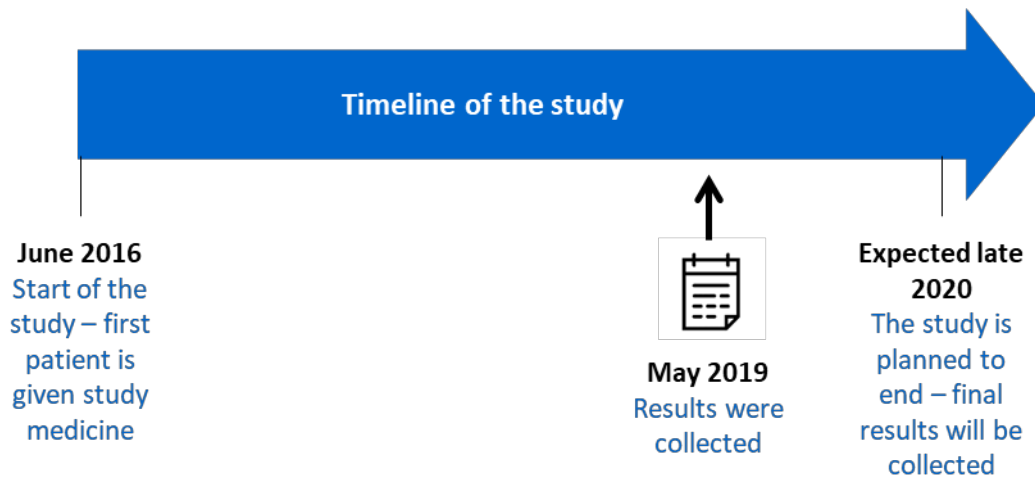
This study was a ‘Phase 3’ study. This means that atezolizumab had been tested in a smaller number of people with bladder cancer before this study. In this study, a larger number of people with bladder cancer were in Groups A (New + Existing), B (New), and C (Existing). The researchers wanted to find out if adding atezolizumab to platinum-based chemotherapy helped prevent people’s cancer from getting worse and helped them live longer.

The study was ‘randomised’. This means that it was decided by chance which of the medicines people in the study would get – like tossing a coin.

This was a ‘partially blinded’ study. This means that the people taking part in the study and the study doctors did not know which of the study medicines people were taking. Only people receiving atezolizumab alone knew they were receiving atezolizumab.

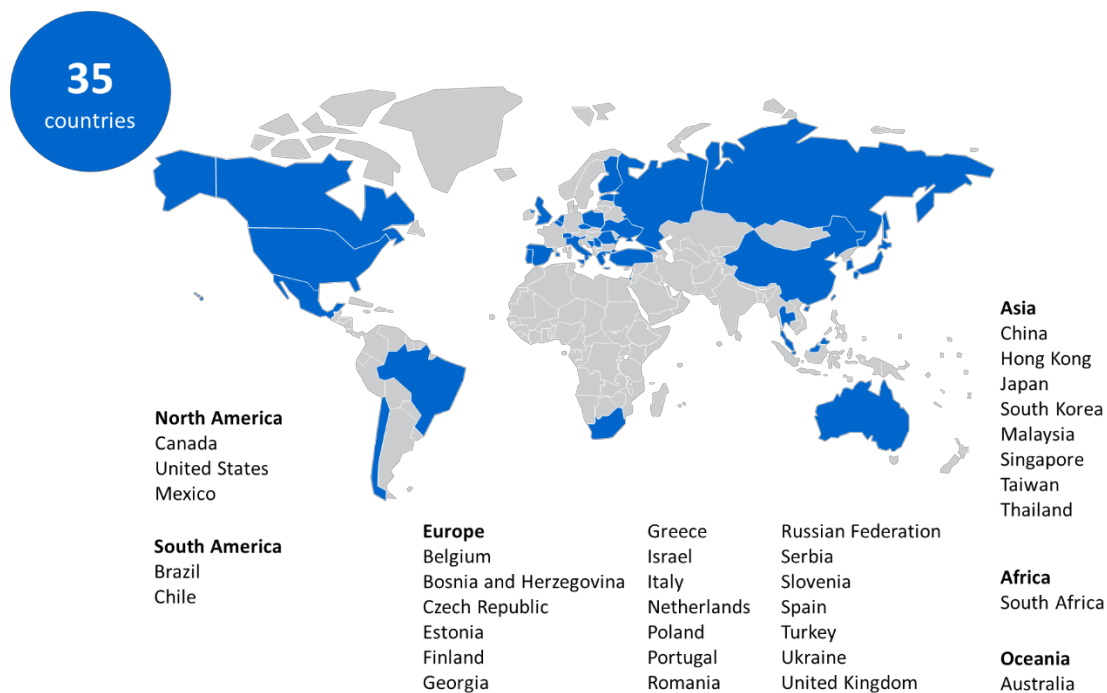
When and where did the study take place?

The study started in June 2016 and is expected to end at the end of 2020. This summary includes the results up until 31 May 2019. At time of writing (November 2019), the study is still continuing – some patients are still being treated and study doctors are still collecting information.



This study is still continuing, so the symbol on the timeline (📅) shows when the information shown in this summary was collected – after 3 years (31 May 2019).

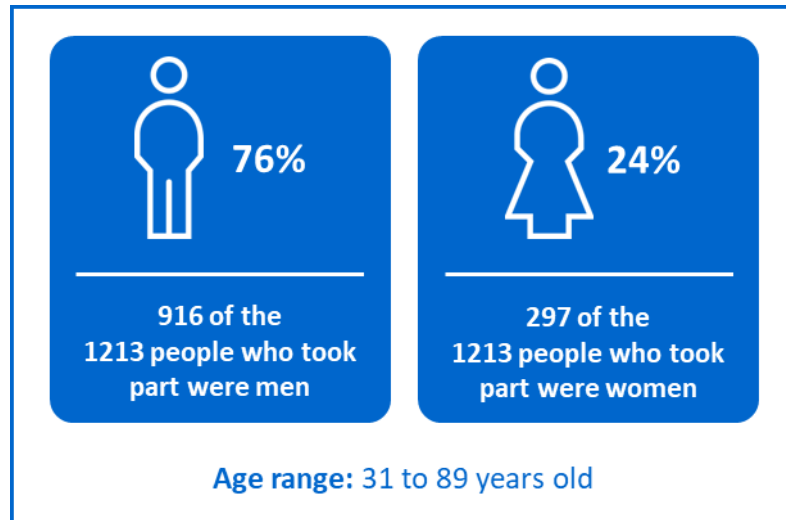
The study took place at 221 study centres in 35 countries in Europe, Central America, South America, North America, Asia, Africa, and Australia. This map shows the countries where this study took place.



2. Who took part in this study?

In this study, 1213 people with bladder cancer that had spread to other parts of the body and hadn't been previously treated took part. The age and sex of the patients in this study reflected that of all patients who have this type of cancer.

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

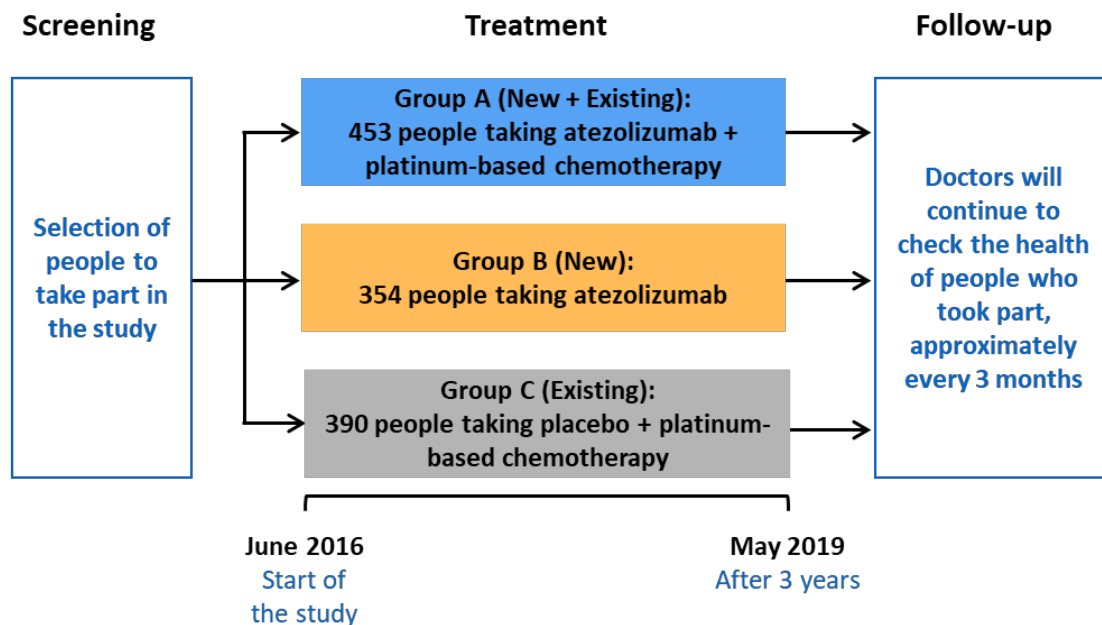


3. What happened during the study?

During the study, people were selected by chance to get one of 3 treatments. The treatments were selected at random – by a computer. This table shows the groups in the study, what drugs they were taking, and when the drugs were taken. All the drugs were taken by drip into a vein (infusion).

	Atezolizumab (the new study medication)	Existing Chemotherapy		Placebo
		Gemcitabine	Cisplatin or carboplatin	
Days of each 21-day cycle	Day 1	Days 1 and 8	Day 1	Day 1
Group A	453 patients	453 patients	453 patients	-
Group B	354 patients	-	-	-
Group C	-	390 patients	390 patients	390 patients

This study is still continuing, so some people are still being treated with the study medicines. When the study finishes, the people who took part will be asked to go back to their study centre for more visits – to check their overall health. Here is more information about what has happened in the study so far – and what the next steps are.



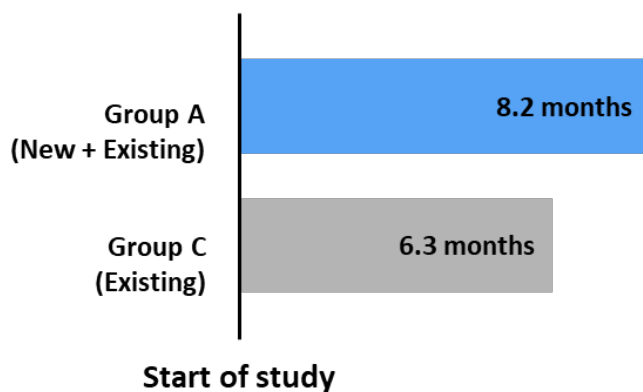
4. What were the results of the study at this point?

Question 1: How much time was there between the start of the study treatment and people's cancer getting worse?

Researchers looked at how long it took for people's cancer to get worse in Groups A and C. Results from Group B were not yet final and therefore not ready to be reported at the time of this summary:

So far, in Group A, people's cancer got worse after an average of 8.2 months (some people's cancer did not get worse at all and some people's cancer got worse more rapidly). In Group C, people's cancer got worse after an average of 6.3 months.

On average, how long did it take for people's cancer to get worse?



Question 2: Were there changes in the size of people’s tumours or how much worse their disease got? Researchers looked at this several times during the study.

- In Group A, 47% of people’s tumours got smaller, and 13% of people’s tumours shrank so much they could no longer be measured.
- In Group C, 44% of people’s tumours got smaller, and 7% of people’s tumours shrank so much they could no longer be measured.

Question 3: How long did people in this study live?

Another piece of information that researchers collected was how long people in this study lived. They compared this information between the 3 groups. People who were in Group A lived for an average of 16.0 months after starting the medicine, although some lived longer and some did not live this long. People who were in Group C lived for an average of 13.4 months.

Out of the 1197 people who were originally given a medicine to take in this study, 649 people died during the study.

- In Group A, 236 out of 453 people (52%) died.
- In Group C, 223 out of 390 people (57%) died.

On average, how long did people in each group live?



5. What were the side effects of the study medicine?

Side effects (also called ‘adverse reactions’) are medical problems (such as a headache) that are believed to be caused by medicines used in the study. Side effects can vary from mild to very serious and may vary from person to person. Not all of the people in this study had all of the side effects.

Common side effects and those that suggest a patient’s immune system might be attacking their own body are listed in the following sections.

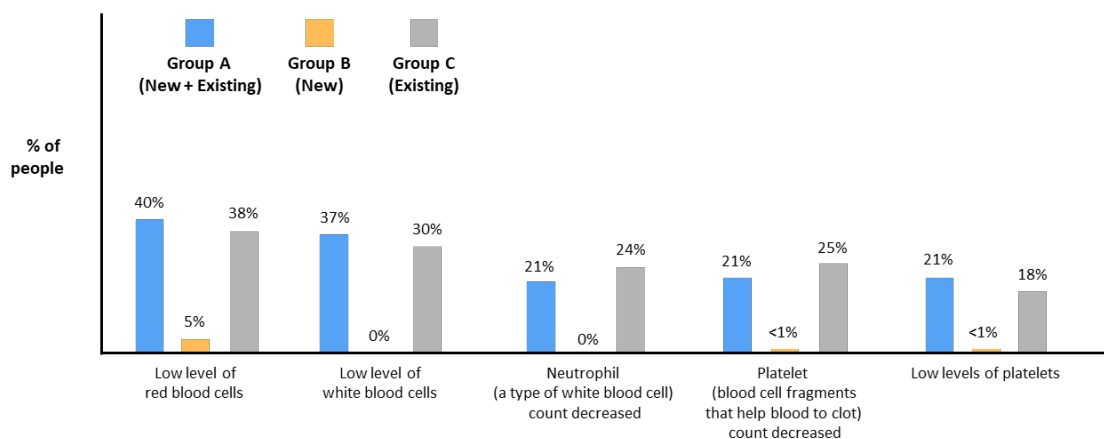
Most common side effects

During this study, about 61 out of every 100 people (61%) had a side effect that doctors thought to be caused by the study medicines they were taking. Here are the people in each group who had these types of side effects:

- About 81% of people taking atezolizumab + platinum-based chemotherapy (Group A – New + Existing).
- About 15% of people taking atezolizumab alone (Group B – New).
- About 81% of people taking placebo + platinum-based chemotherapy (Group C – Existing).

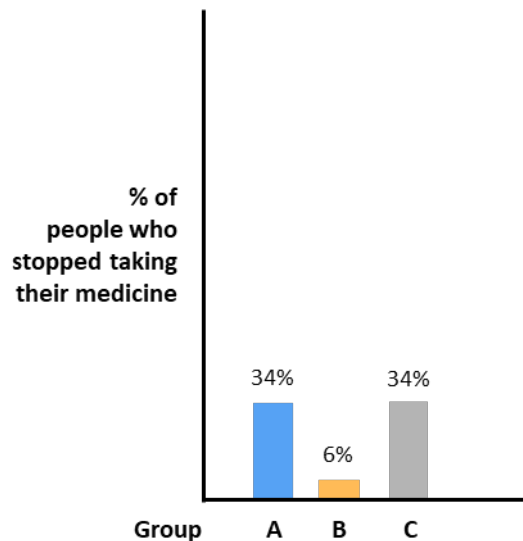
This graph shows the 5 most common Grade 3 (serious but not life threatening) or Grade 4 (life threatening) side effects across all treatment groups.

What percentage of people had each of these side effects?



During the study, some people decided to stop taking at least one of their medicines because of side effects:

- In Group A (New + Existing), 156 out of 453 people (34%) stopped taking their medicine.
- In Group B (New), 22 out of 354 people (6%) stopped taking their medicine.
- In Group C (Existing), 132 out of 390 people (34%) stopped taking their medicine.



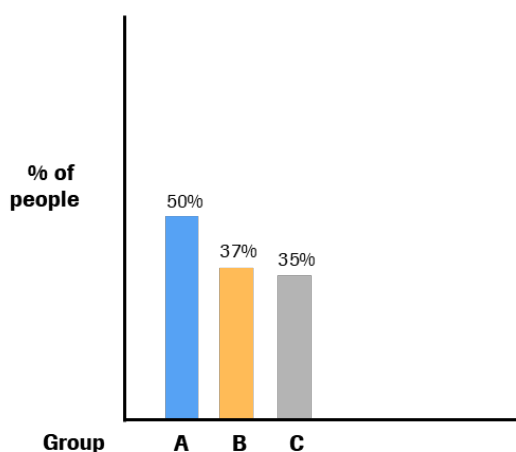
Some people in the study died from side effects that may have been related to one of the study medicines. These were:

- 9 out of 453 people (2%) in Group A (New + Existing).
- 3 out of 354 people (< 1%) in Group B (New).
- 4 out of 390 people (1%) in Group C (Existing).

Most common side effects that suggested immune system activity is involved

During this study, about 41 out of every 100 people (41%) had a side effect that doctors thought could be a reaction of the immune system on the patients' own body. Here are the people in each group who had these types of side effects:

- About 50% of people taking atezolizumab + platinum-based chemotherapy (Group A).
 - About 37% of people taking atezolizumab alone (Group B).
 - About 35% of people taking placebo + platinum-based chemotherapy (Group C).
-



This table shows the 5 most common immune-related side effects across all treatment groups.

Most common immune-related side effects reported in this study	Group A (New + Existing): people taking atezolizumab + platinum-based chemotherapy (453 people total)	Group B (New): people taking atezolizumab (354 people total)	Group C (Existing): people taking placebo + platinum-based chemotherapy (390 people total)
Rash	30% (137 out of 453)	13% (45 out of 354)	19% (74 out of 390)
Hepatitis (diagnosis and laboratory abnormalities) ^a	18% (82 out of 453)	14% (50 out of 354)	13% (49 out of 390)
Hepatitis (laboratory abnormalities)	17% (79 out of 453)	13% (46 out of 354)	11% (44 out of 390)
Hepatitis (diagnosis)	1% (6 out of 453)	2% (6 out of 354)	2% (8 out of 390)
Low thyroid activity	11% (48 out of 453)	10% (36 out of 354)	4% (15 out of 390)
High thyroid activity	7% (31 out of 453)	5% (17 out of 354)	2% (7 out of 390)
Inflammation of lung tissue	3% (12 out of 453)	3% (12 out of 354)	2% (6 out of 390)
Inflammation of the pancreas	1% (3 out of 453)	2% (6 out of 354)	1% (2 out of 390)

^a Some patients were captured in both categories.

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. What do these results mean for doctors and patients?

The information presented here is from a single study of 1213 people with bladder cancer that had spread to other parts of the body and hadn't been previously treated. These results helped researchers learn more about atezolizumab treatment for people with bladder cancer.

Overall, this study showed that for people who were given atezolizumab in addition to platinum-based chemotherapy, their cancer took longer to get worse and they did not experience any new side effects. In addition, people taking atezolizumab with platinum-based chemotherapy seem to live longer compared with those who received platinum-based chemotherapy plus placebo.

One study can't 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 results from other studies of the same medicine.

- This means that you shouldn't 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?

More work is planned to look at the efficacy and safety of atezolizumab in patients participating in this trial.

This study started in June 2016 and is expected to end at the end of 2020. This summary includes the results up until 31st May 2019. The study is still happening – study doctors are still collecting information.

Another trial (IMvigor010; NCT02450331) is happening now where, after surgery to remove the bladder, some patients receive atezolizumab and some do not.

8. Where can I find more information?

You can find more information about this study on these websites:

- <https://clinicaltrials.gov/ct2/show/results/NCT02807636>
- <https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-000250-35>
- <https://forpatients.roche.com/en/trials/cancer/bladder-cancer/study-of-atezolizumab-as-monotherapy-and-in-combination-with-pla.html>

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Atezolizumab with or without chemotherapy in metastatic urothelial cancer (IMvigor130): a multicentre, randomized, placebo-controlled phase 3 trial”. The authors of the scientific paper are: Matthew D. Galsky, José Ángel Arranz Arija, Aristotelis Bamias, Ian D. Davis, Maria De Santis, and others. The paper is published in the journal *The Lancet*, volume number 395, on pages 1547–57, May 16, 2020.

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

If you have more questions:

- Visit the ForPatients website and fill out the contact form – <https://forpatients.roche.com/en/trials/cancer/bladder-cancer/study-of-atezolizumab-as-mono-therapy-and-in-combination-with-pla.html>
- Contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Talk to the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Talk 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 whose headquarters are in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study: “Study of Atezolizumab as Monotherapy and in Combination With Platinum-Based Chemotherapy in Participants With Untreated Locally Advanced or Metastatic Urothelial Carcinoma (IMvigor130)”.

The study is known as ‘IMvigor130’.

- The protocol number for this study is: WO30070.
- The ClinicalTrials.gov identifier for this study is: NCT02807636.
- The EudraCT number for this study is: 2016-000250-35.