

## Clinical Trial Results – Layperson

### **A study to compare three treatment regimens—atezolizumab with chemotherapy, atezolizumab alone and placebo with chemotherapy—in people with advanced or metastatic bladder cancer for which they had not received prior treatment with chemotherapy: final results on how long the people included in the study lived**

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 (May 2023).

The study started in June 2016 and is expected to end by the end of 2023. This summary includes the results until 31 August 2022. At the time of writing this summary, the study is still happening and study doctors are still collecting information. However, new participants are not being enrolled.

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

1. General information about this study (page 3)
2. Who took part in this study? (page 6)
3. What happened during the study? (page 7)
4. What were the results of the study? (page 8)
5. What were the side effects? (page 8)
6. How has this study helped research? (page 11)
7. Are there plans for other studies? (page 12)
8. Where can I find more information? (page 12)

#### Thank you to the people who took part in this study

The people who took part have helped researchers 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 treatment regimens:
    - A new medicine (the ‘study medicine’) used alone.
    - 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 one of these treatments:
    - The study medicine (atezolizumab) with an existing platinum-based chemotherapy (gemcitabine and carboplatin or gemcitabine and cisplatin) (Group A: New + Existing).
    - Atezolizumab alone (Group B: New).
    - A placebo (a dummy drug that 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).
  - People in Groups A and C didn’t know whether they were given the new medicine or not.
- 
- | Group A                                    | Group B           | Group C                               |
|--|-------------------|---------------------------------------|
| (New + Existing)                           | (New)             | (Existing)                            |
| atezolizumab + platinum-based chemotherapy | atezolizumab only | placebo + platinum-based chemotherapy |
- It was decided by chance which treatment each person would take.
  - This study included 1213 people in 35 countries or regions.
  - This summary includes final survival results for each group:
    - In Group A, people lived for about 16.1 months from the start of the study (some died earlier, some lived longer), compared to about 15.2 months in Group B and 13.4 months in Group C.
    - Serious side effects were experienced by 54% of people (243 out of 454 people) in Group A, 46% of people (163 out of 354 people) in Group B, and 50% of people (196 out of 389 people) in Group C.
  - At time of writing (May 2023), the study is still happening. It is expected to end by the end of 2023.

## 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 a poor chance of survival, and there is no current treatment that can cure everyone. People usually take medicines that kill cancer cells called 'platinum-based chemotherapy'. It is preferred for people 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 a person has too many side effects while taking cisplatin, they can 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 attack tumours.

In this study, researchers wanted to see if giving people both chemotherapy and immunotherapy at the same time (or giving them immunotherapy alone) would work better than chemotherapy alone to keep their cancer from getting worse and help people with this type of bladder cancer live longer.

Since the first results were collected (up until 31 May 2019), researchers have continued to look at how well the medicines work by continuing to study things like how long participants have lived and how many side effects they've had. This summary includes the updated and final results showing how long people with this type of cancer lived and how safe the medicines were in this study.

### 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 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 together 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 that it had no medicine-related effect on the body. A placebo is used so that the participant and the doctor do 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 with the final results were:**

- How long did people who received the study medicine (atezolizumab) live? Did the people treated with atezolizumab plus platinum-based chemotherapy live longer than people treated with only platinum-based chemotherapy?

#### **Other questions that researchers wanted to answer were:**

- 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?**

---

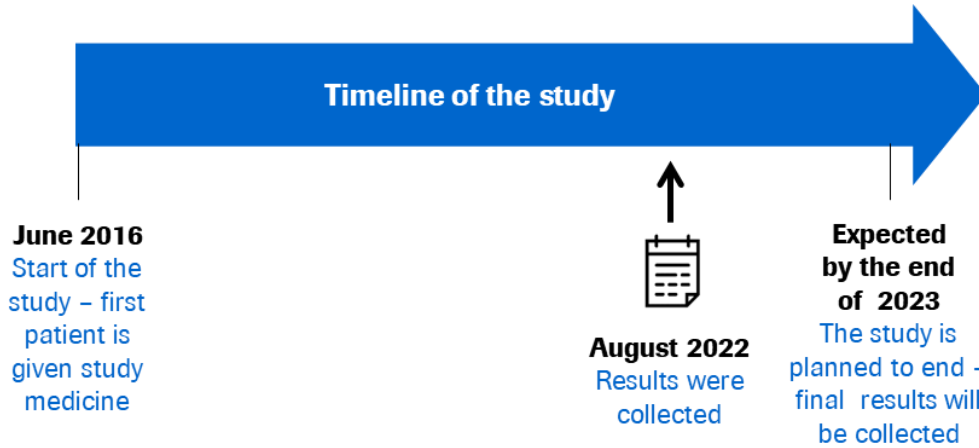
This study is a 'Phase 3' study. This means that atezolizumab had been tested in a smaller number of people with bladder cancer before this study. In this study, a larger number of people with bladder cancer were in Groups A (New + Existing), B (New), and C (Existing). The researchers wanted to find 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 (Group B) knew they were receiving atezolizumab.

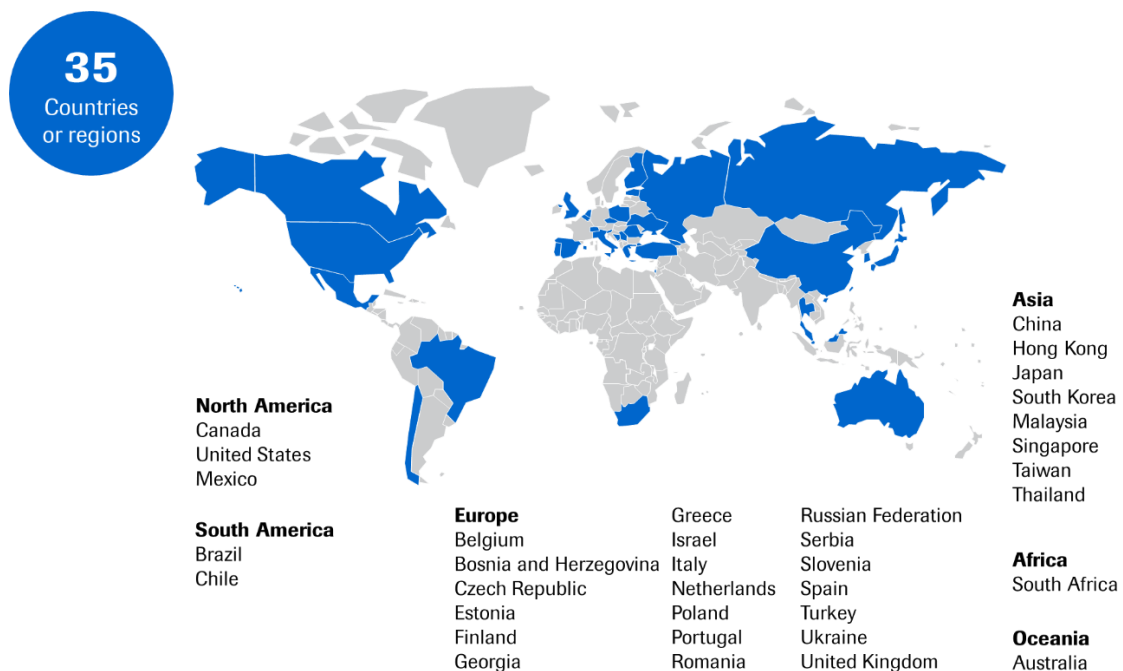
## When and where did the study take place?

The study started in June 2016 and is expected to end by the end of 2023. This summary includes the results up until 31 August 2022. At the time of writing (May 2023), the study is continuing and study doctors are still collecting information.



This study is continuing, so the symbol on the timeline (📅) shows when the information shown in this summary was collected—after about 6 years (31 August 2022).

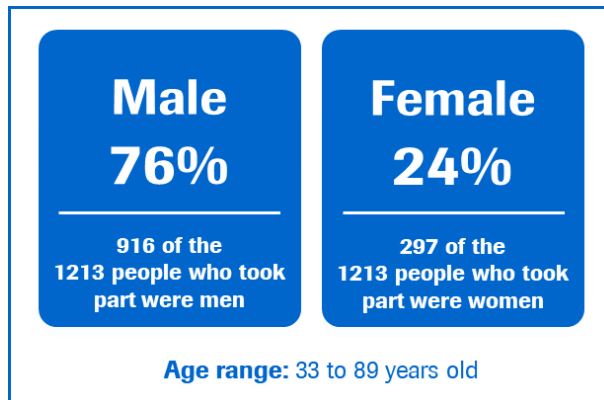
The study took place at 221 study sites in 35 countries or regions in Europe, Central America, South America, North America, Asia, Africa, and Australia. This map shows the locations where this study took place.



## 2. Who took part in this study?

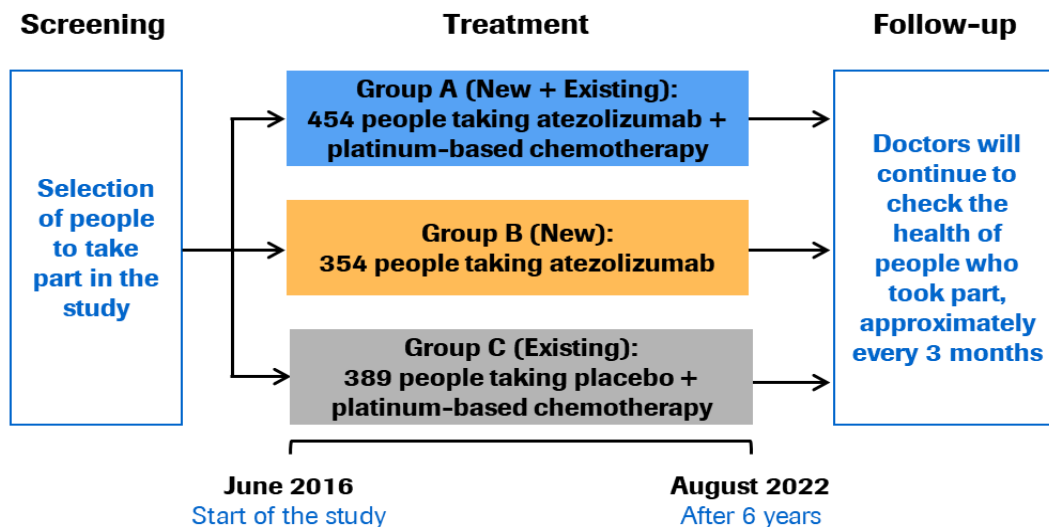
In this study, 1213 people with bladder cancer that had spread to other parts of the body and hadn't been treated previously took part. The age and sex of the participants reflected those of all people who have this type of cancer.

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 three treatments. The treatments were selected at random by a computer. This diagram shows the groups in the study, what drugs they were taking, and when the drugs were taken. All of the drugs were taken by drip into a vein (infusion).



This table shows the number of people who were given each study treatment, and how often the drugs were given. Sometimes people who enrol in a study do not end up taking part. For example, some people may decide not to be involved or may have other reasons for not taking part.

	<b>Atezolizuma b (the new study medication)</b>	<b>Existing chemotherapy</b>		<b>Placebo</b>
		<b>Gemcitabine</b>	<b>Cisplatin or carboplatin</b>	
<b>Days of each 21-day cycle</b>	Day 1	Days 1 and 8	Day 1	Day 1
<b>Group A</b>	454 people	454 people	454 people	–
<b>Group B</b>	354 people	–	–	–
<b>Group C</b>	–	389 people	389 people	389 people

This study is still happening, 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 sites 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?

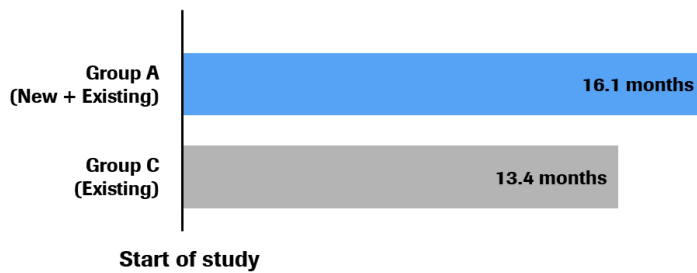
### Question 1: How long did people in this study live?

Researchers looked at 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 16.1 months after starting the medicine, although some lived longer and some did not live this long. People who were in Group B lived for an average of 15.2 months and people who were in Group C lived for an average of 13.4 months.

Of the people who took part in this study, 917 died during the study.

- In Group A, 336 out of 451 people (75%) died.
- In Group B, 271 out of 360 people (75%) died.
- In Group C, 310 out of 400 people (78%) died.

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



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 person’s immune system might be attacking their own body are listed in the following sections.

### Most common side effects

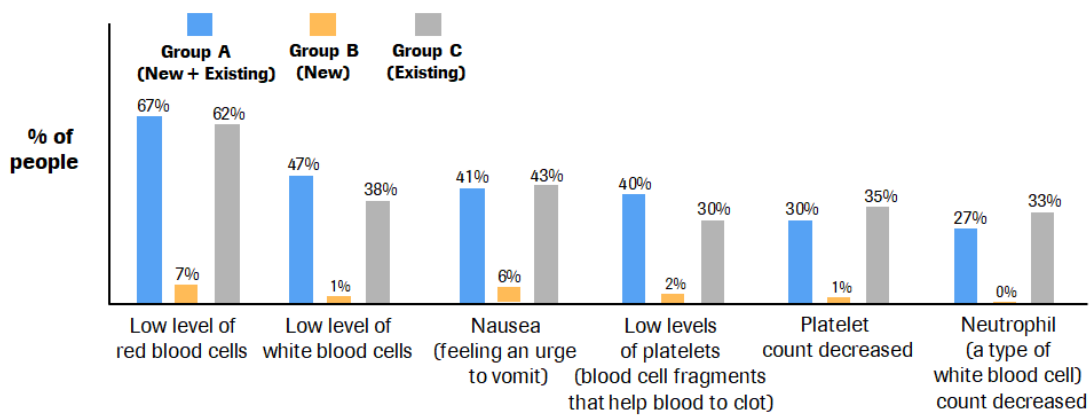
During this study, most people had a side effect that doctors thought was caused by a study medicine they were taking. Here are the people in each group who had these types of side effects:

- About 96% of people (435 out of 454 people) taking atezolizumab + platinum-based chemotherapy (Group A: New + Existing).
- About 61% of people (217 out of 354 people) taking atezolizumab alone (Group B: New).
- About 96% of people (372 out of 389 people) taking placebo + platinum-based chemotherapy (Group C: Existing).

This graph shows the 6 most common side effects (occurring in at least 30% of people) across all treatment groups that doctors thought were caused by any of the study medicines.



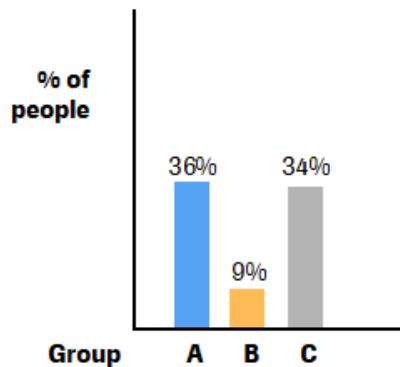
**What percentage of people had each of these side effects?**



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

- In Group A (New + Existing), 165 out of 454 people (36%) stopped taking their medicine.
- In Group B (New), 31 out of 354 people (9%) stopped taking their medicine.
- In Group C (Existing), 132 out of 389 people (34%) stopped taking their medicine.

**What percentage of people stopped taking their medicine because of a side effect?**



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

- 9 out of 454 people (2%) in Group A (New + Existing).
- 3 out of 354 people (1%) in Group B (New).
- 4 out of 389 people (1%) in Group C (Existing).

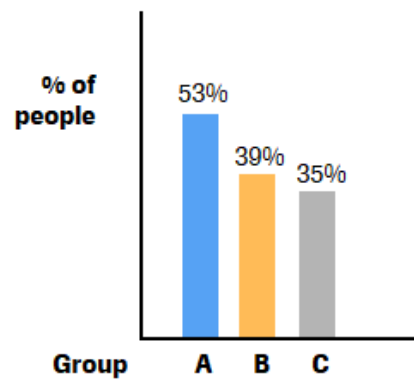
## Most common side effects that suggested immune system activity was involved

---

During this study, some people had a side effect that doctors thought could be a reaction of the immune system on the person's own body. Here are the people in each group who had these types of side effects:

- 242 out of 454 people (53%) in Group A (New + Existing).
- 139 out of 354 people (39%) in Group B (New).
- 138 out of 389 people (35%) in Group C (Existing).

### What percentage of people had a side effect that suggested an immune system reaction?



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

<b>Most common immune-related side effects reported in this study</b>	<b>Group A (New + Existing)</b>  <b>People taking atezolizumab + platinum-based chemotherapy</b> (454 people total)	<b>Group B (New)</b>  <b>People taking atezolizumab</b> (354 people total)	<b>Group C (Existing)</b>  <b>People taking placebo + platinum-based chemotherapy</b> (389 people total)
Rash	32% (145 out of 454)	14% (49 out of 354)	19% (75 out of 389)
Hepatitis (diagnosis and laboratory abnormalities) <sup>a</sup>	20% (89 out of 454)	16% (57 out of 354)	13% (52 out of 389)
Hepatitis (laboratory abnormalities)	19% (86 out of 454)	15% (53 out of 354)	12% (47 out of 389)
Hepatitis (diagnosis)	1% (6 out of 454)	2% (6 out of 354)	2% (8 out of 389)
Low thyroid activity	12% (54 out of 454)	11% (38 out of 354)	4% (17 out of 389)
High thyroid activity	8% (35 out of 454)	5% (18 out of 354)	2% (7 out of 389)
Inflammation of lung tissue	3% (15 out of 454)	3% (12 out of 354)	2% (6 out of 389)

<sup>a</sup> Some people were included in both categories.

## Other side effects

You can find information about other side effects (not shown in the sections above) in some of the resources 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 treated previously. These results helped researchers learn more about treatment with atezolizumab for people with bladder cancer.

Overall, this study showed that for people who were given atezolizumab in addition to platinum-based chemotherapy (Group A) and people who were given atezolizumab alone (Group B), their cancer took longer to get worse than for people who were given placebo in addition to platinum-based chemotherapy (Group C). These people did not experience any new side effects beyond to what was already known. The differences between Groups A and C and between Groups B and C were not big enough to show researchers that atezolizumab combined with platinum-based chemotherapy or atezolizumab alone increased how long people lived compared to placebo combined with platinum-based chemotherapy.

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?

This study started in June 2016 and is expected to end by the end of 2023. This summary includes the results up until 31 August 2022. The study is still happening and study doctors are still collecting information.

There are other studies looking at the safety and effects of atezolizumab in people with bladder cancer. In these studies, atezolizumab is given alone or together with other anti-cancer medicines in people with bladder cancer that has spread to the muscle or other parts of the body or in people with bladder cancer that has not spread to the muscle.

## 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/trial/2016-000250-35/GB>
- <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 titles of the relevant scientific papers are:

- “Atezolizumab plus chemotherapy versus placebo plus chemotherapy in untreated locally advanced or metastatic urothelial carcinoma (IMvigor130): final overall survival analysis results from a randomised, controlled, phase 3 study”. The authors of the scientific paper are: Enrique Grande, José Á. Arranz, Maria De Santis, and others. The paper is published in the journal *The Lancet Oncology* [online ahead of print; [https://doi.org/10.1016/S1470-2045\(23\)00540-5](https://doi.org/10.1016/S1470-2045(23)00540-5)].
- “Atezolizumab monotherapy versus chemotherapy in untreated locally advanced or metastatic urothelial carcinoma (IMvigor130): final overall survival analysis from a randomised, controlled, phase 3 study”. The authors of the scientific paper are: Aristotelis Bamias, Ian D. Davis, Matthew D. Galsky, and others. The paper is published in the journal *The Lancet Oncology* [online ahead of print; [https://doi.org/10.1016/S1470-2045\(23\)00539-9](https://doi.org/10.1016/S1470-2045(23)00539-9)].

The first results from the study can be found in this scientific paper: “Atezolizumab with or without chemotherapy in metastatic urothelial cancer (IMvigor130): a multicentre, randomized, placebo-controlled phase 3 trial”. The paper is published in the journal *The Lancet*, volume number 395, on pages 1547-57.

### **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: “A phase III, multicenter, randomized, placebo-controlled study of atezolizumab (anti-pd-l1 antibody) as monotherapy and in combination with platinum-based chemotherapy in patients with untreated locally advanced or metastatic urothelial carcinoma”.

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.