# Summary of Clinical Trial Results

## A study of atezolizumab and cabozantinib compared with cabozantinib alone in people with kidney cancer after immune checkpoint inhibitor treatment has not worked

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 it was written (April 2023).

The study started in July 2020 and is planned to end in early 2024. This summary includes the results that were analysed up to January 2023. At the time of writing this summary, the study is still happening – study doctors are still collecting information. The study was fully enrolled by December 2021.

The purpose of this study was to see if adding atezolizumab, a new type of medicine called an 'immune checkpoint inhibitor', to cabozantinib, compared to cabozantinib only, helped stop or slow a type of kidney cancer called renal cell carcinoma, or RCC, from getting worse and kept people with the kidney cancer alive longer after previous treatment with a different immune checkpoint inhibitor. The results from this study may be different than results from other studies with the same medicine. One study cannot tell us everything about how safe a medicine is and how well it works. It takes a lot of people in many studies to find out everything we need to know.

- **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.**

### Contents of the summary



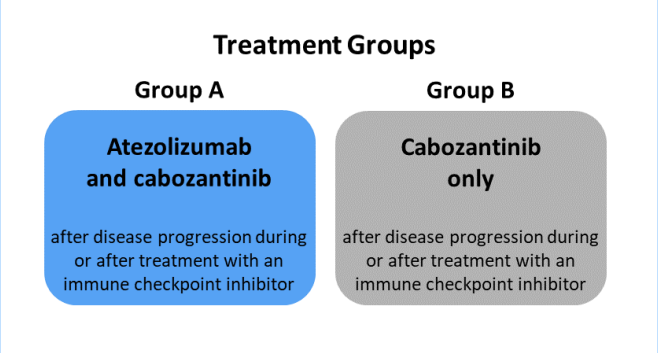
### Thank you to the people who took part in this study

The people who took part in this study have helped researchers answer important questions about kidney cancer and about treatment with two drugs called 'atezolizumab' and 'cabozantinib', which were given in this study after a person's cancer got worse during or after treatment with an immune checkpoint inhibitor.

## Key information about this study

**Why was this study done?**

- This study was done to compare the medicines being studied (called atezolizumab and cabozantinib) with cabozantinib alone. These medicines were given to people with kidney cancer whose cancer got worse (also known as 'disease progression') during or after treatment with a type of medicine called an immune checkpoint inhibitor.
    - The purpose of this study was to see if adding atezolizumab to cabozantinib after treatment with an immune checkpoint inhibitor didn't work would help to stop or slow the worsening of kidney cancer and keep people alive longer compared to cabozantinib alone.
    - The treatment each person was given was decided by chance.




- This study included 522 people in 15 countries (see map on page 6).

**What were the results?**

- The main findings were that:
    - In **Group A**, people's cancer got worse 10.6 months on average after starting the treatment, compared with 10.8 months on average after starting the treatment for those in **Group B**.
    - People in **Group A** lived for about 25.7 months on average after starting the treatment. How long people lived in **Group B** could not be calculated because fewer than 50% had died.
    - The difference between **Group A** and **Group B** was not big enough to show researchers that giving atezolizumab and cabozantinib together stopped or slowed the worsening of people's cancer or increased how long people lived after starting the treatment compared to giving cabozantinib only.

**How many people had side effects?**

- About 24% of people (63 out of 262 people) in **Group A** had serious side effects related to their treatment, compared to 12% of people (30 out of 256 people) in **Group B**.
- At the time of writing (April 2023), the study is still ongoing and information about side effects is still being collected. The study is expected to end in early 2024.

# 1. General information about this study

## Why was this study done?

People with cancers that have spread to other parts of the body (locally advanced or metastatic) are very ill and have a poor chance of survival. These people are sometimes given a treatment called 'immunotherapy'—this is a medicine that helps the person's own immune system attack their cancer (tumour).

A type of immunotherapy called an 'immune checkpoint inhibitor' works by blocking substances called checkpoint proteins. Normally, these proteins stop a person's immune system from attacking healthy cells, but cancer cells can use them to stop the immune system from killing the tumour. Immune checkpoint inhibitors help to treat cancers by blocking these proteins, which allows the immune system to attack tumours. One checkpoint protein that can be blocked by immune checkpoint inhibitors is called 'programmed death-ligand 1' or 'PD-L1'.

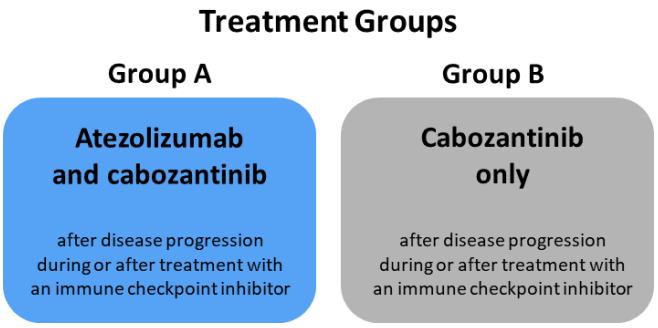
In some cases where the kidney cancer hasn't spread to other parts of the body (localized), immune checkpoint inhibitors are given after the cancer has been removed by surgery. In cases where the kidney cancer is locally advanced or metastatic, immunotherapy is sometimes given together with a type of medicine called an 'anti-angiogenic'. Anti-angiogenic medicines help to stop cancer cells from growing and spreading by blocking the formation of new blood vessels that supply the tumour with oxygen and food. Anti-angiogenic medicines can also help immunotherapy medicines kill cancer cells.

When an anti-cancer treatment doesn't work, people are given a different medicine to treat the cancer. In this study, researchers wanted to see if giving an immune checkpoint inhibitor that blocks PD-L1 (atezolizumab) and an anti-angiogenic medicine (cabozantinib) stopped or slowed the worsening of the cancer and kept people alive longer after previous treatment with an immune checkpoint inhibitor didn't work. They compared people who were given both drugs to people who were given only cabozantinib. The people who took part in this study had already been given previous treatment with an immune checkpoint inhibitor and their cancer got worse before they were given these medicines.

## What were the medicines being studied?

This study looked at a medicine called atezolizumab and another medicine called cabozantinib given together compared with only cabozantinib in people with kidney cancer whose disease worsened during or after treatment with a type of medicine called an immune checkpoint inhibitor:

- **Group A: atezolizumab and cabozantinib**
- **Group B: cabozantinib**
    - People in this group were not given atezolizumab. They were given only cabozantinib.




One of the medicines being studied is **'atezolizumab'** (known by its brand name, Tecentriq®):

- You say this as 'a – teh – zo – liz – oo – mab'.
- You say 'Tecentriq' as 'tee – sen – trik'.

- 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.
- When people are given atezolizumab, it may stop or delay their tumour (cancer) from coming back.
- This medicine is a type of medicine called 'immunotherapy'. More specifically, it is a type of immunotherapy known as an 'immune checkpoint inhibitor'.

The other medicine being studied is **'cabozantinib'** (known by its brand name, Cabometyx®):

- You say this as 'cab– oh – zan – tin – nib'.
- You say 'Cabometyx' as 'cab – bow – met - ticks'.

- Tumours can use proteins known as receptor tyrosine kinases to form new blood vessels (in a process called angiogenesis) that supply oxygen and food to the tumour, helping them grow and spread. Cabozantinib blocks receptor tyrosine kinases, meaning that the cancer cells do not get what they need to develop and grow.
- When people are given cabozantinib, it may stop or delay their cancer from worsening.
- This medicine is a type of medicine called a 'tyrosine kinase inhibitor'. It is also known as an "anti-angiogenic'.

## What did researchers want to find out?

- Researchers did this study to compare atezolizumab and cabozantinib together with cabozantinib alone to see how well the combination of atezolizumab and cabozantinib worked in people with kidney cancer after an immune checkpoint inhibitor didn't work (see section 4 "What were the results of the study?").
    - People in **Group A** were given both atezolizumab and cabozantinib.
    - People in **Group B** were given only cabozantinib.
    - Researchers compared the two groups to see how well atezolizumab and cabozantinib worked together.
- Researchers also looked at how safe the combination of atezolizumab and cabozantinib was by seeing how many people in each treatment group had side effects and how serious these side effects were (see section 5 "What were the side effects?").

**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 did it take longer for the cancer to get worse in the people treated with both atezolizumab and cabozantinib compared to the people treated with only cabozantinib?
2. How long did people in this study live, and did the people treated with both atezolizumab and cabozantinib live longer than people treated with only cabozantinib?
3. How many people had side effects when taking the medicines, and how serious were the side effects?

## What kind of study was this?

This study was a '**Phase 3**' study. This means that a large number of people with kidney cancer took either both atezolizumab and cabozantinib or only cabozantinib; this was to find out if combining atezolizumab and cabozantinib stopped people's cancer from getting worse and helped them live longer, compared to only cabozantinib. Phase 3 studies are done in a large number of people to see if a medicine works better than the usual treatment and is safe enough to be approved by the authorities as a treatment that can be prescribed by your doctor.

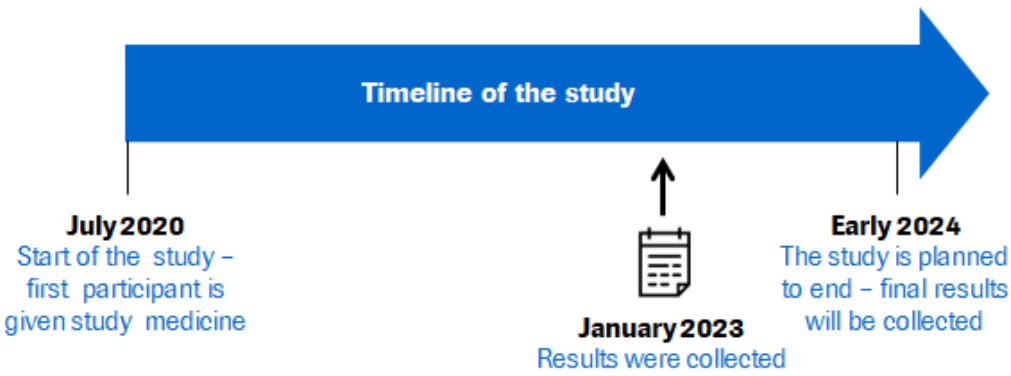
The study was '**randomised**'. This means that which of the two treatment groups people in the study would be in was decided by chance—like tossing a coin. Deciding by chance which group people will be in makes it more likely that the types of people in both groups will be similar (for example, age and race). Other than the different study treatments given to people in each group (atezolizumab and cabozantinib in **Group A** and cabozantinib only in **Group B**), all other care was the same.

This was an '**open label**' study. This means that the people taking part in the study and the study doctors knew which of the treatment groups (**Group A** or **Group B**) people were in.

## When and where did the study take place?

The study started in July 2020 and is planned to end in early 2024. Study doctors are still collecting information until the end of the study. However, people are no longer being enrolled.

At the time of writing this summary, the study is still happening. This summary only includes the results until January 2023.



The symbol on the timeline (📋) shows when the information shown in this summary was collected (January 2023, which was about 2.5 years after the study started).

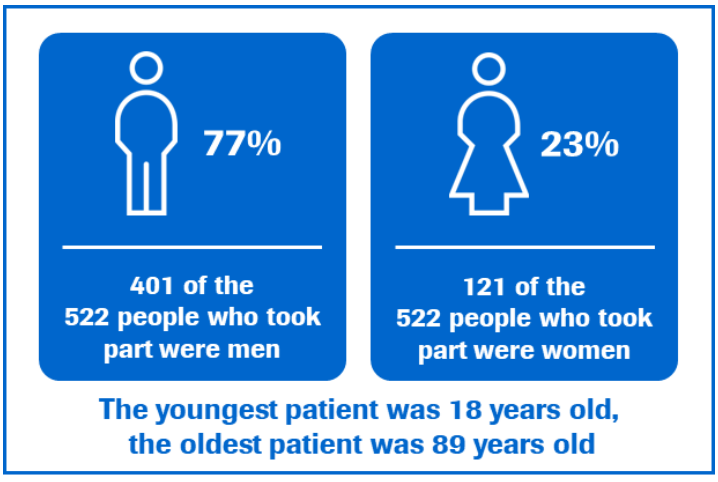
The study took place at 135 hospitals and clinics in 15 countries. This map shows where this study took place.

- Argentina
- Australia
- Canada
- Denmark
- France
- Germany
- Greece
- Italy
- Japan
- Korea
- Poland
- Russia
- Spain
- United Kingdom
- United States

## 2. Who took part in this study?

A total of 522 people with kidney cancer took part in this study.

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



People could take part in the study if:

- They had kidney cancer that spread to other parts of the body (locally advanced or metastatic).
- Their cancer worsened either during or after treatment with an immune checkpoint inhibitor (metastatic disease), or during or within 6 months after the last dose of an immune checkpoint inhibitor following surgery to remove their cancer (localized disease).

People could not take part in the study if they:

- Had previously received cabozantinib for their kidney cancer.
- Had received more than one immunotherapy treatment for their locally advanced or metastatic disease.

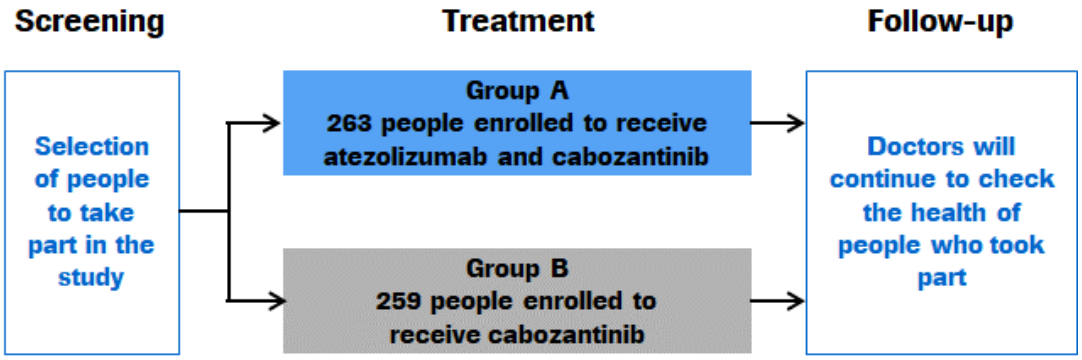
These are just some of the requirements that people needed to meet to be able to take part in this study. There were also other requirements that are not listed here.

## 3. What happened during the study?

During the study, people were selected by chance to be in one of two treatment groups.

The treatment groups were:
**Group A:** atezolizumab and cabozantinib.
**Group B:** cabozantinib only.

This study is still happening, so people are still going back to their study centre for visits to check their overall health and collect information on side effects until the study ends in early 2024. This picture shows more information about what has happened in the study so far—and what the next steps are.




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

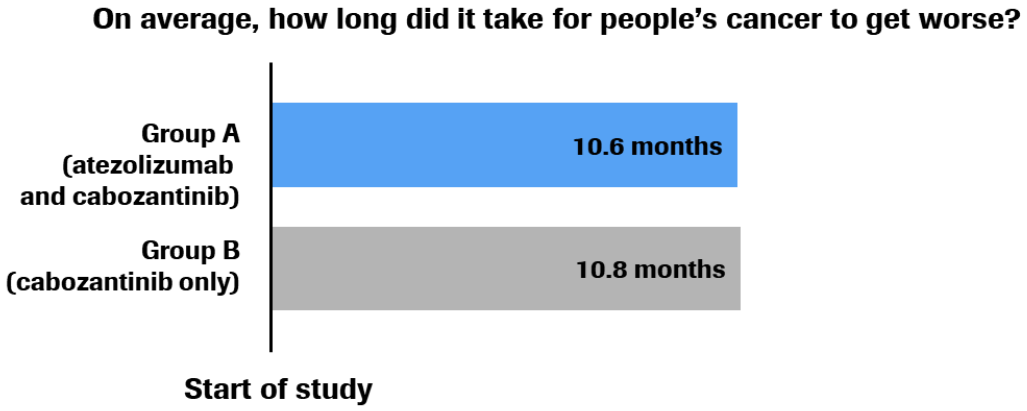
| | Group A<br>Atezolizumab and cabozantinib | Group B<br>Cabozantinib only |
|---|---|---|
| **Number of enrolled people selected by chance to be included in each group** | 263 | 259 |
| **Number of people given medicine (both atezolizumab and cabozantinib or only cabozantinib)** | 262 | 256 |
| **How and when the medicine was given** | Atezolizumab given by injection once every 21 days, and cabozantinib given by mouth daily | Cabozantinib given by mouth daily |

## 4. What were the results of the study?

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

Researchers looked at how much time there was before the cancer got worse in **Group A** and **Group B**. This information was collected from all the people in both groups from July 2020 until January 2023.

- In **Group A**, the cancer got worse after 10.6 months on average (in some people it took longer to come back, and in others it came back sooner).
- In **Group B**, the cancer got worse after 10.8 months on average (in some people it took longer to come back, and in others it came back sooner).
- The difference between **Group A** and **Group B** was not big enough to show researchers that giving both atezolizumab and cabozantinib helped stop the worsening of the cancer compared to cabozantinib alone.
- This picture shows how long it took for the cancer to come back in each group.



### **Question 2:** 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 two groups. People who were in **Group A** lived for an average of 25.7 months after starting the medicine, although some lived longer and some did not live this long. How long on average people in **Group B** lived could not be calculated because fewer than 50% had died.

Out of the 522 people who were originally given a medicine to take in this study, 176 people died during the study.

- In **Group A**, 89 out of 263 people (34%) died.
- In **Group B**, 87 out of 259 people (34%) died.

## 5. What were the side effects?

- Side effects are medical problems (like feeling dizzy) that may happen during the study.
- Not all of the people in this study had all of the side effects.
- Side effects may be mild to severe, or even life-threatening, 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 in the medicine leaflets.
- Common and serious side effects are listed in the following sections.

### Most common side effects

- In this study, 100% of people who received both atezolizumab and cabozantinib had a side effect of any kind, compared to 99% of people who received cabozantinib alone.
- This table shows the most common side effects; these are the side effects that at least 20% of people in either group had. The side effects could have been serious (meaning an unwanted effect that is life-threatening, needs hospital care or causes lasting problems) or not serious (an unwanted effect, but one that was not life-threatening and did not require hospital care or have lasting effects). 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 (occurring in at least 20% of people in either group)** | **Group A** Atezolizumab and cabozantinib (262 people total) | **Group B** Cabozantinib only (256 people total) |
|---|---|---|
| Diarrhoea | **65%** (171 out of 262) | **71%** (181 out of 256) |
| Skin reaction on the hands and feet (hand-foot syndrome) | **39%** (101 out of 262) | **41%** (105 out of 256) |
| Poor appetite | **38%** (100 out of 262) | **38%** (97 out of 256) |
| Low thyroid activity | **36%** (95 out of 262) | **38%** (97 out of 256) |

| | | |
|---|---|---|
| Feeling sick (nausea) | **29%** (77 out of 262) | **36%** (92 out of 256) |
| Lack of energy (asthenia) | **29%** (77 out of 262) | **29%** (75 out of 256) |
| High blood pressure | **28%** (72 out of 262) | **34%** (87 out of 256) |
| Feeling tired (fatigue) | **28%** (72 out of 262) | **24%** (61 out of 256) |
| Liver damage, shown by higher levels of something called 'ALT' in the blood | **24%** (62 out of 262) | **22%** (57 out of 256) |
| Liver, heart, or kidney damage, shown by higher levels of something called 'AST' in the blood | **23%** (60 out of 262) | **24%** (61 out of 256) |
| Low level of red blood cells (anaemia) | **20%** (53 out of 262) | **19%** (48 out of 256) |
| Weight loss | **18%** (46 out of 262) | **25%** (64 out of 256) |

## Most common side effects related to the study medicines

- The side effects shown in this section are thought to be caused by the treatments being studied—atezolizumab and cabozantinib.
- During this study, 252 of the 262 people (96% of people) in **Group A** had at least one side effect that was related to the study medicines, either atezolizumab or cabozantinib.
- During this study, 249 of the 256 people (97% of people) in **Group B** had at least one side effect that was related to the study medicine, cabozantinib.

This table shows the most common side effects related to the study medicines. These are the side effects occurring in at least 20% of people in either group. The side effects could have been serious (meaning an unwanted effect that is life-threatening, needs hospital care or causes lasting problems) or not serious (an unwanted effect, but one that was not life-threatening and did not require hospital care or have lasting effects). Some people have had more than one side effect—this means that they are included in more than one row in the table.

| **Most common side effects related to the study medicines (occurring in at least 20% of people in either group)** | **Group A** Atezolizumab and cabozantinib (262 people total) | **Group B** Cabozantinib only (256 people total) |
|---|---|---|
| Diarrhoea | **63%** (164 out of 262) | **69%** (177 out of 256) |
| Skin reaction on the hands and feet (hand-foot syndrome) | **39%** (101 out of 262) | **41%** (104 out of 256) |
| Low thyroid activity | **34%** (89 out of 262) | **30%** (76 out of 256) |
| Poor appetite | **32%** (84 out of 262) | **32%** (81 out of 256) |
| High blood pressure | **25%** (66 out of 262) | **29%** (75 out of 256) |
| Lack of energy (asthenia) | **25%** (66 out of 262) | **24%** (62 out of 256) |
| Feeling sick (nausea) | **25%** (65 out of 262) | **31%** (80 out of 256) |
| Liver damage, shown by higher levels of something called 'ALT' in the blood | **23%** (59 out of 262) | **20%** (50 out of 256) |
| Feeling tired (fatigue) | **22%** (57 out of 262) | **21%** (53 out of 256) |
| Liver, heart or kidney damage, shown by higher levels of something called 'AST' in the blood | **21%** (56 out of 262) | **19%** (48 out of 256) |

## Serious side effects

- During this study, 63 of the 262 people (24%) in **Group A** and 30 of 256 people (12%) in **Group B** had at least one serious side effect that was related to the study medicines. A side effect is considered 'serious' if it is life-threatening, needs hospital care or causes lasting problems.

## Other side effects

- In **Group A**, 29 of the 262 people (11%) had a side effect that required them to stop receiving atezolizumab and 25 of the 262 people (10%) had a side effect that required them to stop receiving cabozantinib.
- In **Group B**, 10 of the 256 people (4%) had a side effect that required them to stop receiving cabozantinib.

You can find information about additional side effects (not shown in the sections above) at some of the resources listed at the end of this summary (see section 8).

## 6. How has this study helped research?

Overall, giving atezolizumab and cabozantinib together was not better than cabozantinib alone; there was no difference between **Group A** and **Group B** in how long it was until peoples' cancer got worse or how long they lived. Therefore, there was no evidence to show researchers that giving atezolizumab and cabozantinib together was better than giving only cabozantinib to people who were previously treated with an immune checkpoint inhibitor that didn't work. Researchers also found that **Group A** had more side effects than **Group B**.

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?

Researchers are constantly monitoring new agents to use in people with kidney cancer. Currently, studies are ongoing to evaluate other agents that may provide benefit to patients with kidney 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/NCT04338269
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=2020-000502-29
- https://forpatients.roche.com/en/trials/cancer/rcc/a-study-of-atezolizumab-in-combination-with-cabozantini-46186.html

If you want to find out more about the results of this study, the full title of the relevant scientific paper is: "Atezolizumab plus cabozantinib versus cabozantinib for patients with renal cell carcinoma after progression with prior immune checkpoint inhibitor treatment (CONTACT-03): a multicentre, randomized, open-label, phase 3 trial". The authors of the scientific paper are: Sumanta Kumar Pal, Laurence Albiges, Piotr Tomczak, Cristina Suárez, Thomas Powles, Toni K. Choueiri, and others. The paper is published in the journal *The Lancet*, volume number XXX, on pages XXX-XXX. *<<to be updated upon publication>>*

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

If you have more questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form: https://forpatients.roche.com/en/trials/cancer/rcc/a-study-of-atezolizumab-in-combination-with-cabozantini-46186.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, in collaboration with Exelixis, Inc, and Chugai Pharmaceutical Co, Ltd.

## Full title of the study and other identifying information

The full title of this study is: “A Study of Atezolizumab in Combination With Cabozantinib Compared to Cabozantinib Alone in Participants With Advanced Renal Cell Carcinoma After Immune Checkpoint Inhibitor Treatment (CONTACT-03)”.

The study is known as ‘CONTACT-03’.

- The protocol number for this study is: WO41994.
- The ClinicalTrials.gov identifier for this study is: NCT04338269.
- The EudraCT number for this study is: 2020-000502-29.