

Summary of Clinical Trial Results

A study of ipatasertib plus abiraterone compared with abiraterone alone in men with prostate cancer that has spread to other parts of the body

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of a clinical trial (called a 'study' in this document) and was written for:

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

This summary is based on information known at the time it was written (June 2021)

The study started in June 2017. This summary includes the results that were collected until March 2020. At the time of writing this summary, this study is still happening – study doctors are still collecting information. This summary will be updated when the study ends.

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

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Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about prostate cancer and about treatment with ipatasertib taken with abiraterone.

Key information about this study

- This study was done to see if adding a new medicine to already existing medicines would help keep cancer from getting worse in men with prostate cancer that has spread to other parts of the body.
- In this study, men were given either the new medicine being studied (called 'ipatasertib', a drug that blocks the activity of a protein that helps control how cells grow) or 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). It was determined completely by chance which treatment each person was given.
- All of the men were given the existing medications abiraterone, a drug that reduces production of male hormones in the body, and prednisone, a drug that helps control some side effects related to abiraterone.
- This study included 1101 men in 26 countries/regions.
- The first analysis for this study – which included data collected until March 2020 – has shown that for men taking ipatasertib plus abiraterone and prednisone, their cancer did not get worse until about 19.2 months after the start of the study drugs, compared with about 16.6 months for those taking placebo plus abiraterone and prednisone. This difference may have been due to chance.
- When looking only at men with tumours that had lost the PTEN protein (a protein that helps control how cells grow), among those taking ipatasertib plus abiraterone and prednisone, their cancer did not get worse until about 18.5 months after the start of the study drugs, compared with about 16.5 months for those taking placebo plus abiraterone and prednisone. This difference appeared to be due to the new medicine, ipatasertib.
- About 40% of men (4 out of 10 men) taking ipatasertib plus abiraterone had serious side effects, compared to a little more than 20% of men (2 out of 10 men) taking the placebo plus abiraterone.
- At the time of writing this summary (June 2021), the study is still happening. It is expected to be completed at the end of 2023.

1. General information about this study

Why was this study done?

Men with prostate cancer that has spread to other parts of the body are often treated with drugs that lower the amount of male hormones in the body. Male hormones may help the tumours grow, so taking drugs that reduce the amount of male hormones in the body can stop the tumours from getting bigger or even make them shrink. However, some tumours start growing again, even with the hormone-reducing drugs. Doctors may then use combinations of drugs that act in different ways to help prevent tumours from growing for a longer period of time.

One of these types of tumours are those that have a protein called PTEN that stops working, or in other words, loses the ability to function (has PTEN loss). That typically happens in almost half of prostate cancer tumours that have spread to other parts of the body. PTEN is a protein that helps control how cells grow and maintain themselves. Tumours that have PTEN loss tend to grow faster, make people sicker, and make it so hormone-reducing drugs don't work as well.

In this study, researchers wanted to see if combining a male hormone-reducing drug with a new drug that acts differently would stop cancer from growing for longer than the hormone-reducing drug by itself. They wanted to look at this for all men in the study and then specifically in the men who had tumours that had lost the PTEN protein. They also wanted to see whether the combination would be safe for people to take.

What are the study medicines?

This study looked at a new medicine called 'ipatasertib' taken together with 2 other study medications called 'abiraterone' (known by its brand name Zytiga®) and 'prednisone' (known by multiple brand names, including Deltasone®, Meticorten® and Orasone®).

Abiraterone and prednisone are the existing medicines given to men with prostate cancer that has spread to other parts of the body.

- You say this as 'ah - ber - at - er - own'. Abiraterone reduces the production of male hormones in the body. These hormones can help the cancer grow, so reducing the amount of hormones in the body can shrink the tumours or make them grow more slowly.
- You say this as 'pred - ni - zone'.
- Prednisone is a drug given with abiraterone to help prevent some side effects, such as high blood pressure or fluid build up.

The new medicine being studied is 'ipatasertib'.

- You say this as 'eye – pat – uh – sir – tib'.
- Ipatasertib blocks a protein called 'Akt' that helps to control how cells grow. In cancer cells, Akt can become too active and uncontrolled, causing the tumour to grow. Akt and PTEN are in the same pathway, meaning they work together to control cell growth. Problems that cause Akt or PTEN to not function normally can lead to tumour formation.

In this study, ipatasertib plus abiraterone/prednisone (**Group A**) was compared to 'placebo' plus abiraterone/prednisone (**Group B**).

- You say this as 'plah – see – bo'.
- The placebo looked the same as ipatasertib but did not contain any real medicine. This means that it did not have any medicine-related effects on the body.
- The researchers gave all the men abiraterone and prednisone, but half of the men got extra medicine (ipatasertib) and the other half did not (placebo) so they could see which benefits or side effects are caused by the extra medicine. Side effects are medical problems (such as feeling dizzy) that happen during the study.

What did researchers want to find out?

- Researchers wanted to see whether treating men who have prostate cancer that has spread with a combination of medicines (ipatasertib plus abiraterone/prednisone) would extend the amount of time before their cancer got worse or they died, compared with abiraterone/prednisone by itself.
 - See section 4 "What were the results of the study?"
- They also wanted to find out how safe the combination of medicines is – by seeing what the side effects were and counting how many men had side effects (plus seeing how severe these side effects were) when taking both medicines together during this study.
 - See section 5 "What were the side effects?"

The main questions that researchers wanted to answer were, in Group A and Group B, how much time was there between the start of treatment until:

1. The cancer getting worse or the person dying in all men in the study?
2. The cancer getting worse or the person dying in just the men with tumours that have lost the PTEN protein?

Other questions that researchers wanted to answer included:

3. How safe, as in what kind of side effects occurred, is the combination of ipatasertib plus abiraterone/prednisone? How many men in **Group A** and **Group B** had side effects and how severe were they?

What kind of study was this?

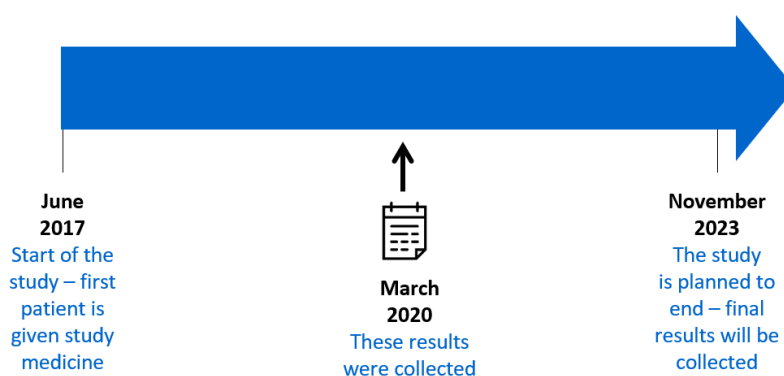
This study was a '**Phase 3**' study. This means that a large number of men with prostate cancer took either abiraterone/prednisone with ipatasertib or abiraterone/prednisone with a placebo – this was to find out if adding ipatasertib to abiraterone/prednisone helped prevent the men's cancer from getting worse. Phase 3 studies are done in a large number of people to see if a drug works better than the usual treatment and is safe enough for it to be 'approved' by the authorities as a treatment that can be prescribed by your doctor.

The study was '**randomised**'. This means that it was determined by chance which of the medicines each man would be given – like tossing a coin. Randomly choosing which medicine people take makes it more likely that the types of people in both groups (for example, age, race) will be similar. Other than the medicines being tested in each group, all other care was the same in both groups.

This was a '**double-blind**' study. This means that neither the men taking part in the study nor the study doctors or nurses knew which of the study medicines they were taking. 'Blinding' of a study is done so that any effect seen from the medicine is not due to something people expected to happen – if they had known which medicine they were taking.

When and where did the study take place?

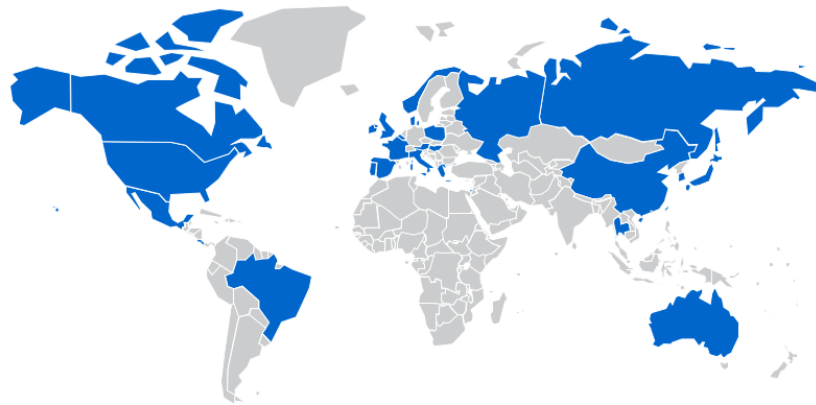
The study started in June 2017 and will end in November 2023. This summary includes the data collected up until March 2020. At the time of writing this summary (June 2021), the study is still happening – study doctors are still collecting information.



The timeline (📅) shows when the information shown in this summary was collected – 3 years (March 2020) after the study started.

The study took place at 200 study centres in 26 countries/regions around the world. The following map shows the countries where this study took place.

- Australia
- Austria
- Belgium
- Brazil
- Canada
- China
- Costa Rica
- Denmark
- France
- Greece
- Hungary
- Ireland
- Israel
- Italy
- Japan
- Mexico
- Norway
- Poland



- Portugal
- Russia
- South Korea
- Spain
- Taiwan
- Thailand
- United Kingdom
- United States

2. Who took part in this study?

In this study, 1101 men with prostate cancer that had spread to other parts of the body took part. Those who took part in the study were between 44 and 93 years old.

Men could take part in the study if:

- They had a score between 0 and 3 out of 10 on a measure of how much pain the man has been having. A score of 0 to 3 means the man has no symptoms or mild symptoms related to the cancer

Men who had been treated with chemotherapy (a medicine that kills cancer cells) for their current disease could not take part but could if they had received chemotherapy along with hormone-reducing drugs as a treatment during an earlier stage of the disease.

3. What happened during the study?

During the study, men were selected by chance (using a computer) to get one of the 2 treatments.

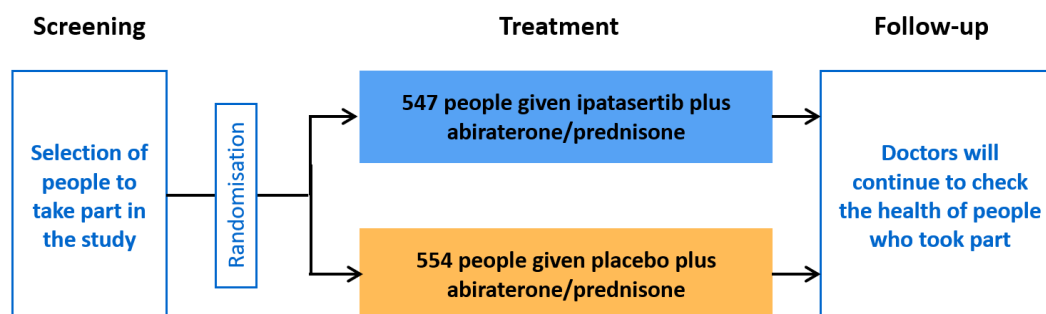
The treatment groups were:

- **Group A:** ipatasertib (new medicine) plus abiraterone/prednisone (existing medicine)
- **Group B:** placebo plus abiraterone/prednisone (existing medicine)

All drugs were taken orally (by mouth) every day. This table shows the number of men in Group A and Group B.

	Group A Ipatasertib plus abiraterone/prednisone	Group B Placebo plus abiraterone/prednisone
Number of men taking this medicine	547	554

This study is still happening, so some men are still being treated with the study medicines. The men will continue taking study medicines until their disease gets worse or side effects are too bad that they cannot continue treatment. After treatment discontinuation, the men enter a follow-up period where information on how much pain they are experiencing, what other anti-cancer treatments they are taking, and survival are collected, until the man has died or decided not to participate in the study anymore. This picture shows more information about what has happened in the study so far – and what the next steps are.

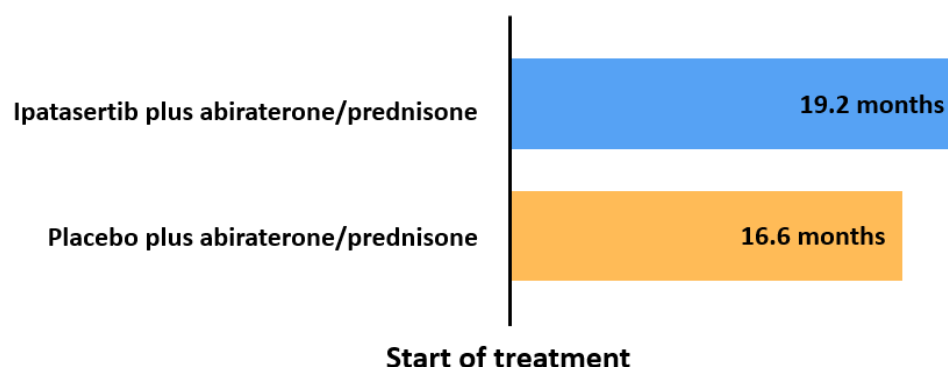


4. What were the results of the study?

Question 1: In **Group A** and **Group B**, how much time was there between the start of treatment and the cancer getting worse or the person dying in all men in the study?

Researchers looked at how much time there was before the cancer became worse (in other words, spread further or grew larger as shown by their scans) or the person died in each group for all 1101 men in the study.

On average, how long did it take for the men’s cancer to get worse?



So far, in **Group A**, the men’s cancer got worse after an average of 19.2 months (some men’s cancer took longer to become worse and some became worse sooner than 19.2 months). In **Group B**, the men’s cancer got worse after an average of 16.6 months.

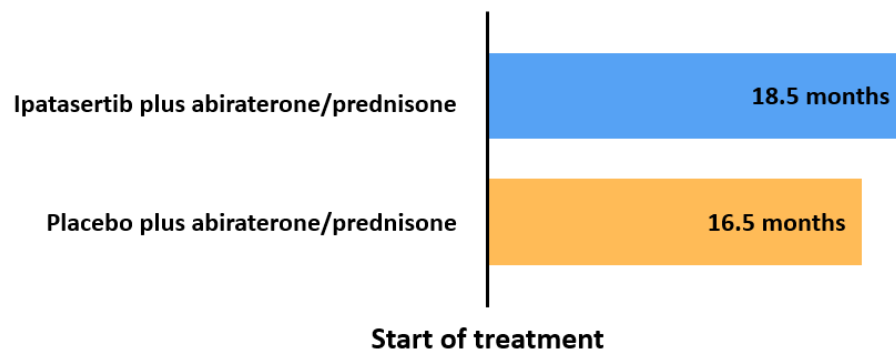
- In **Group A**, just under half of the men (252 out of 547 or 46%) had their cancer get worse or they died.
- In **Group B**, over half of the men (306 out of 554 or 55%) had their cancer get worse or they died.

Men in Group A had a 16% lower chance of their cancer getting worse or dying compared with men in Group B, but we do not know if this difference was caused by the medicine or if it was caused by chance.

Question 2: In Group A and Group B, how much time was there between the start of treatment and the cancer getting worse or the person dying in just the men with tumours that have lost the PTEN protein?

Another piece of information that researchers collected was how much time there was before the cancer became worse (spread further or grew larger as shown by their scans) or the person died in each group when only looking at the 521 men who had tumours that had lost PTEN.

On average, how long did it take for the men’s cancer to get worse when looking only at those with tumours that lost PTEN?



So far, in **Group A**, the men’s cancer got worse after an average of 18.5 months (some men’s cancer took longer to become worse and some became worse sooner than 18.5 months). In **Group B**, the men’s cancer got worse after an average of 16.5 months.

- In **Group A**, just under half of the men (124 out of 260 or 48%) had their cancer get worse or they died.
- In **Group B**, over half of the men (154 out of 261 or 59%) had their cancer get worse or they died.

Among men whose tumours had lost the PTEN protein, those in Group A had a 23% lower chance of their cancer getting worse or dying compared with men in Group B. The researchers determined that this difference was likely not due to chance – it was due to the addition of the new medicine, ipatasertib.

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see section 8).

5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happen during the study.

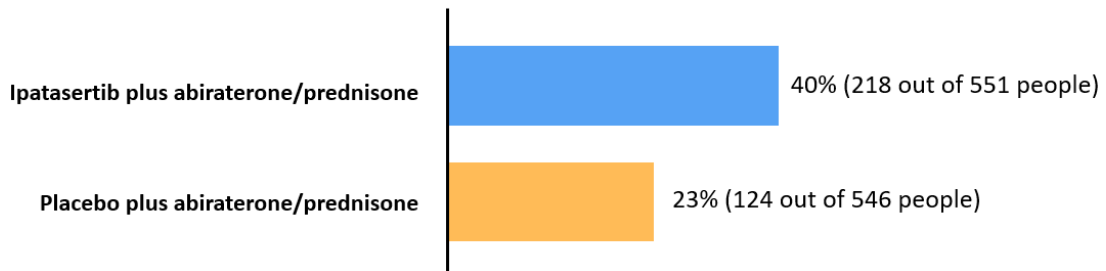
- Some side effects were caused by treatments in the study.
- Not all of the men in this study had all of the side effects.
- Side effects were mild to serious.
- The side effects were different from person to person.
- It is important to be aware that the side effects reported here are from this one study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflets.
- Serious and common side effects are listed in the following sections.

Serious side effects

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

During this study, 31 in every 100 men (31%) had at least one serious side effect. About 40% of the men taking ipatasertib plus abiraterone/prednisone had a serious side effect, compared with about 23% of the men taking placebo plus abiraterone/prednisone.

How many people had at least one serious side effect?



Some men died due to side effects that occurred during the time they were taking the study treatment. These were:

- 24 out of 551 men (4%) in the ipatasertib plus abiraterone/prednisone group.
- 20 out of 546 men (4%) in the placebo plus abiraterone/prednisone group.

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

- In the ipatasertib plus abiraterone/prednisone group, 116 out of 551 men (21%) stopped taking ipatasertib.
- In the placebo plus abiraterone/prednisone group, 28 out of 546 men (5%) stopped taking the placebo.

Most common side effects

In this study 99% of men taking ipatasertib plus abiraterone/prednisone had a side effect of any kind (not serious or serious), compared with 95% of men taking placebo plus abiraterone/prednisone.

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

Most common side effects reported in this study	Men taking ipatasertib plus abiraterone/prednisone (551 men in total)	Men taking placebo plus abiraterone/prednisone (546 men in total)
Diarrhoea	80%	23%
Low energy levels	38%	28%
High level of sugar in the blood	48%	18%
Rash	41%	11%
Liver problems	31%	19%
Feeling sick (nausea)	28%	10%
Low level of red blood cells	21%	12%

Some men left the study without taking any study medicines, so they were not included in the total number in the table.

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. How has this study helped research?

The information presented here is from one study of 1101 men with prostate cancer that has spread to other parts of the body. These results helped researchers learn more about prostate cancer and a new medicine, ipatasertib.

So far the study has shown that:

- In **Group A**, the men's cancer got worse or they died after an average of 19.2 months and in **Group B**, the men's cancer got worse or they died after an average of 16.6 months. The men in Group A had a 16% lower chance of their disease getting worse or dying, but we do not know if this is a real difference – it could have been caused by chance.
- When only looking at men who had tumours that lost the PTEN protein – in **Group A**, the men's cancer got worse or they died after an average of 18.5 months and in **Group B**, the men's cancer got worse or they died after an average of 16.5 months. The men in Group A had a 23% lower chance of their disease getting worse or dying, and this was due to the new medicine, ipatasertib.
- Serious side effects were more common in **Group A** (40%) than in **Group B** (23%).
- In **Group A**, 24 out of 551 men (4%) and in **Group B**, 20 out of 546 men (4%) died due to side effects that occurred while they were taking the study drugs.
- The most common side effects in **Group A** were diarrhoea (80%), high level of sugar in the blood (48%), rash (41%), low energy level (38%), liver problems (31%), feeling sick (28%), and low level of red blood cells (21%).
- The most common side effects in **Group B** were low energy level (28%), diarrhoea (23%), liver problems (19%), high sugar level in the blood (18%), low level of red blood cells (13%) rash (11%) and feeling sick (10%).

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?

More analyses are planned to look at the efficacy and safety of ipatasertib in men taking part in this trial. Additionally, an analysis of data from this study was performed to evaluate different ways to test for PTEN loss and determine how effective ipatasertib plus abiraterone was in tumours that have PTEN loss tested by these different methods or that have lost proteins other than PTEN (such as AKT).

This study started in June 2017 and will end November 2023. This summary includes the data collected up until March 2020. The study is still happening – study doctors are still collecting information on survival and other clinical outcomes.

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/NCT03072238>
- <https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-004429-17>
- <https://forpatients.roche.com/en/trials/cancer/prostate-cancer/ipatasertib-plus-abiraterone-plus-prednisone-prednisolone--relat.html>

If you want to find out more about the results of this study, the full title of the scientific paper we described here is: “Ipatasertib plus abiraterone and prednisone in metastatic castration-resistant prostate cancer”. The authors of the scientific paper are: Christopher Sweeney, Sergio Bracarda, Cora N. Sternberg, Kim N. Chi, David Olmos, Johann de Bono and others. The paper is published in the journal ‘Lancet’, volume number 398, on pages 131-142.

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/prostate-cancer/ipatasertib-plus-abiraterone-plus-prednisone-prednisolone--relat.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 with the doctor in charge of your treatment.

Who organised and paid for this study?

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: “Ipatasertib plus abiraterone plus prednisone/prednisolone, relative to placebo plus abiraterone plus prednisone/prednisolone in adult male patients with metastatic castration-resistant prostate cancer”.

The study is known as ‘IPATential150’.

- The protocol number for this study is: CO39303.
- The ClinicalTrials.gov identifier for this study is: NCT03072238.
- The EudraCT number for this study is: 2016-004429-17.