Summary of Clinical Trial Results

A study of ipatasertib plus rucaparib in men with prostate cancer that has spread to other parts of the body after male-hormone lowering medication 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) and was 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 (November 2022).

The study started in June 2019 and ended in January 2022. This summary was written after the study ended.

You should not make decisions based on this one summary – always speak to 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 have helped researchers to answer important questions about prostate cancer and about treatment with ipatasertib and rucaparib.

Key information about this study

- In this study, men with prostate cancer that has spread to other parts of the body were given a combination of 2 medicines being studied (called ipatasertib and rucaparib).
- This study included 37 men in 5 countries.
- The main finding was that the combination of ipatasertib plus rucaparib lowered the level of prostate specific antigen, or 'PSA' (a protein that is higher in men with prostate cancer), in the blood of about a quarter of the men (9 out of 35, or 26%) by half (50%) or more.
- Around a quarter of the men (9 out of 37 men, or 24%) taking ipatasertib plus rucaparib had serious side effects.
- Less than half (46%) of the men had severe side effects, but about two-thirds (70%) of the men had side effects that required a change in treatment.
- This study has ended and this summary includes data up to the end of the study.

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 (testosterone) 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.

Often, cancer develops when changes in cells cause them to grow or function abnormally. Some anti-cancer drugs work by reversing or blocking these changes. Rucaparib is a drug that helps prevent tumours from growing by blocking a natural way that cells can repair their genetic material, causing the tumour cells to die. Rucaparib works best against tumours that already have changes that make this natural cell repair system not work as well. Ipatasertib is a drug that targets a protein that is abnormally active in several cancers. When this protein becomes too active, it can cause the cells to grow out of control. Ipatasertib can block the protein and slow or stop tumour growth. Both drugs have been shown to prevent or slow cancer cells from growing.

In this study, researchers wanted to see if combining the 2 drugs together would work better than the drugs by themselves. Previous reports have suggested that drugs like ipatasertib can make drugs like rucaparib work well against more types of tumours, not just ones that have cell repair problems. They also wanted to study different doses of the drugs and see whether the combination of drugs would be safe for people to take.

What are the study medicines?

This study looked at a new medicine called 'ipatasertib' taken together with another study medication called 'rucaparib' (known by its brand name Rubraca®).

One medicine that was 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, which makes the tumour grow.

The other medicine that was studied is 'rucaparib'.

- You say this as 'roo – ka – par – ib'.
- Rucaparib blocks a protein called PARP that help cells to repair their genetic material. Blocking PARP triggers cancer cell death and has been shown to work in treating prostate cancer tumours.

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 rucaparib) would help to reduce the blood levels of prostate-specific antigen, or 'PSA', which is a protein that is often higher in men with prostate cancer. When PSA levels decrease, that is seen as a sign that the treatment is working and the cancer is shrinking.
- Researchers also wanted to see if there was a change in how big the tumour was or if the cancer had gotten worse.
    - See section 4 "What were the results of the study?".
- They also wanted to find out how safe the combination of medicines is. They do this by seeing what the side effects were, counting how many men had side effects and seeing how severe these side effects were when taking both medicines together during this study.
    - See section 5 "What were the side effects?".

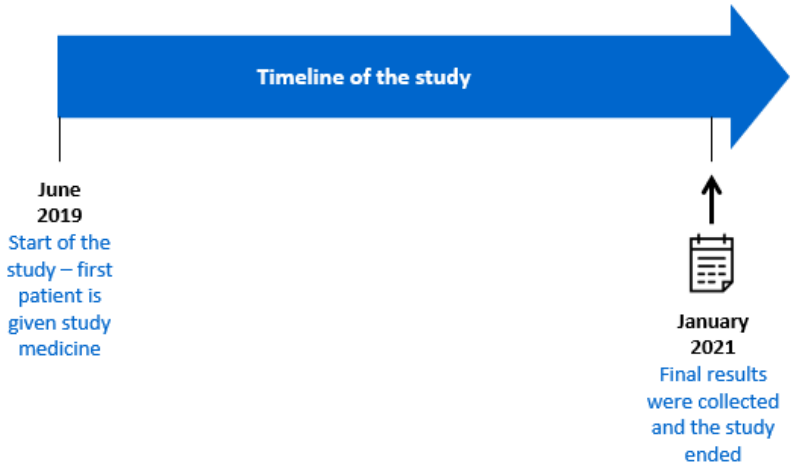
What kind of study was this?

This study was a '**Phase 1**' study, which means that this was one of the first studies of ipatasertib and rucaparib together. A small number of men with prostate cancer that had spread to other parts of the body took ipatasertib plus rucaparib. The researchers did medical tests on the people to find out more about ipatasertib plus rucaparib.

This was an '**open-label**' study. This means that both the people taking part in the study and the study doctors or nurses knew which of the study medicines they were taking.

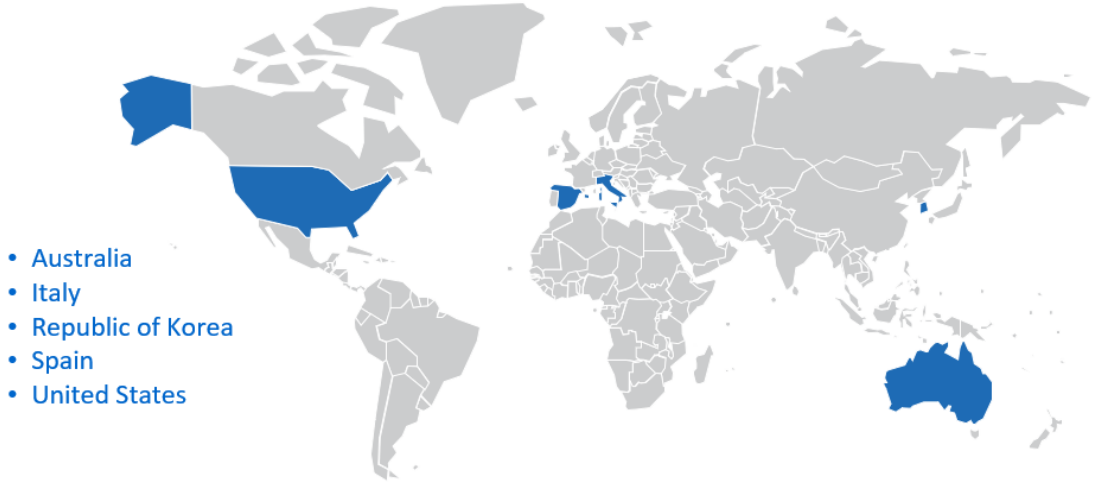
When and where did the study take place?

The study started in June 2019 and ended in January 2021. This summary includes the data collected up until the end of the study. This summary was written after the study ended.



The timeline (📋) shows when the information shown in this summary was collected, which was at the end of the study (January 2021).

The study took place at 14 study centres in 5 countries/regions around the world. The following map shows the countries where this study took place.



2. Who took part in this study?

Overall, 51 people took part in the study, including 47 men with prostate cancer that had spread to other parts of the body. The remaining people in the study had either ovarian or breast cancer; these people were included in the study since PARP inhibitors on their own have also shown activity against these kinds of tumours. However, the focus of this study was on the men with prostate cancer. Some people received different amounts of the medicines, to see which doses were the safest but still strong enough to fight the cancer. A dosing combination was identified, and 37 men with prostate cancer received the selected dose of ipatasertib plus rucaparib (**Group A**). These 37 men were between 52 and 88 years old.

Men with prostate cancer that had spread to other parts of the body could take part in the study if:

- They had previously been treated with one or more male hormone–reducing drug.
- They were at least 18 years old.

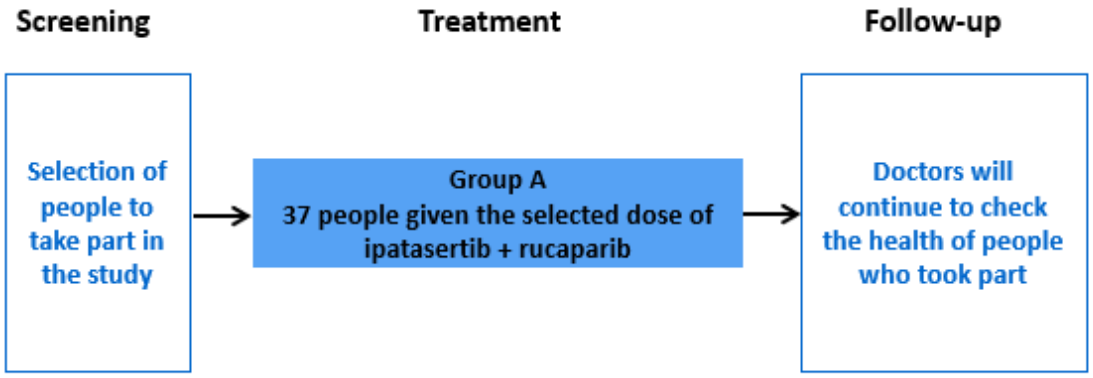
Men with high blood sugar levels and men who had been previously treated with other anti-cancer drugs that act the same way as ipatasertib or rucaparib could not take part.

3. What happened during the study?

During the study, 37 men received the selected dose of ipatasertib plus rucaparib (**Group A**).

All drugs were taken orally (by mouth). Ipatasertib was taken once every day, and rucaparib was taken twice a day.

People in the study took the treatments until the disease came back or got worse, until side effects got too bad to continue treatment, or until they left the study or the study was stopped. When the study treatment finished, the people who took part were asked to go back to their study centre for more visits to check their overall health.



4. What were the results of the study?

Question 1: In men who received the selected dose of ipatasertib plus rucaparib, how many men had the PSA levels in their blood reduced by half or more?

Researchers looked at how many men had the PSA level in their blood reduced by half or more from their level at the beginning of the study. PSA is a protein that is often elevated in men with prostate cancer. When this protein is reduced, that is seen as a sign that the treatment is working.

	Group A **Ipatasertib + rucaparib**
Number of enrolled men who received the selected dose of ipatasertib plus rucaparib	37
Number of men who could be analysed for PSA levels	35
Men who had PSA level in their blood reduced by half or more	26% (9 out of 35)

In **Group A**, about a quarter of the men (9 out of 35, or 26%) had PSA levels in their blood reduced by half or more from their level at the beginning of the study.

Question 2: In men who received the selected dose of ipatasertib plus rucaparib, was there a change in the size of the tumour or had their cancer gotten better?

Researchers looked at how many men had an improvement in their disease. This was measured by how big the tumour was or if the cancer had gotten worse. This could only be done in men who had tumours that could be measured at the beginning of the study. In this case, there were 21 men.

	Group A **Ipatasertib + rucaparib**
Number of enrolled men who received the selected dose of ipatasertib plus rucaparib	37
Number of men who had tumours that could be measured at the beginning of the study	21
Men who had tumours that went away or got smaller	10% (2 out of 21)

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

5. What were the side effects?

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

- Some side effects were caused by treatments in this study.
- Not all of the men in this study had all of the side effects.
- The side effects were mild to serious.
- The side effects were different for each person.
- It is important to be aware that the side effects reported here are from this study. Therefore, the side effects shown here may be different from those seen in other studies and 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.

In this study, 9 of the 37 men (24%) with prostate cancer who received the selected dose of ipatasertib plus rucaparib had a serious side effect.

Severe side effects

Doctors describe the severity of each side effect. A side effect can be severe without being serious, such as a rash that is very bad but does not cause hospitalization or lasting problems. In this study, 17 of the 37 men (46%) who had prostate cancer that had spread to other parts of the body and who received the selected dose of ipatasertib plus rucaparib had a side effect that doctors described as severe.

Side effects leading to modification of treatment

Some side effects require the doctor to change the treatment (such as stop, pause, or reduce the amount of drug given). In this study, 26 of the 37 men (70%) who had prostate cancer that had spread to other parts of the body and who received the selected dose of ipatasertib plus rucaparib had a side effect that required their doctor to change the treatment, including ipatasertib alone, rucaparib alone or both agents.

Most common side effects

- In this study, all men in Group A, or 37 out of 37 (100%), had a side effect.

This table shows the most common side effects. These are the side effects that occurred in more than 5 men in **Group A**. 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 hospitalization or have lasting effects). Some men had more than one side effect. This means that they are included in more than 1 row in the table.

Side effects reported in at least 15% of men in this study	**Group A** Ipatasertib + rucaparib (37 people total)
Diarrhoea	95% (35 out of 37)
Feeling sick (nausea)	68% (25 out of 37)
Weight loss	54% (20 out of 37)
Feeling tired	54% (20 out of 37)
Decreased appetite	46% (17 out of 37)
Vomiting	41% (15 out of 37)
Liver damage (shown by higher levels of a protein called 'ALT' in the blood)	30% (11 out of 37)
Low level of blood cells	27% (10 out of 37)
Lack of energy	24% (9 out of 37)
Pain in the stomach area	22% (8 out of 37)
Liver damage (shown by higher levels of a protein called 'AST' in the blood)	22% (8 out of 37)
High sugar level in the blood	16% (6 out of 37)
Constipation	16% (6 out of 37)

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

6. How has this study helped research?

The information presented here is from a single study of 51 people, with a focus on 37 men with prostate cancer that spread to other parts of the body who received the selected dose of ipatasertib plus rucaparib. These results helped researchers to learn

more about prostate cancer and the combination of ipatasertib plus rucaparib. The doctors concluded that the side effects associated with the selected dose of ipatasertib plus rucaparib were manageable, sometimes requiring a change in the treatment, but that the treatment combination did not show signs of being better at controlling cancer than each medicine alone.

7. Are there plans for other studies?

This study has ended. At this time, there are no other studies planned for this combination of medicines.

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/NCT03840200
- https://forpatients.roche.com/en/trials/cancer/oc/a-study-evaluating-the-safety--pharmacokinetics-and-eff-46472.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: "A phase Ib, open-label study evaluating the safety and efficacy of ipatasertib plus rucaparib in patients with metastatic castration-resistant prostate cancer". The authors of the scientific paper are: David Pook, Daniel M. Geynisman, Joan Carles, Fillippo de Braud, Anthony M. Joshua, Howard Gurney and others. The paper is published in the journal *Clinical Cancer Research*, published online 20 June 2023. https://doi.org/10.1158/1078-0432.CCR-22-2585.

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/oc/a-study-evaluating-the-safety--pharmacokinetics-and-eff-46472.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 organized and paid for this study?

This study was organized 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: “A Study Evaluating the Safety, Pharmacokinetics and Efficacy of Ipatasertib Administered With Rucaparib in Participants With Advanced Breast, Ovarian Cancer, and Prostate Cancer”.

- The protocol number for this study is: BO40933.
- The ClinicalTrials.gov identifier for this study is: NCT03840200.
- The EudraCT number for this study is: 2018-003293-2.