Summary of Clinical Trial Results

A study to look at how safe ipatasertib given in combination with standard treatment (palbociclib and fulvestrant) was for people with breast cancer – and how ipatasertib was processed through 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 part 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 of writing.

The study started in November 2019 and stopped early – in August 2023 – because Roche made the decision to prioritise the development of other medicines.

No single study can tell us everything about the risks and benefits of a medicine. 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 to your doctor before making any decisions about your treatment**

Contents of the summary

- HER2 = human epidermal growth factor receptor 2
- Hormones = chemical messengers that are produced by various glands in the body. They circulate in the bloodstream and help regulate and coordinate different bodily functions

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about hormone-receptor positive HER2-negative breast cancer and the medicines studied – 'ipatasertib' given in combination with standard treatment (palbociclib and fulvestrant).

Key information about this study

Why was this study done?

- This study was done to look at how safe ipatasertib is in combination with standard treatment for people with breast cancer – and how ipatasertib was processed through the body

Which medicines were being studied and who took part?

- In this study, people were given the medicine being studied (called 'ipatasertib') in combination with standard treatment – palbociclib and fulvestrant
- This portion of the study included 20 people in 7 countries

What were the results?

- The main findings were:
  - The combination of medicines was safe enough for people to take, and there were no new safety concerns
  - More ipatasertib was available to the body when it was given with palbociclib compared with when it was given on its own
- Out of 20 people, 1 person (5%) had serious unwanted effects
- This study stopped early because Roche made the decision to prioritise the development of other medicines

1. General information about this study

Why was this study done?

Hormone receptor-positive and HER2-negative breast cancer is a type of cancer that starts in the breast. It is made up of cells that have hormone receptors but not HER2. These cells grow quickly because of the hormones. Some of these hormones are oestrogen and progesterone.

Standard treatment for hormone receptor-positive HER2-negative breast cancer includes medicines called 'targeted' treatments. These are usually given with hormone therapy.

But better medicines are needed for people with this type of breast cancer when cancer cells spread to nearby tissue, to other parts of the body, and/or cannot be taken out or completely removed with surgery.

What were the study medicines?

This study looked at a combination of 3 medicines:

- **Ipatasertib** – the medicine that was studied
- **Palbociclib and fulvestrant** – existing medicines used as standard treatment

A medicine called '**ipatasertib**' was the focus of this study.

- You say this as 'eye-pat-uh-sir-tib'
- Ipatasertib works by blocking a protein called 'AKT' in cancer cells
- This may mean that ipatasertib could benefit people with hormone-receptor positive HER2-negative breast cancer that has spread or cannot be removed with surgery

'Palbociclib' and 'fulvestrant' are existing medicines given to people with hormone receptor-positive and HER2-negative breast cancer as standard treatment.

- You say palbociclib as 'pal-boh-SYE-klib'
    - Palbociclib is a targeted cancer treatment
    - It works by blocking 2 proteins in cancer cells called CDK4 and CDK6. This blocks the cancer cells from growing
- You say fulvestrant as 'full-VEST-tront'
    - Fulvestrant is a hormone therapy
    - It works by blocking the hormone receptor for oestrogen on cancer cells. This blocks the cancer cells from growing

What did researchers want to find out?

Researchers did the first part of this study to see how safe ipatasertib, palbociclib and fulvestrant were when taken together – by checking how many people had unwanted effects and seeing how serious they were (see Section 4 'What were the results of the study?', and Section 5 'What were the unwanted effects?').

The main questions that researchers wanted to answer were:

1. How many people had unwanted effects from the study medicines, and how serious were they?
2. Did palbociclib affect levels of ipatasertib in the blood?

What kind of study was this?

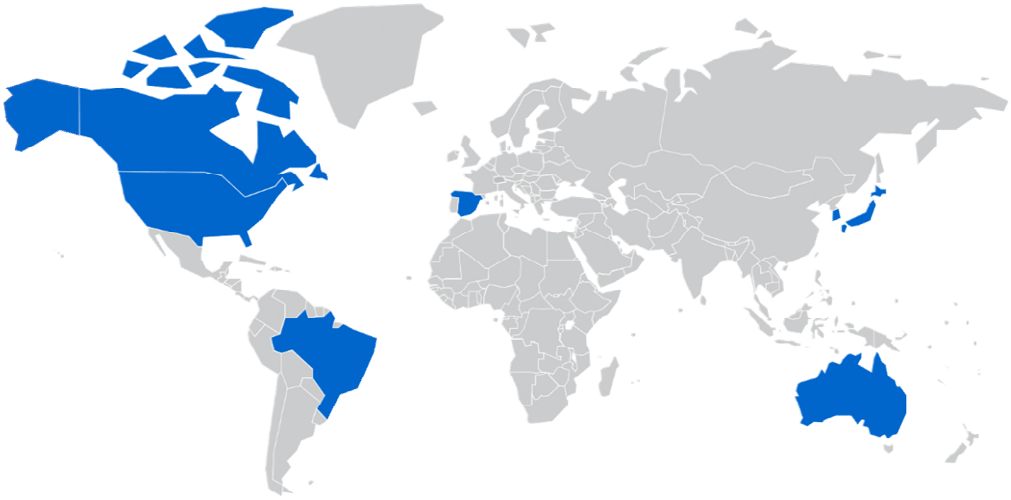
This study was in 2 parts. The first part of the study was the 'Phase 1' portion where ipatasertib was combined for the first time with both palbociclib and fulvestrant. A small number of people with hormone receptor-positive HER2-negative breast cancer took the study medicine (ipatasertib combined with palbociclib and fulvestrant), and the researchers did medical tests on the people who took part to find out more about the study medicine in combination with standard treatment. The Phase 1 part was 'open-label'. An open-label study means everyone involved, including the participant and the study doctor, know which study medicine the participant is given.

The second part was to look at how well the study medicines worked in a larger group of people. The second part of the study did not take place because the study was stopped early.

When and where did the study take place?

The study started in November 2019 and stopped early. This summary presents the results of the study up until it was stopped in August 2023.

The study took place at 12 study centres – across 7 countries in Asia, Australia, Europe and North and South America. The following map shows the countries where this study took place.



- Australia
- Brazil
- Canada
- Japan
- Republic of Korea
- Spain
- United States of America

2. Who took part in this study?

In this study, 20 people with hormone receptor-positive HER2-negative breast cancer took part.

People who took part in the study were between 37 and 74 years of age and all were female.

People could take part in the study if they:

- Were male or female and at least 18 years old
- Had hormone receptor-positive HER2-negative breast cancer that had spread to nearby tissue, to other parts of the body, and/or could not be taken out or completely removed with surgery
- Had cancer that got worse after hormone therapy

People could not take part in the study if:

- Their breast cancer had spread to bones but nowhere else in their body

3. What happened during the study?

The study medicine was given in 'treatment cycles' lasting 28 days. A treatment cycle is the period of treatment and recovery time before the next set of treatment is given.

The first group of 10 people were given:

- Ipatasertib for 5 to 7 days before Cycle 1, as a tablet to be swallowed daily
    - This was done to see the effects of ipatasertib on its own in the body compared to when given in combination starting in Cycle 1

Then, in Cycle 1 onwards, these people and the second group of 10 people were given:

- Ipatasertib and palbociclib daily on Days 1 to 21, as tablets to be swallowed, AND
- Fulvestrant on Day 1 (and Day 15 in Cycle 1 only) as an injection into a muscle

The study stopped early because Roche made the decision to prioritise the development of other medicines. After people finished taking their medicine for this study, they were asked to go back to their study centre for 1 more visit – to check their overall health.

4. What were the results of the study?

Question 1: How many people had unwanted effects from the study medicines, and how serious were they?

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

- They are described in this summary because the study doctor believes the unwanted effects were related to the treatments in the study
- Not all of the people in this study had all of the unwanted effects
- Unwanted effects may be mild to very serious and can be different from person to person
- It is important to be aware that the unwanted effects reported here are from this single study. Therefore, the unwanted effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflets

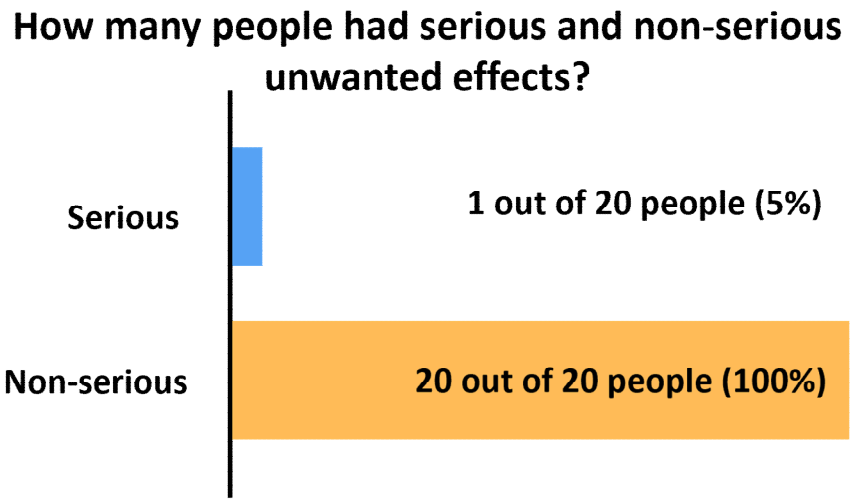
Serious unwanted effects

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

- No-one in the study had a serious unwanted effect that was thought to be related to ipatasertib or fulvestrant
- Out of the 20 people who took part in this study, 1 person (5%) had a serious unwanted effect that was thought to be related to taking palbociclib

Non-serious unwanted effects

- Everyone (20 out of 20 people; 100%) had at least 1 non-serious unwanted effect due to ipatasertib
- Everyone had at least 1 non-serious unwanted effect due to palbociclib
- Most people (16 out of 20 people; 80%) had at least 1 non-serious unwanted effect due to fulvestrant.



More information about the types of unwanted effects that people had can be found in Section 5 ('What were the unwanted effects?').

Question 2: Did palbociclib affect levels of ipatasertib in the blood?

Another piece of information that researchers collected was the level of ipatasertib in the blood when it was given on its own compared with when it was given with palbociclib. This was because palbociclib may interfere with how ipatasertib works in the body.

Ipatasertib and its smaller parts were seen for a slightly longer time in the blood and reached slightly higher levels when it was given with palbociclib compared with when it was given on its own.

The lowest levels of palbociclib seen in the blood were the same with and without 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 'Where can I find more information?').

5. What were the unwanted effects?

Serious unwanted effects

During this study, 1 out of 20 people (5%) had at least 1 serious unwanted effect. This person had a low level of a type of white blood cell that helps the body fight infections.

No-one taking part in the study died.

During the study, 1 person decided to stop taking ipatasertib and palbociclib because of unwanted effects (low levels of different types of white blood cells).

Most common unwanted effects

During this study, everyone (100%) had an unwanted effect that was not considered serious.

The most common unwanted effects are shown in the following table – these were seen in at least 5 people (25%), or in at least 2 people (10%) for effects related to fulvestrant. Some people had more than 1 unwanted effect – this means that they are included in more than 1 row in the table.

Most common unwanted effects reported in this study	Related to ipatasertib	Related to palbociclib	Related to fulvestrant
Frequent, watery stools	75% (15 out of 20 people)	30% (6 out of 20 people)	5% (1 out of 20 people)
Wanting to throw up	70% (14 out of 20)	40% (8 out of 20)	5% (1 out of 20)
Throwing up	45% (9 out of 20)	20% (4 out of 20)	0%
Rash	35% (7 out of 20)	10% (2 out of 20)	0%
Low number of red blood cells	30% (6 out of 20)	40% (8 out of 20)	10% (2 out of 20)
Lower than usual levels of neutrophils – a type of white blood cell that helps the body fight infections	25% (5 out of 20)	40% (8 out of 20)	5% (1 out of 20)
Condition in which the body does not have enough neutrophils	30% (6 out of 20)	45% (9 out of 20)	0% (0 out of 20)
Low levels of the blood cell fragments that help the blood to clot	30% (6 out of 20)	30% (6 out of 20)	5% (1 out of 20)
Feeling tired or weak	25% (5 out of 20)	20% (4 out of 20)	0%
Inflamed or sore mouth	0%	25% (5 out of 20)	0%
Not having energy or strength	20% (4 out of 20)	25% (5 out of 20)	15% (3 out of 20)
Hot flush	0%	0%	10% (2 out of 20)

Other unwanted effects

You can find information about other unwanted effects (not shown in the sections above) on the websites listed at the end of this summary – see Section 8 'Where can I find more information?'.

6. How has this study helped research?

The information presented here is from a single study of 20 people with hormone-receptor positive HER2-negative breast cancer. These results helped researchers learn more about ipatasertib in combination with palbociclib and fulvestrant in this type of breast cancer.

7. Are there plans for other studies?

Studies with ipatasertib are still happening but currently no new studies are planned.

8. Where can I find more information?

You can find more information about this study on the websites listed below:

- https://forpatients.roche.com/en/trials/cancer/bc/a-study-of-ipatasertib-plus-palbociclib-and-fulvestrant-28505.html

If you would like to find out more about the results of this study, the full title of the relevant conference presentation is: 'Ipatasertib (ipat) in combination with palbociclib (palbo) and fulvestrant (fulv) in patients (pts) with hormone receptor-positive (HR+) HER2-negative advanced breast cancer (aBC)'. The authors are: Mafalda Oliveira, Aditya Bardia, Sung-Bae Kim, Naoki Niikura, Cristina Hernando, and others. The abstract of the conference publication was published in the journal 'Cancer Research', volume number 82, issue 4 supplement.

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

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/trials/cancer/bc/a-study-of-ipatasertib-plus-palbociclib-and-fulvestrant-28505.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.

Full title of the study and other identifying information

The full title of this study is: 'A phase Ib/III study of ipatasertib plus palbociclib and fulvestrant versus placebo plus palbociclib and fulvestrant in hormone receptor positive and human epidermal growth factor receptor 2 negative (HER–) locally advanced unresectable or metastatic breast cancer'.

The study is known as 'IPATunity150'.

- The protocol number for this study is: CO41012
- The ClinicalTrials.gov identifier for this study is: NCT04060862
- The EudraCT number for this study is: 2019-001072-11