

Summary of Clinical Trial Results

A study to compare inavolisib with placebo, each combined with palbociclib and fulvestrant, in people with a type of breast cancer called *PIK3CA*-mutated, hormone receptor (HR)-positive breast cancer, whose disease recurred or spread during or within 12 months of stopping hormonal therapy following surgery

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 (October 2024).

The study started in January 2020, and this summary includes the results that were collected and analysed in September 2023. At the time of writing this summary, the study is still ongoing – this summary presents the complete results for the main part of the study. This summary will be updated when the study ends.

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.**

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about a specific type of breast cancer called *PIK3CA*-mutated, HR-positive breast cancer that has spread, and the medicines studied – 'inavolisib', 'palbociclib' and 'fulvestrant'.

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Key information about this study

- This study was done to see how well a new medicine – ‘inavolisib’ – when combined with palbociclib and fulvestrant, could lengthen the amount of time it took for people’s cancer to get worse (in other words, spread or grow larger) or help people live longer compared with a placebo combined with palbociclib and fulvestrant.
- In this study, people were given either the medicine being studied (inavolisib) or a placebo, each in combination with palbociclib and fulvestrant. It was decided by chance which treatment each person was given.
- This study included 325 people in 28 countries.
- On average, for people who were given inavolisib plus palbociclib and fulvestrant, their cancer got worse or they died after 15.0 months; while for people who were given placebo plus palbociclib and fulvestrant, their cancer got worse or they died after 7.3 months. This means that, on average, people receiving inavolisib plus palbociclib and fulvestrant lived more than twice as long, without their cancer getting worse, than people receiving only palbociclib and fulvestrant in this study.
- Around 9% of people (14 out of 162 people) taking inavolisib plus palbociclib and fulvestrant had serious side effects related to a study treatment, compared with around 4% of people (6 out of 162 people) taking placebo plus palbociclib and fulvestrant.
- At the time of writing this summary, the study is still ongoing.

1. General information about this study

Why was this study done?

This study includes people with a type of breast cancer called '*PIK3CA*-mutated' and 'HR-positive' breast cancer. These people have received treatment with hormonal therapy after surgery, but the treatment stopped working during treatment or within a year of stopping, and their cancer spread to other parts of the body.

When the cancer spreads to other parts of the body and can no longer be cured, it is called 'advanced' cancer. People with advanced breast cancer are given medicines to help them live as long as possible with the disease.

People with 'HR-positive' breast cancer have a high number of HRs on the surface of their cancer cells. These HRs bind hormones circulating in the blood – this tells the cell to perform a specific function; for example, to make copies of itself. Cancer cells with more HRs make copies of themselves more often than normal, making the tumour grow.

Breast cancers are also classified by their 'HER2' protein status. If your breast cancer is 'HER2-negative', the cancer cells do not have a high number of HER2 protein receptors. People in this study have 'HER2-negative' breast cancer and would not have benefited from standard treatments for 'HER2-positive' breast cancer.

People included in this study also have '*PIK3CA*-mutated' breast cancer, meaning that their tumours have at least one specific alteration (a '*PIK3CA* mutation'). Anticancer treatments may not work as well for people whose tumours have these alterations compared with people whose tumours do not have these alterations.

People with *PIK3CA*-mutated, HR-positive advanced breast cancer need better therapies to help them live as long as possible and maintain their quality of life with minimal side effects.

In this study, researchers wanted to find out how inavolisib compares with a placebo, when combined with standard therapy (palbociclib and fulvestrant) in people with *PIK3CA*-mutated, HR-positive advanced breast cancer. The study measured the length of time between the start of the study and people's cancer getting worse or people dying.

What were the study medicines?

'Inavolisib' is one of the medicines that is being studied here.

- You say this as 'in – avo – lisib'.
- Inavolisib is a type of medicine taken by mouth that blocks a protein called phosphatidylinositol 3-kinase (also known as PI3K) that helps cancer cells grow and make copies of themselves. Inavolisib also causes mutated forms of this protein to be destroyed.
- This may mean that inavolisib stops tumours from growing.

'Palbociclib' is another one of the medicines that is being studied here.

- You say this as 'pal – boe – sye – klib'.
- It is a type of medicine taken by mouth that blocks proteins called cyclin-dependent kinases 4 and 6 that help cancer cells grow and make copies of themselves.
- This may mean that palbociclib stops tumours from growing.

'Fulvestrant' is another one of the medicines that is being studied here.

- You say this as 'full – veh – strant'.
- It is a type of hormonal therapy that is given as an injection into a muscle.
- Fulvestrant blocks access to the HR on the surface of cells and also breaks it down, stopping the cells from growing and making copies of themselves.
- This may mean that fulvestrant stops tumours from growing.

In this study, inavolisib plus palbociclib and fulvestrant is compared to a 'placebo' with palbociclib and fulvestrant.

- You say this as 'plah – see – bo'
- The placebo looks the same as inavolisib but does not contain any real medicine. This means it has no medicine-related effect on the body.
- Researchers are comparing palbociclib and fulvestrant plus inavolisib or a placebo so they can show which benefits or side effects are actually caused by the medicine.

What did researchers want to find out?

- Researchers did this study to compare inavolisib plus palbociclib and fulvestrant with placebo plus palbociclib and fulvestrant – to see how well inavolisib plus palbociclib and fulvestrant worked (see section 4 "What were the results of the study?").
- They also wanted to find out how safe the medicine was – by checking how many people had side effects and seeing how serious they were, when taking the medicines during this study (see section 5 "What were the side effects?").

The main question that researchers wanted to answer was:

1. Did giving inavolisib plus palbociclib and fulvestrant to people lengthen the amount of time it took for their cancer to get worse or for them to die compared with giving people placebo plus palbociclib and fulvestrant?

Other questions that researchers wanted to answer included:

2. How many people taking inavolisib plus palbociclib and fulvestrant had side effects caused by the treatments compared with placebo plus palbociclib and fulvestrant – and how serious were they?

What kind of study was this?

This study is a 'Phase III' study. This means that inavolisib plus palbociclib and fulvestrant had already been tested in a smaller number of people with *PIK3CA*-mutated, HR-positive breast cancer before this Phase III study started. In this Phase III study, a larger number of people with *PIK3CA*-mutated, HR-positive disease either took inavolisib plus palbociclib and fulvestrant or placebo plus palbociclib and fulvestrant – this was to find out about the side effects of the inavolisib combination, and if the inavolisib combination lengthened the amount of time it took for people's cancer to get worse or until they died. It can then be decided whether the treatment can be approved for doctors to give to people.

The study was 'randomised'. This means that it was decided by chance which of the medicines people in the study would have – 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 a similar mix. Apart from the exact medicines being tested in each group, all other aspects of care were the same between the groups.

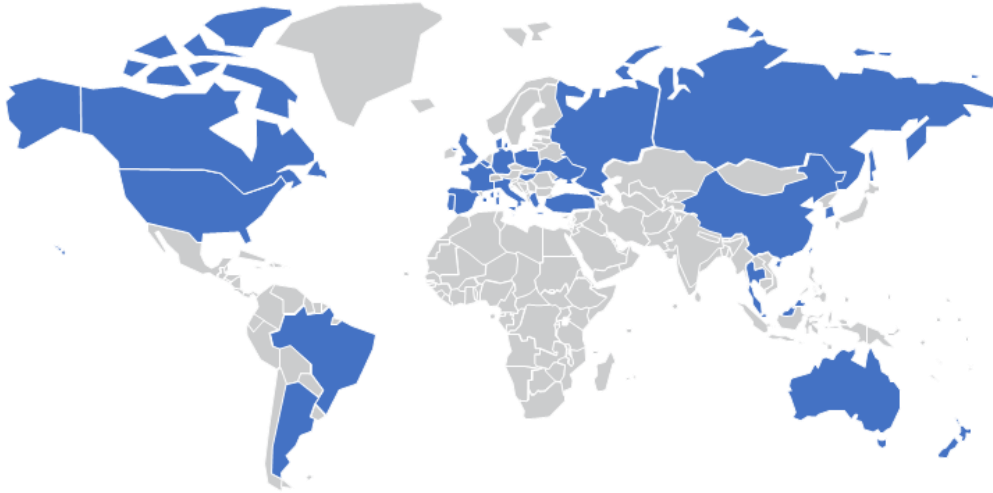
When and where did the study take place?

The study started in January 2020, and this summary includes the complete results until September 2023. At the time of writing this summary, further information is still being collected.



This study is still happening, so the symbol (📅) on the timeline shows when the information shown in this summary was collected – after 3 years and 8 months (September 2023).

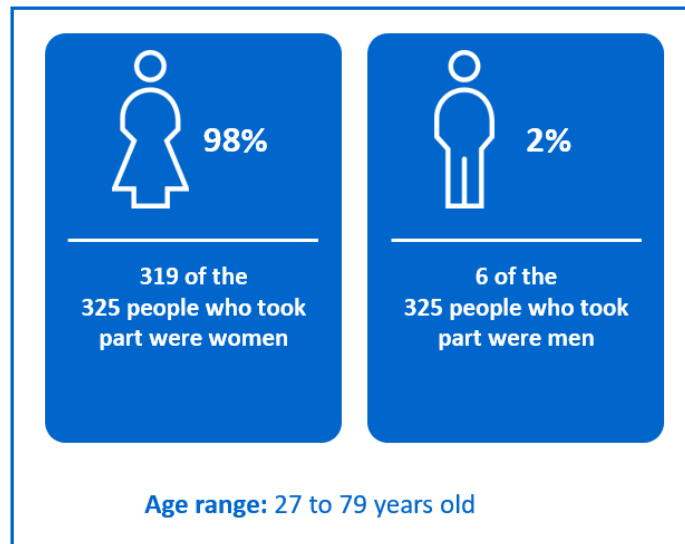
The study took place at 183 study centres – across 28 countries in Asia, North America, South America, Europe, Australia and New Zealand. The following map shows the countries where this study took place.



- Argentina
- Australia
- Belgium
- Brazil
- Canada
- China
- Denmark
- France
- Georgia
- Germany
- Greece
- Hong Kong
- Hungary
- Italy
- Republic of Korea
- Malaysia
- New Zealand
- Poland
- Portugal
- Russia
- Singapore
- Spain
- Taiwan
- Thailand
- Turkey
- Ukraine
- United Kingdom
- United States

2. Who took part in this study?

In this study, 325 people with *PIK3CA*-mutated, HR-positive advanced breast cancer took part. More information on the people who took part is given below.



People could take part in the study if they had:

- breast cancer that had spread to other parts of the body ('advanced' breast cancer)
- HR-positive breast cancer with at least one *PIK3CA* mutation
- some tumours that could be accurately measured in size
- received treatment with hormonal therapy after surgery, but their disease came back during treatment or within 12 months of stopping.

People could not take part in the study if they had:

- received previous treatment for their advanced breast cancer.

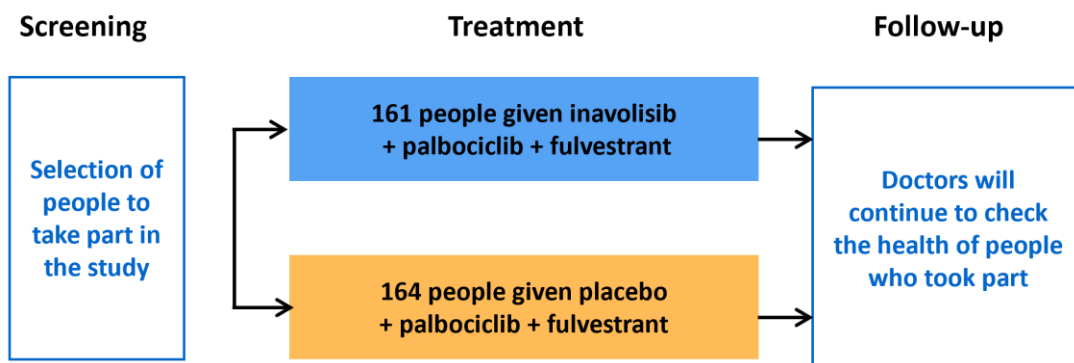
3. What happened during the study?

During the study, people were selected by chance to get one of two treatments. The treatments were selected at random – by a computer. Treatments were continued until people's cancer got worse, or until they experienced unacceptable side effects.

The treatment groups were:

- Inavolisib plus palbociclib and fulvestrant: inavolisib and palbociclib were taken by mouth. Inavolisib was taken every day. Palbociclib was taken every day for the first 21 days out of every 28 days. Fulvestrant was given as an injection into the thigh muscle, generally once a month.
- Placebo plus palbociclib and fulvestrant: the placebo and palbociclib were taken by mouth. The placebo was taken every day. Palbociclib was taken every day for the first 21 days out of every 28 days. Fulvestrant was given as an injection into the thigh muscle, generally once a month.

This study is still happening so some people are still being treated with the study medicines. When people finish their study treatments, they will be asked to go back for more follow-up visits to check their overall health. Look below to see more information about what has happened in the study so far, and what the next steps are.

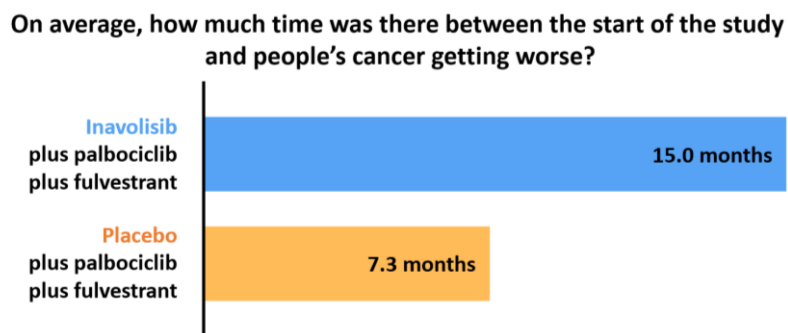


4. What were the results of the study?

Question 1: Did giving inavolisib plus palbociclib and fulvestrant to people lengthen the amount of time it took for their cancer to get worse or for them to die compared with giving people placebo plus palbociclib and fulvestrant?

Researchers looked at whether inavolisib plus palbociclib and fulvestrant increased the length of time it took for people’s cancer to get worse or until they died compared with placebo plus palbociclib and fulvestrant.

On average, for people who were given inavolisib plus palbociclib and fulvestrant, their cancer got worse or they died after 15.0 months; for people who were given placebo plus palbociclib and fulvestrant, their cancer got worse or they died after 7.3 months. Some people’s cancer got worse or they died earlier than this, and some people’s cancer got worse or they died later than this.



This section 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 the study.

- They are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Not all of the people in this study had all of the side effects.
- It is important to be aware that the unwanted effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflets.
- Side effects can vary from mild to very serious, and may vary from person to person.
- Serious and common unwanted 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, 6 out of 100 people (6%) had at least one serious side effect caused by a study medicine. Around 9% of people taking inavolisib plus palbociclib and fulvestrant had a serious side effect caused by a study medicine, compared with around 4% of people taking placebo plus palbociclib and fulvestrant.

Serious side effects related to study treatments that were experienced by more than one patient in either treatment group are shown in the following table. Some people may have had more than one side effect – this means that they may have been included in more than one row in the table.

Serious side effects reported in more than one patient in either treatment group in this study	People taking inavolisib + palbociclib + fulvestrant (162 people total)	People taking placebo + palbociclib + fulvestrant (162 people total)
Low levels of red blood cells (<i>anaemia</i>)	2% (3 out of 162)	0% (0 out of 162)
Low level of neutrophils, a type of white blood cell, with fever (<i>febrile neutropenia</i>)	2% (3 out of 162)	0% (0 out of 162)

No people in the study died due to side effects related to one of the study medicines.

During the study, some people decided to stop taking their medicine because of side effects:

- In the inavolisib plus palbociclib and fulvestrant group, 11 out of 162 people (7%) stopped taking their medicine.
- In the placebo plus palbociclib and fulvestrant group, 1 out of 162 people (1%) stopped taking their medicine.

Most common side effects

During this study, 96 out of 100 people (96%) had at least one side effect caused by a study medicine. Around 98% of people taking inavolisib plus palbociclib and fulvestrant had a side effect, compared with around 94% of people taking placebo plus palbociclib and fulvestrant.

The 10 most common side effects related to study treatments in the inavolisib treatment group are shown in the following table. Some people may have had more than one side effect – this means that they may have been included in more than one row in the table.

Most common side effects reported in this study	People taking inavolisib + palbociclib + fulvestrant (162 people total)	People taking placebo + palbociclib + fulvestrant (162 people total)
Severely low levels of neutrophils, a type of white blood cell (<i>neutropenia</i>)	54% (88 out of 162)	55% (89 out of 162)
High level of sugar in the blood (<i>hyperglycaemia</i>)	51% (82 out of 162)	6% (10 out of 162)
Low (not severely) levels of neutrophils, a type of white blood cell	37% (60 out of 162)	39% (63 out of 162)
Frequent, watery stools (<i>diarrhoea</i>)	36% (59 out of 162)	10% (16 out of 162)
Low levels of red blood cells (<i>anaemia</i>)	33% (53 out of 162)	33% (53 out of 162)
Sore or inflammation inside of the mouth (<i>stomatitis</i>)	31% (50 out of 162)	15% (25 out of 162)
Low (not severely) levels of cell fragments (platelets) that help blood to clot	25% (40 out of 162)	21% (34 out of 162)
Feeling sick (<i>nausea</i>)	22% (36 out of 162)	10% (16 out of 162)
Severely low levels of cell fragments (platelets) that help blood to clot, (<i>thrombocytopenia</i>)	22% (35 out of 162)	25% (40 out of 162)
Low levels of white blood cells	22% (35 out of 162)	21% (34 out of 162)

Other side effects

You can find information about other less common 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 a single study of 325 people with advanced *PIK3CA*-mutated, HR-positive breast cancer. These results helped researchers learn more about this type of cancer and inavolisib.

Adding a new medicine – inavolisib – to the existing treatment combination of palbociclib and fulvestrant helped increase the length of time it took for people’s cancer to get worse or until they died compared with placebo plus palbociclib and fulvestrant. For people who were given inavolisib plus palbociclib and fulvestrant, their cancer got worse or they died after 15.0 months, on average. For people who were given a placebo plus palbociclib and fulvestrant, their cancer got worse, or they died after 7.3 months, on average.

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.**

7. Are there plans for other studies?

Other studies are ongoing to investigate inavolisib in other combinations or at different times in the treatment journey.

8. Where can I find more information?

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

- <https://clinicaltrials.gov/study/NCT04191499>.
- <https://www.clinicaltrialsregister.eu/ctr-search/search?query=2019-002455-42>.
- <https://forpatients.roche.com/en/trials/cancer/bc/a-study-evaluating-the-efficacy-and-safety-of-gdc-0077--75564.html>.

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: ‘Inavolisib-Based Therapy in *PIK3CA*-Mutated Advanced Breast Cancer’. The authors of the scientific paper are: Nicholas C. Turner, Seock-Ah Im, Cristina Saura, Dejan Juric, Sibylle Loibl, and others. The paper is published in the journal ‘*The New England Journal of Medicine*’, volume number 391, on pages 1584–1596.

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-evaluating-the-efficacy-and-safety-of-gdc-0077--75564.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 Study Evaluating the Efficacy and Safety of Inavolisib + Palbociclib + Fulvestrant vs Placebo + Palbociclib + Fulvestrant in Patients With *PIK3CA*-Mutant, Hormone Receptor-Positive, HER2-Negative, Locally Advanced or Metastatic Breast Cancer (INAVO120)”.

The study is known as ‘INAVO120’.

- The protocol number for this study is: WO41554.
- The ClinicalTrials.gov identifier for this study is: NCT04191499.
- The EudraCT number for this study is: 2019-002455-42.