Summary of Clinical Trial Results

A study to find out what happens to a new medicine (inavolisib) inside the human 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).

This summary is written for:

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

This summary is based on information known at the time of writing.

The study started in March 2021 and finished in May 2021. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. It takes many people in several 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.**

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Thank you to the people who took part in this study

The people who took part have helped researchers answer important questions about the medicine studied – "inavolisib".

Key information about this study

- This study was done to find out what happens to the study medicine, inavolisib, inside the human body.
- This study included eight people at one study center in USA.
- The main finding was that less medicine was available in the body when it was given as a capsule – in comparison to being given through an IV.
- The medicine and its breakdown products were passed from the body in urine and feces.
- There were no serious side effects experienced by anyone in this study.

1. General information about this study

Why was this study done?

Most patients with breast cancer (about 60-70%) have a type that is known as, "hormone receptor positive", which is commonly referred to as, "**HR+**".

HR+ breast cancer uses a protein in the body, called "**endocrine**", to turn on a way (**pathway**) for cancer cells to grow and spread without control.

Patients with HR+ breast cancer are treated with "**endocrine therapies**". These medicines interfere with endocrine and disrupt its pathway for uncontrolled cell growth.

Unfortunately, not all HR+ breast cancers respond to endocrine therapies. Sometimes, the cancer can use other cell growth pathways not affected by endocrine therapy.

About 40% of patients who have HR+ breast cancer have a change (**mutation**) in a gene called, "***PIK3CA***". This gene makes a protein (**p110α**) that is part of a larger protein, called "**PI3K**".

The PI3K protein is part of another cell growth pathway - the **PI3K/AKT/mTOR pathway**. When p110α is mutated, the P13K protein turns the PI3K/AKT/mTOR pathway "on" for uncontrolled cell growth – that allows the cancer to grow and spread.

Inavolisib is a medicine that stops the activity of PI3K. Inavolisib is especially effective on PI3K that has p110α, which is defective (mutated). There are several studies going on to test inavolisib in breast cancer.

This study was done to find out some basic information about inavolisib. Researchers wanted to find out how much inavolisib is available in the body after it is given to people. They also wanted to know how it is removed from the body.

What was the medicine being studied?

Inavolisib is a study medicine taken by mouth, or injected into the vein (given intravenously) – through an **IV**.

- Inavolisib is also known as "**GDC-0077**".
- Inavolisib breaks down the p110α protein and interferes with the incorrect (**aberrant**) activation of the PI3K/AKT/mTOR pathway.
- Inavolisib causes the death of cancer cells that have a mutation in the *PIK3CA* gene.
- Inavolisib is a type of medicine known as a "**PI3K inhibitor**".

One form of the study medicine was in the form of **[^{14}C]-inavolisib**.

- The [^{14}C] is a **radiolabel**.
- Radiolabeling is a technique used for tracking (tracing) a medicine.
- Even if the study medicine breaks down or undergoes a chemical change in the body, the radiolabel will still be present in the breakdown products.
- [^{14}C] shows up in tests that detect the radiolabel – "liquid scintillation test".
- [^{14}C]-inavolisib was prepared as a **capsule** of 9 milligrams (mg) inavolisib with a known amount of the radiolabel.

Another form of the study medicine was in the form of **[$^{13}C_6$]-inavolisib**.

- [$^{13}C_6$] is another type of label that can be traced – it shows up in tests – "LC/MS/MS test for [$^{13}C_6$]".
- [$^{13}C_6$]-inavolisib was prepared as a 100 microgram (mcg) **solution** to be given by IV.

What did researchers want to find out?

Researchers did this study to find out details about the study medicine.

The main questions that researchers wanted to answer were:

1. How much of the medicine went in and out of the body (**mass balance**), and which way (**route**) did the medicine leave the body?
2. How much of the medicine was available in the blood (**bioavailability**) when taken as a 9 mg capsule by mouth?

What kind of study was this?

Here are the terms used to describe this study:

- **Phase 1 study**
  This was one of the early studies to find out basic information about inavolisib. A small number of healthy people were given treatments. Information from this study will be useful in other studies with more people.
- **Open-label study**
  This study was open label which means all the people in this study knew which medicine they were getting.

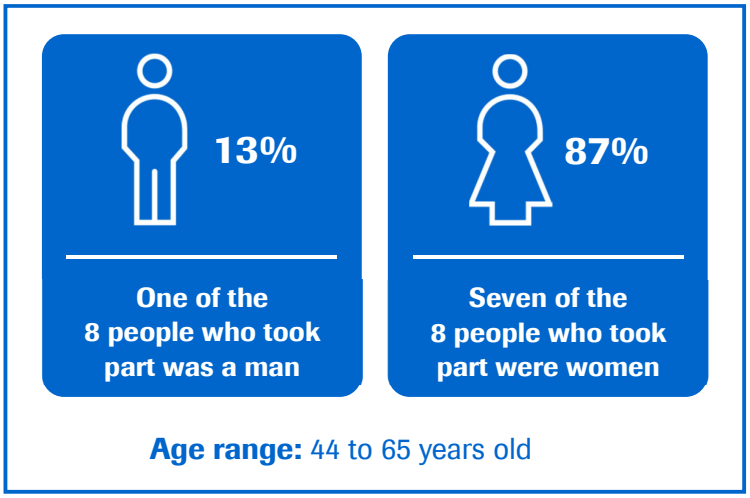
When and where did the study take place?

The study started in March 2021 and finished in May 2021. This summary was written after the study had ended.

The study took place at one study center in USA.

2. Who took part in this study?

There were 8 healthy people who took part in this study.



People could take part in the study if:

- They were men who were sterile and could not have children.
- They were women who were not pregnant or nursing and who could not get pregnant.
- They were between 18 and 65 years old.
- They had a certain weight to height ratio (body mass index 18.5 to 32.0 kg/m^2).
- Study doctors found them to be in good health through examinations including regular blood tests, other tests for HIV, TB, hepatitis B and C.
- They had a history of using the toilet daily – having at least one bowel movement per day.

People could not take part in the study if:

- They had a history of having had certain diseases or allergies in the past.
- They used tobacco or nicotine-containing products within the last 6 months.
- They had a history of drug or alcohol addiction.
- They tested positive for drug or alcohol.
- They had used medicine that was not acceptable in this study.
- They had participated in more than 3 other radiolabeled medicine studies within one year.

3. What happened during the study?

What happened before treatment was given:

- People were examined (screened) up to 28 days before treatment.
- They were admitted to the study center one day before treatment.
- They were not allowed to used tobacco or nicotine-containing products prior-to and during the study.
- They were not allowed to consume alcohol, grapefruit, or caffeine-containing food and drinks for 3 days before and during the study.
- They were not allowed to do any extreme physical activity 2 days before and during the study.

How was the medicine given:

- People had regular meals. They fasted overnight for about 8 hours and then got their medicine.
- A single radioactive capsule was given by mouth with water. They didn't eat for another 4 hours but they could drink water during this time.
- At about 3 hours after taking the capsule, a single IV dose of inavolisib solution was pushed into the vein over a 2-minute time period.

What happened after getting the medicine:

- People stayed at the study center for 10 to 15 days after getting their treatment.
- The study staff asked questions and took samples for different tests.
- Blood samples were collected at time points before and after treatment.
- Urine samples and fecal samples were collected at several time points.
- If there was any vomiting in the first 6 hours after dosing, the material (vomitus) was collected for tests.

4. What were the results of the study?

Question 1: How much of the medicine went in and out of the body (mass balance), and which way (route) did the medicine leave the body?

Researchers did several different tests on blood, plasma, urine, and feces samples collected from people in the study. (Plasma is the liquid part of blood without red blood cells).

Mass balance

After taking the [14C]-inavolisib capsule by mouth, most of the radioactivity was removed from the body through passing urine and feces. About 96.5% of the radioactivity was removed in 336 hours.

Removal routes

Passing urine and feces were the main routes for removal of the radioactive material – which was distributed about equally in urine and feces. The radioactivity that was measured included the radiolabel in inavolisib and in its breakdown products.

Question 2: How much of the medicine was available in the blood (bioavailability) when taken as a 9 mg capsule?

Inavolisib given by IV

When the [13C6]-inavolisib was given through an IV, it went straight into the plasma. The highest (peak) inavolisib concentration was measured in plasma at about 5 minutes. It took about 13.7 hours for [13C6]-inavolisib to drop to half of its peak concentration in plasma.

Inavolisib taken as a capsule

After taking a 9 mg inavolisib capsule by mouth, it took 4 ½ hours for inavolisib in the capsule to be absorbed to reach its peak concentration in plasma. It took 17 ½ hours for inavolisib to drop to half of its peak concentration in the plasma.

Bioavailability of inavolisib

When inavolisib was taken as a 9 mg capsule, about 76% of the inavolisib in the capsule made its way into the plasma to work as a medicine in the body. When inavolisib was given through an IV, all of the inavolisib went into the plasma (100%).

The bioavailability of the 9 mg inavolisib capsule was 76%.

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 happened 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.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side 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 leaflet.
- 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.

There were no serious side effects reported by anyone in this study. Nobody withdrew from the study because of any side effects.

Most common side effects

Two of the eight people in the study (25%) had a side effect that was not considered serious, but was thought to be caused by the study medicine. The side effects were:

- One person had diarrhea.
- One person felt tired and sleepy (somnolence).

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 a single study of 8 healthy people. These results helped researchers learn more about the study medicine, inavolisib.

Researchers learned how inavolisib was cleared from the body and how much of the medicine was absorbed into the plasma when taken as a 9 mg capsule.

No single study can tell us everything about the risks and benefits of a medicine. It takes many people in several 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.**
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7. Are there plans for other studies?

Several studies with inavolisib are ongoing.

8. Where can I find more information?

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

> https://forpatients.roche.com/en/trials/cancer/bc/a-study-to-find-out-what-happens-to-a-new-medicine--inavolisib--.html

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/About.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 organized and paid for this study?

This study was organized and paid for by Genentech, Inc., South San Francisco, CA, USA. Genentech is part of F. Hoffmann-La Roche Ltd., with headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is:

> "A phase 1, open-label, single-center study to investigate the absorption, metabolism, excretion, and absolute bioavailability of a single oral dose of [^{14}C]-labeled inavolisib and IV tracer dose of [$^{13}C_6$]-labeled inavolisib in a single cohort of healthy volunteers".

The protocol number for this study is **GP42652**.

The clinical trial number for this at ISRCTN registry is 60043317.