

Summary of Clinical Trial Results

A study to find out if taking different forms of a medicine (GDC-6036) results in the same amount of medicine in your body – and the effect of food on the medicine

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 July 2021 and finished in October 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 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.**

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Thank you to the people who took part in this study

The people who took part in this study have helped researchers answer important questions about the study medicine – GDC-6036.

Key information about this study

- This study was done to find out how much GDC-6036 was available in the body when taken – in tablet and capsule form – on an empty stomach. Researchers also wanted to know the effect of food – what happened when the tablet form was taken after eating.
- People took three treatments at three different times. They took the tablet with no food, capsule with no food, and tablet with food.
- This study included 17 people in one country.
- The main finding was that similar levels of GDC-6036 were absorbed into the body – when taken as either tablet or capsule form – on an empty stomach.
- There was slightly less GDC-6036 absorbed into the body in tablet form after a meal – in comparison to the tablet form taken on an empty stomach. Absorptions was also slower with food.
- There were no serious side effects – thought to be caused by the study medicine.
- One person had non-serious side effects – thought to be caused by the study medicine.

1. General information about this study

Why was this study done?

The **KRAS** gene makes the KRAS protein, found in cells. The KRAS protein is a type of switch that can be in the “on” or “off” state.

In the “on” state, KRAS turns on a pathway in the cell that allows cells to:

- Make more cells (**proliferation**)
- Grow into different cell types (**differentiation**)
- Turn off cell death signals (**inhibit apoptosis**)

Sometimes, a change (**mutation**) can happen in a particular gene in the cell. When there is a mutation in a protein gene, there is a change in the protein that is made using the mutated gene. Often times, the mutated protein works differently – in comparison to a normal protein.

The **KRAS** gene is known to sometimes have mutations that keep the KRAS protein in the “on” state all the time. This causes uncontrolled cell growth – leading to cancer.

Researchers have found a medicine called “GDC-6036” that stops (inhibits) the **KRAS** gene that has a certain mutation – **KRAS G12C**. Following gene inhibition, the gene can no longer make a defective KRAS protein.

As a **KRAS G12C inhibitor**, GDC-6036 may be effective for cancer. There are several studies testing GDC-6036 on cancers found in different tissues and organs – cancers that are positive for the **KRAS G12C** mutation.

This study was done to gather information about GDC-6036 that would be helpful in other studies. Researchers wanted to know if GDC-6036 delivered the same amount of medicine in the body – in tablet versus capsule form – taken with or without food.

What was the medicine being studied?

The study medicine was called “**GDC-6036**”.

- It is also known as “**KRAS G12C inhibitor**”.
- GDC-6036 has already been given to people. Researchers have found doses that are safe enough for people – doctors can manage side effects at those doses.
- GDC-6036 is being developed for a type of lung cancer (NSCLC), colorectal cancer, and other solid types of cancers that have the *KRAS G12C* mutation.
- In this study, people took 100 milligram (**mg**) GDC-6036 – in tablet or capsule form.

What did researchers want to find out?

The main questions that researchers wanted to answer were:

1. When GDC-6036 was taken on an empty stomach, how much was available in the body when taken in tablet form – in comparison to capsule form?
2. When GDC-6036 was taken in tablet form after a meal, how much medicine was available in the body – in comparison to taking it on an empty stomach?

What kind of study was this?

There are several ways to describe this study.

Phase 1 study

This was a “Phase 1” study, an early study looking at GDC-6036. Only a small number of people took part in this study to find answers that would be useful for continuing to study GDC-6036 in other studies.

Open-label study

Researchers and people in the study knew which medicine the people were getting. That made it an “open-label” study.

Randomized study

A computer randomly decided who joined which treatment group. Researchers and people in the study had no control over this.

Three-period crossover study

There were 3 groups and they took 3 treatments (A, B, C) in different orders. That made it a “three-period crossover study”.

- Group 1 took A→B→C.
- Group 2 took B→C→A.
- Group 3 took C→A→B.

When and where did the study take place?

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

The study took place at one study center in one country – USA.

2. Who took part in this study?

Seventeen healthy men took part in this study. The youngest person in this study was 26 years. The oldest person was 60 years.

People could take part in the study if they met all of the following conditions:

- Men and women between 18 and 60 years old.
- Men who agreed to use birth control methods so that their female partners could not become pregnant while the men were on the study.
- Women who were not pregnant and could not become pregnant while on the study.
- They had a certain weight-to-height ratio (BMI: 18 to 32 kg/m²).
- They were found to be in good health after undergoing blood tests, urine tests, and doctor visits.
- They underwent a drug test with negative results.
- They were able to finish a high-fat breakfast of eggs, bacon, toast with butter, hash brown potatoes, and a glass of milk.
- They understood and signed an informed consent form.

People could not take part in the study if they met any of the following conditions:

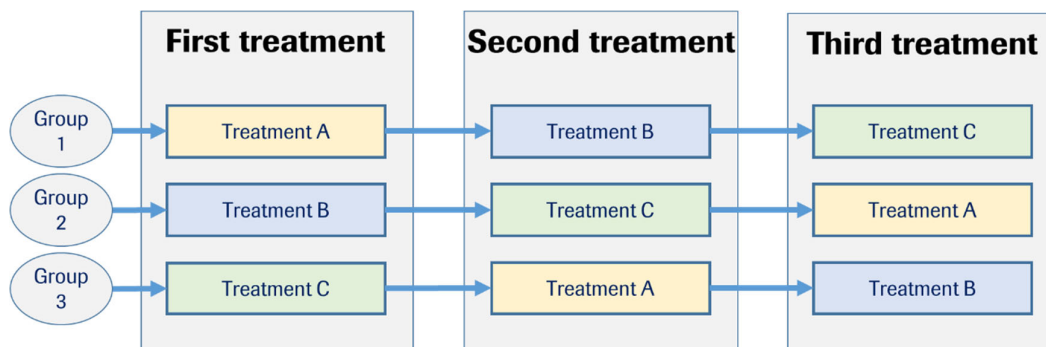
- They had a history of health conditions not allowed in this study.
- They had drug or alcohol addiction within the last year.
- They recently participated in another study.
- They received Covid-19 vaccine 28 days before the first dosing day in this study.
- They recently took over-the-counter or prescription medicines that were not allowed in this study.
- They recently used – or planned to use during the study – any tobacco or nicotine-containing products.
- They recently had – or planned to have during the study – certain foods and drinks that were not allowed for a specified time.
- They participated in strenuous exercise two days before starting the study – or planned to do so during the study.
- They recently donated blood or plasma outside of the study.
- They recently received blood or blood products.

3. What happened during the study?

During the study, people were selected by chance – to join one of three study groups. A computer selected the group for each person – at random.

People were screened to see if they met the conditions for being in the study. They checked into the study center on “Day -1”, one day before the first treatment. They checked out on Day 4 of the third treatment period. They stayed at the study center for a maximum of 18 days.

Each group received study treatments in a certain order:



These were the study treatments:

	Treatment A	Treatment B	Treatment C
GDC-6036 dose	100 mg	100 mg	100 mg
GDC-6036 form	Capsule	Tablet	Tablet
Overnight fast	Yes	Yes	No
Dosing details	Taken with a glass of water – on an empty stomach. Food was not allowed for another 4 hours after dosing.	Taken with a glass of water – on an empty stomach. Food was not allowed for another 4 hours after dosing.	Taken with a glass of water – on a full stomach. Breakfast was eaten and the medicine was taken within 30 minutes of starting breakfast.

At least 5 days passed between the first and second treatments, and between the second and third treatments. This “washout period” was planned so that one treatment would not interfere with the next.

Before, during, and after treatments, people underwent exams at the study center, lab tests on blood and urine samples, answered questions, and reported any side effects.

After the people went home, researchers asked them follow-up questions for 28-30 days after the last dose they took – so researchers could learn more about the study medicine.

4. What were the results of the study?

Seventeen people started the study. Not everyone finished all three treatments.

- Fourteen people provided data for Treatment A.
- Fifteen people provided data for Treatment B.
- Fourteen people provided data for Treatment C.

Question 1: When GDC-6036 was taken on an empty stomach, how much was available in the body when taken in tablet form – in comparison to capsule form?

When the **tablet** and **capsule** forms of GDC-6036 were taken on an **empty** stomach:

- Both resulted in similar maximum (peak) concentrations of GDC-6036 in the body.
- The time it took to reach the peak concentration was similar for both - between 0.5 to 4 hours for both medicine forms.
- After reaching the peak concentration, the time it took to fall to half of the peak concentration was similar for both:
 - Capsule: Around 14 hours
 - Tablet: Around 14 hours

Question 2: When GDC-6036 was taken in tablet form after a meal, how much medicine was available in the body – in comparison to taking it on an empty stomach?

When comparing GDC-6036 **tablet** taken on a **full** stomach versus on an **empty** stomach:

- The peak concentration of GDC-6036 was slightly lower when taken with food.
- The time it took to reach the peak concentration was slower when taken with food.
- After reaching the peak concentration, the time it took to fall to half of the peak concentration was similar for both:
 - On a full stomach: Around 14 hours
 - On an empty stomach: Around 14 hours

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 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.

Nobody experienced a serious side effect caused by GDC-6036 in this study.

There were no deaths in this study.

One person (6%) was taken off the study because he had a toothache. The study doctor did not think the toothache was caused by GDC-6036.

Most common side effects

During this study, one person (6%) got a side effect that was not serious, but was thought to be caused by the study medicine. He had diarrhea and was feeling sick to his stomach (nausea).

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 17 healthy people. These results helped researchers compare GDC-6036 in tablet and capsule forms. They also learned what effect food had on how the medicine was absorbed in the body.

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7. Are there plans for other studies?

Studies with GDC-6036 are still happening, and further studies are planned.

8. Where can I find more information?

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

<https://www.isrctn.com/ISRCTN10450075>

<https://forpatients.roche.com/en/trials/cancer/lung-cancer/a-study-to-measure-how-much-of-the-study-drug-gdc-6036-is-absorb.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-dose, randomized, three-period crossover study to evaluate the relative bioavailability and food effects of GDC-6036 in healthy subjects

- The protocol number for this study is GP43039.
- The ISRCTN clinical trial registry number for this study is 10450075.