Clinical Trial Results – Layperson Summary

A study to look at how safe different doses of GDC-0334 were for healthy people and how this medicine 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 clinical trial called a "study" in this document. This summary is written for:

- members of the public
- **participants** – these are the healthy people who took part in the study

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

The study started in November 2017 and finished in May 2019. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. Many people volunteer in several studies to help us 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

1. General information about this study
2. Who took part in this study?
3. What happened during the study?
4. What were the results of the study?
5. What were the side effects?
6. How has this study helped research?
7. Are there plans for other studies?
8. Where can I find more information?

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about the study medicine and the effects of food.

Key information about this study

- This study was done to find out which dose of the study medicine was safe for people and what effect food had on the medicine.
- In this study, participants were given a new medicine (GDC-0334) or no medicine (placebo).
- This study included 86 people in the United Kingdom.
- This study found that GDC-0334 was safe at the doses tested in this study.
- Taking the medicine on an empty stomach versus after eating had different effects on how much medicine was absorbed in the body.
- No one in this study had any serious side effects.
- No one in this study had side effects that led to stopping the treatment.
- This report was written after the study was completed.

1. General information about this study

Why was this study done?

Asthma is a disease of the airways leading to the lungs. Patients with asthma may have coughing, wheezing, and difficulty breathing.

Approximately 300 million people in the world have asthma. Many people (about 250,000) die each year because of asthma.

Several different types of medicine are used to control asthma. However, many patients continue to have asthma that cannot be controlled by any available medicine.

GDC-0334 is a new medicine being studied for the treatment of patients with severe asthma. Researchers think that GDC-0334 could reduce airway blocking that happens in asthma patients.

GDC-0334 has not been given to humans before this study.

This study investigated the effects of GDC-0334 when taken by healthy people. Some people took their medicine without food while others took their medicine after eating.

Patients with severe asthma are very sick. It is therefore safer to test GDC-0334 in healthy people starting at a low dose. The results from this study could be used to decide whether the medicine is safe to give to asthma patients.

What was the study medicine?

GDC-0334 is a new medicine.

- GDC-0334 is an oral medicine (taken by mouth) that may reverse the symptoms of asthma in patients.

GDC-0334 was compared to a "**placebo**".

- Some patients got GDC-0334 while others got a placebo.
- The placebo looked the same as GDC-0334 but did not contain any real medicine.

What did researchers want to find out?

Researchers did this study to compare the study medicine against the placebo.

The main questions that researchers wanted to answer were:

1. What dose of GDC-0334 was safe?
2. What happened to GDC-0334 in the body?
3. Was there any difference if GDC-0334 was taken with food or on an empty stomach?
4. What were the side effects of GDC-0334?

What kind of study was this?

There are several ways to describe this study.

- **Phase 1 study**
  This was a "Phase 1" study, which means that this was the first study for GDC-0334 in humans. A small number of healthy people got GDC-0334 starting at a low dose.
- **Placebo-controlled study**
  Some people got GDC-0334 while others got a placebo. This was done so that the real effect of the medicine could be compared against the placebo.
- **Randomized study**
  People were randomly assigned by a computer to receive the study medicine or the placebo in every dose group.
- **Double-blind study**
  Groups of people got different doses of the study medicine. In each group, some people got GDC-0334 while others got the placebo. In this double-blind study, the researchers and the participants did not know who was getting the placebo and who was getting the study medicine.

When and where did the study take place?

The study started in November 2017 and finished in May 2019. The study took place in the United Kingdom. This summary was written after the study had ended.

2. Who took part in this study?

There were 86 people (healthy volunteers) who took part in this study, which consisted of 3 parts.

Part 1 (Total = 46 people)	**Part 2** (Total = 16 people)	**Part 3** (Total = 24 people)
People who got medicine Age range: 19-54 years 7 men, 28 women 91% white	**People who got medicine** Age range: 27-56 years 5 men, 7 women 100% white	**People who got medicine** Age range: 19-55 years 16 men, 4 women 90% white
People who got placebo 4 men, 7 women Age range: 21-54 years 91% white	**People who got placebo** 1 man, 3 women Age range: 23-48 75% white	**People who got placebo** 2 men, 2 women Age range: 29-48 50% white

Requirements for healthy volunteers to participate in this study

1. They had to provide written consents to volunteer in this study.
2. Be between 18 and 55 years old and have a body mass index of 18 to 32 kg/m^2.
3. Be able and willing to communicate and participate in the study.
4. Agree to use family planning methods to prevent pregnancies while participating in this study.

Conditions that disqualified healthy volunteers from this study

1. History of drug or tobacco use or excessive alcohol use.
2. People without suitable veins for blood draw.
3. Abnormal lab test results.
4. Positive for hepatitis B, C, or for HIV.
5. History of seizure, poor organ function, or psychiatric disorder.
6. People with gall stones or those who had their gall bladder removed.
7. People who failed the study screening test for allergies.
8. People who took herbal medicine in the two weeks before this study.
9. People with arms that would interfere with data collection, such as thick forearm hair, tattoos, and surgical scars.

3. What happened during the study?

The participants joined a group and received a "**treatment"** that was either the study medicine or placebo. The treatment was selected for each person at random by a computer.

Treatment groups

- There were 3 parts to this study, and different dose groups in each of the 3 parts.
- All groups received their treatments once a day except for one group in Part 1 whose treatment got divided into 3 doses over a day.
- In Part 2, the same people participated in each of the 3 groups, on different days.

Food and water taken with the treatment

Water was not allowed for 1 hour before and 1 hour after taking the medicine. One glass of water was allowed while taking the medicine.

- **No food**: No food was allowed for 8 hours before and 4 hours after treatment.
- **High fat food**: Participants in these groups ate a high fat breakfast. The treatment was given 30 minutes after starting breakfast.
- **Low fat food**: Participants in these groups ate a low fat breakfast. The treatment was given 30 minutes after starting breakfast.

Groups in this study	Received GDC-0334	Received Placebo
PART 1		
No food	**24 people** (25 mg, 75 mg, 200 mg, and 600 mg; 6 participants per each dose group)	**7 people**
High fat food	**5 people** (600 mg)	**2 people**
Low fat food	**6 people** (1200 mg; treatment was divided into 3 doses taken over 1 day)	**2 people**
PART 2		
No food	**12 people** (300 mg)	**4 people**
High fat food	The above 12 people (300 mg)	The above 4 people
Low fat food	The above 12 people (300 mg)	The above 4 people
The same people took part in the 3 groups in Part 2. The first treatment was given without food, the second treatment was given with high fat food, and the last treatment was given with low fat food. Between each of the single dose treatments, there was at least a 21-day delay before the next treatment.		
PART 3		
No food	**10 people** (100 mg)	**2 people**
Low fat food	**10 people**	**2 people**

	(125 mg)	

How was the treatment administered? The treatment (GDC-0334 or placebo) was in tablet form that was swallowed with a glass of water.

Single ascending dose (SAD): Part 1 and Part 2 were SAD studies where participants received one treatment only. They were observed for 32-38 days after treatment. Participants were treated in order from low to high dose groups.

Multiple ascending doses (MAD): Part 3 was a MAD study where participants were treated for multiple days (28 days). They were observed for 32 to 38 days after the last day of treatment. Participants were treated in order from low to high dose groups.

What happened after treatment started? Tests and physical examinations were carried out by researchers at times including before, during, and after the completion of the study. All side effects were reported.

4. What were the results of the study?

One participant in Part 2 and one in Part 3 dropped out of the study. The others completed the study.

Question 1: What was a safe dose of GDC-0334?

Researchers compared side effects of patients who got the study medicine with those who got the placebo.

A single dose of GDC-0334 was as safe as taking the placebo when taken without food or with high fat food (up to 600 mg GDC-0334). It was also safe when taken with low fat food (up to 1200 mg GDC-0334).

Multiple doses (28 days) of GDC-0334 taken without food (100 mg once daily) or with low fat food (125 mg once daily) were as safe as taking the placebo.

Question 2: What happened to GDC-0334 in the body?

The concentration of GDC-0334 increased in blood after treatment, and then decreased over time. Researchers found the blood concentration to increase with increasing dose level of the study medicine.

Question 3: Was there any difference if GDC-0334 was taken with food or on an empty stomach?

When a single dose of GDC-0334 was taken with food (high fat or low fat), there was a larger concentration on medicine in the body in comparison to taking the medicine on an empty stomach.

When multiple daily doses of GDC-0334 were taken without food, it took 15 days of treatment before the concentration of medicine in the body became stable. With food, it took 22 days.

5. What were the side effects?

Side effects are unwanted medical problems (such as a headache) that happen during the study and are related to the treatment given during the study.

- Not every patient in a study has all or any of the side effects seen in the study.
- Common side effects and serious side effects are listed in the following sections.

Most common side effects

Side effects are listed in a Table on the next page.

In Part 1, one participant in the “no food” group reported headache as the side effect of the study medicine.

In Part 2, three participants in the “high fat food” reported side effects.
Two participants had side effects from the study medicine. One person had a headache and the other person was not feeling well (malaise).
One participant in the placebo group had a stomach ache that was considered to a side effect of getting the placebo treatment.

In Part 3, three participants reported getting side effects from the study medicine in the “low fat food” group. The side effects were vomiting, stomach ache, and dizziness.

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 in this study.

Most common side effects reported by participants:

Study Group and Medical Problems	Received GDC-0334	Received Placebo
PART 1		
No food		
Reported at least one side effect	4%	0%
What were the side effects?	Headache	None
High fat food		
Reported at least one medical problem that was a side effect	0%	0%
What were the side effects?	None	None
Low fat food		
Reported at least one side effect	0%	0%
What were the side effects?	None	None
PART 2		
No food		
Reported at least one side effect	0%	0%
What were the side effects?	None	None
High fat food		
Reported at least one side effect	17%	25%
What were the side effects?	Feeling unwell (malaise) Headache	Stomach ache
Low fat food		
Reported at least one side effect	0%	0%
What were the side effects?	None	None
PART 3		
No food		
Reported at least one side effect	0%	0%
What were the side effects?	None	None
Low fat food		
Reported at least one side effect	30%	0%
What were the side effects?	Vomiting Stomach ache Dizziness	None

6. How has this study helped research?

This study was the first time that the study medicine, GDC-0334, was given to any human. This study helped researchers learn that the study medicine was as safe as the placebo for humans at the doses tested.

Researchers also learned that it took about 15 days of treatment taken without food before the concentration of GDC-0334 became stable in the body. With food, it took 22 days.

It took about 130 to 228 hours for GDC-0334 to drop to half of its initial concentration in the body after stopping the medicine. This will help with decisions surrounding how often patients need to take the medicine in the future.

7. Are there plans for other studies?

While this study was ongoing, other studies were happening as well. Based on the results of other studies, researchers decided not to continue developing GDC-0334 for asthma patients.

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/NCT03381144

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
  or 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.

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: “Phase I, randomized, double-blind, placebo-controlled, 3-part, study designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamic effects of single and multiple ascending doses of GDC-0334 and the effect of food on the pharmacokinetics of GDC-0334 in healthy adult subjects”.

- The protocol number for this study is GB40223.
- The clinical trial number for this study is NCT03381144.