

Summary of Clinical Trial Results

A study to find out how safe is it to give people a new medicine for asthma (GDC-4379), and to see how this medicine is processed in 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
- People who took part in the study

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

The study started in June 2019 and finished in April 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 have helped researchers to answer important questions about asthma and the study medicine, called “GDC-4379”.

Key information about this study

- This study was done to find out how safe is it to give people a single dose and multiple doses of a new medicine called, “GDC-4379”.
- In this study, people were given either GDC-4379 or a pill with no medicine (called a “placebo”). It was decided by chance which treatment each person was given.
- This study included 128 people in a single country.
- The main finding was that GDC-4379 was safe enough to give to people at all doses that were tested in this study.
- No one in this study experienced any serious side effects, regardless of whether they got GDC-4379 or the placebo.

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.

Researchers who study asthma now know that there are different types of asthma. One type is caused by a mechanism in the body called “Type 2 inflammation”.

During Type 2 inflammation, cytokines are released by immune cells. Cytokines are protein structures that signal to other cells and spread (propagate) the inflammation process.

Researchers have found that blocking the cytokine signaling process is effective for patients with Type 2 asthma.

GDC-4379 is a new medicine known as a “Janus kinase 1 inhibitor” (also called “JAK1 inhibitor”). JAK1 is an enzyme that is important in the cytokine signaling process.

GDC-4379 can block JAK1 and could be useful for patients with Type 2 asthma. Researchers wanted to find out if it was safe to give this new medicine to people.

What was the medicine being studied?

GDC-4379 is a new medicine.

- GDC-4379 works by blocking an enzyme called JAK1.
- When JAK1 is blocked, cytokine signaling is interrupted.
- Cytokine signaling is part of the process for Type 2 inflammation.
- Type 2 inflammation is associated with Type 2 asthma.

GDC-4379 was compared to a “**placebo**”.

- Some patients got GDC-4379 while others got a placebo.
- The placebo looked the same as GDC-4379 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. Is it safe for people to get a single dose of GDC-4379? Is it safe for healthy people and patients with asthma to get multiple doses of GDC-4379?

Other questions that researchers wanted to answer included:

2. What happened to GDC-4379 in the body?
3. Was there any indication that GDC-4379 may be useful in patients with asthma?

What kind of study was this?

There are several ways to describe this study.

- **Phase 1 study**
This was a “Phase 1” study. This was the first time GDC-4379 was given to people. A small number of healthy people without asthma and some patients who had asthma got GDC-4379.
- **Placebo-controlled study**
Some people (healthy people and patients) got GDC-4379 while others got the placebo. This was done so that the real effect of the medicine could be compared against the placebo.
- **Randomized study**
People (healthy people and patients) were randomly assigned to different groups that got different doses of the medicine or placebo.
- **Double-blind study**
In each group, some people (healthy people and patients) got GDC-4379 while others got the placebo. In this double-blind study, the investigators and the people/patients did not know who was getting what.

When and where did the study take place?

The study started in June 2019 and finished in April 2021. The study took place at two study centers in New Zealand. This summary was written after the study ended.

2. Who took part in this study?

Overall, 128 people took part in this study. The study consisted of three parts.

	Part A	Part B	Part C
Number of participants	48	32	48
Men and Women	20 men (42%) 28 women (58%)	16 men (50%) 16 women (50%)	22 men (46%) 26 women (54%)
Age (average)	29 years	29 years	25 years
Age (range)	19–62 years	19–55 years	18–60 years

Requirements for participating in this study

1. Participants had to provide a written consent to volunteer in this study.
2. Be between 18 and 65 years old and weigh between 50 to 120 kg.
3. Meet certain requirements for health and breathing ability.
4. Be able to follow directions for administering the study medicine.
5. Agree to use family planning methods to prevent pregnancies while participating in this study.
6. In addition to the above, patients in Part C were required to have mild asthma that was diagnosed by a doctor. Patients needed breathing tests to confirm the presence of inflammation.

Conditions that disqualified participation in this study

1. History of cancer except skin cancer that was treated.
2. History of other diseases related to several organs, blood, or immune system.
3. Presence of growths inside the nose (nasal polyps).
4. Allergies to medicine or milk proteins.
5. The use of tobacco products, drugs, or alcohol.
6. The use of certain medicine or if you underwent certain medical procedures prior to the start of this study.

Additional conditions that disqualified asthma patients (Part C)

1. Any one of the conditions above.
2. Patients whose asthma could not be brought under control.
3. Patients with a history of asthma that made it unsafe to participate in this study.
4. Patients who used a certain medicine (inhaled corticosteroids) within the last 60 days before starting this study.

3. What happened during the study?

- Healthy volunteers were assigned to Parts A and B. Patients with asthma were assigned to Part C. Each study part (A, B, and C) had different dose groups.
- The dose group and study treatment (medicine or placebo) were selected for each person at random by a computer.
- All dose groups received the treatment (study medicine or placebo) **once a day**, except for one – Group T (Part C) received treatments **twice a day**.

How was the treatment given?

The study medicine (GDC-4379 or placebo) was breathed in (inhaled) in powdered form through the mouth using an inhaler device.

Single ascending dose (SAD):

Part A was a SAD study. Participants received only one treatment. Treatment was given starting from the low dose group to the next higher one.

Multiple ascending doses (MAD):

Part B was a MAD study. Participants received one daily treatment for multiple days (14 days). Treatment was given starting from the low dose group to the next higher one.

Proof of activity (POA):

Part C was a POA study. Patients received one daily treatment for multiple days. One group received two treatments every day (Group T).

Part A SAD study Healthy volunteers	Part B MAD study Healthy volunteers	Part C POA study Patients (mild asthma)
Group A Dose = 1 mg Participants = 6	Group E 3 mg QD 6 participants	Group M 10 mg QD 8 participants
Group B Dose = 3 mg Participants = 6	Group F 10 mg QD 6 participants	Group S 30 mg QD 8 participants
Group C Dose = 10 mg Participants = 6	Group Q 30 mg QD 6 participants	Group T 40 mg BID 8 participants
Group D Dose = 20 mg Participants = 6	Group L 80 mg QD 6 participants	Group P 80 mg QD 8 participants
Group H Dose = 40 mg Participants = 6		
Group I Dose = 80 mg Participants = 6		
Placebo Pills with no medicine (2 participants in each dose group above)	Placebo Pills with no medicine (2 participants in each dose group above)	Placebo Pills with no medicine (4 participants in each dose group above)

What happened after treatment started? Doctors examined all participants and ran tests at times including before, during, and after completion of the study. All side effects were reported. Participants were observed for up to 4 weeks following the last dose of the study medicine.

4. What were the results of the study?

Question 1: Is it safe for people to get a single dose of GDC-4379? Is it safe for healthy people and patients with asthma to get multiple doses of GDC-4379?

This was the first study where GDC-4379 treatment was given to humans. Researchers found that people tolerated GDC-4379 when they received a single dose as well as multiple doses. Researchers did not discover any new side effects or any known side effects that they thought needed to be investigated further (no safety signals).

Question 2: What happened to GDC-4379 in the body?

The concentration of GDC-4379 spiked in the blood after treatment, and then decreased over time. Researchers found out that the blood concentration of GDC-4379 increased with increasing dose levels. Healthy people and patients with asthma had similar amounts of GDC-4379. It took about 6 days for GDC-4379 to reach stable levels in the blood.

Question 3: Was there any indication that GDC-4379 may be useful in patients with asthma?

Asthma patients breathe out a chemical called “nitric oxide”. This is measured in the air breathed out, and called “fractional exhaled nitric oxide” or “**FeNO**” for short. The amount of FeNO breathed out is related to the level of inflammation in the lungs.

Researchers measured FeNO in patients – before and after starting treatment. They found that all doses of GDC-4379 were effective in reducing FeNO scores. Therefore, GDC-4379 showed some activity in reducing inflammation in patients with asthma.

This section (Section 4) 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. There were no serious side effects reported by any of the 128 participants in this study. There were no deaths in this study.

Most common side effects

During this study, some people had one or more side effects that were not serious, but were thought to be caused by the treatment that they received.

All side effects are shown in the following table followed by the number of people who had them (in parentheses).

Some people had more than one side effect. That means there are more side effects than the number of people who had them. The same person can be included in more than one row (for different side effects) in the table below.

Part A	Part B	Part C
Placebo treatment: 1 out of 12 people (8%) had side effects: <ul style="list-style-type: none">• Headache (1)	Placebo treatment: 2 out of 8 people (25%) had side effects: <ul style="list-style-type: none">• Back of throat (oropharyngeal) pain (1)• Chest pain (1)• Excessive sweating (hyperhidrosis) (1)• Involuntary muscle contractions (1)	Placebo treatment: 1 out of 16 people (6%) had side effects: <ul style="list-style-type: none">• Asthma (1)
GDC-4379 treatment: 5 out of 36 people (14%) had side effects: <ul style="list-style-type: none">• Constipation (1)• Diarrhea (1)• Headache (1)• Stomach discomfort (1)• Throat irritation (1)• Toothache (1)	GDC-4379 treatment: 3 out of 24 people (13%) had side effects: <ul style="list-style-type: none">• Dry throat (1)• Throat irritation (1)• Upper respiratory tract infection (1)	GDC-4379 treatment: 6 out of 32 people (19%) had side effects: <ul style="list-style-type: none">• Low white cell count (neutropenia) (4)• Throat irritation (2)

One participant in Part B (placebo treatment) experienced a side effect (excessive sweating that led to stopping treatment).

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 128 people. These results helped researchers learn more about asthma and GDC-4379.

Researchers found single and multiple doses of GDC-4379 were tolerated by people. There were no serious side effects and no deaths. While this study was not designed to test whether GDC-4379 was an effective medicine for asthma, there was indication of some activity. Based on this study, researchers have decided not to develop GDC-4379 any further because the results showed that patients will need a very high dose of this medicine to control asthma.

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.**
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7. Are there plans for other studies?

At the time of writing this summary, there are no plans for studying GDC-4379 in asthma any further.

8. Where can I find more information?

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

<https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=376919&isReview=true>

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: Phase 1 study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of inhaled GDC-4379 conducted in three parts: A single-ascending dose study in healthy volunteers, a multiple-ascending dose study in healthy volunteers, and a proof-of-activity study in patients with mild asthma.
- The protocol number for this study is GA41024.
- The ANZCTR identifier for this study is ACTRN12619000227190.