# Clinical Trial Results – Layperson Summary

## A study to find out if a new medicine, GDC-0214, is safe in healthy people and in patients with asthma

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 and written for:

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

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

The study started in December 2017 and finished in March 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



### 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 asthma, which is a condition of the lungs that results in difficulties in breathing.

## Key information about this study

- This study was done to find out which dose of the study medicine was safe for people.
- In this study, participants were given a new medicine called GDC-0214.
- This study included 102 people in New Zealand.
- The main finding was that GDC-0214 was safe for healthy people as well as for patients with mild asthma.
- The highest dose of GDC-0214 tested in this study was 15 mg taken twice daily for 14 days.
- No one in this study had a serious side effect.
- No one in this study had side effects that led to stopping the treatment.
- People in this study were observed for up to 4 weeks following the last dose of the study medicine.
- This study did not have enough people to observe side effects that are rare and only seen in very few people.
- 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.

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 cells. Cytokines are protein structures. Cytokines signal to other cells and contribute to the inflammation process.

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

GDC-0214 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-0214 is a medicine that blocks JAK1 and therefore the cytokine signaling process. GDC-0214 may be effective for patients with Type 2 asthma.

## What was the study medicine?

**GDC-0214** is a new medicine.

- GDC-0214 works by blocking an enzyme called JAK1.
- When JAK1 is blocked, the cytokine signaling process is interrupted.
- Cytokine signaling is part of the process for Type 2 inflammation.
- Type 2 inflammation is associated with Type 2 asthma.

GDC-0214 was compared to a "**placebo**".

- Some patients got GDC-0214 while others got a placebo.
- The placebo looked the same as GDC-0214 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-0214 was safe?
2. What happened to GDC-0214 in the body?
3. What dose of GDC-0214 shows activity in patients with asthma?
4. What were the side effects of GDC-0214?

## 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-0214 in humans. A small number of healthy people without asthma and some patients who had asthma got GDC-0214.
- **Placebo-controlled study**
  Some people (healthy people and patients) got GDC-0214 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-0214 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 December 2017 and finished in March 2019. The study took place at two study centers in New Zealand. This summary was written after the study had ended.

## 2. Who took part in this study?

There were 102 people who took part in this study, which consisted of 3 parts.

- **Part A**: 34 healthy volunteers
- **Part B**: 32 healthy volunteers
- **Part C**: 36 patients with mild asthma

**Part A participants** were between 18 to 56 years of age, with more women (59%) than men (41%) in the study. The majority (85%) were white.

**Part B participants** were between 18-44 years of age, with more men (66%) than women (34%) in the study. The majority (88%) were white.

**Part C participants** were between 19 to 58 years of age, with more women (56%) than men (44%) in the study. The majority (64%) were white while race was unknown for a high proportion of the patients (19%).

**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 65 years old and weigh between 50 to 120 kg
3. Be able to follow directions for administering the study medicine
4. Agree to use family planning methods to prevent pregnancies while participating in this study

**Requirements for asthma patients to participate in this study**

1. They had to meet the 4 conditions from above
2. In addition, each patient needed to have a diagnosis of mild asthma from the doctor at least 6 months before this study
3. Patients had to meet other health and lab test requirements, including a breathing test to show that they have high levels of lung inflammation which is typical for patients with asthma.

**Conditions that disqualified healthy volunteers from 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

**Conditions that disqualified asthma patients from this study**

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?

During the study, participants joined a group and got the study medicine or the placebo. The treatment (study medicine or placebo) 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 in the 3 parts received the treatment (study medicine or placebo) once a day. One group each in Part B and Part C received treatment twice daily.

| Part A | Part B | Part C |
|---|---|---|
| Dose = **0.15 mg**<br>3 people | Dose = **1 mg**<br>6 people | Dose = **1 mg**<br>4 patients |
| Dose = **0.5 mg**<br>3 people | Dose = **3 mg**<br>6 people | Dose = **4 mg**<br>4 patients |
| Dose = **1.5 mg**<br>6 people | Dose = **10 mg**<br>6 people | Dose = **15 mg**<br>8 patients |
| Dose = **5 mg**<br>6 people | Dose = **15 mg twice daily**<br>3 people | Dose = **15 mg twice daily**<br>8 patients |
| Dose = **15 mg**<br>3 people | | |
| **Placebo** (no medicine)<br>10 people | **Placebo** (no medicine)<br>8 people | **Placebo** (no medicine)<br>12 patients |

**How was the treatment given?** The study medicine (GDC-0214 or placebo) was inhaled (breathed in) in powdered form through the mouth using an inhaler device.

**Single ascending dose (SAD):** Part A was a SAD study where people on the study 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 where people on the study received one daily treatment for multiple days (14 days). One group got two treatments in a day. Treatment was given starting from the low dose group to the next higher one.

**Proof of activity (POA):** Part C was a POA study where patients received one daily treatment for multiple days. One group received two treatments in a day.

There were two treatment periods for Part C. The first one was for 4 days when everyone received a placebo. The second treatment period lasted 10 days during which the patients received their assigned treatment (GDC-0214 or placebo).

**What happened after treatment started?** Tests and physical examinations were carried out by investigators at times including before, during, and after the completion of the study. All side effects were reported. People in this study were observed for up to 4 weeks following the last dose of the study medicine. This study did not have enough people to observe side effects that are rare and only seen in very few people.

## 4. What were the results of the study?

Everyone on the study (102 participants) completed the study. No one missed any treatment that they were assigned.

### **Question 1:** What was a safe dose of GDC-0214?

Researchers compared side effects of volunteers and patients who were given the study drug with those who received the placebo.

**Part A**: The side effects in volunteers who took a single dose of GDC-0214 up to 15 mg dose level were similar to those in volunteers who took the placebo (no medicine).

**Part B**: The side effects in volunteers who took multiple doses (14 days) of GDC-0214 up to 15 mg dose level taken twice daily were similar to those in volunteers who took the placebo (no medicine).

**Part C**: The side effects in patients with mild asthma who took multiple doses (10 days) of GDC-0214 up to 15 mg dose level taken twice daily were similar to those in patients who took the placebo (no medicine).

### **Question 2:** What happened to GDC-0214 in the body?

The concentration of GDC-0214 spiked in the blood after treatment, and then declined over time. Researchers found out that the blood concentration increased with increasing dose level of the study medicine. It took about 6 days for the study medicine to reach stable levels in the blood.

### **Question 3:** Was there any relationship between the dose of GDC-0214 and its effect on inflammation in the lung?

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 proportional to the level of inflammation in the lungs.

Researchers wanted to know which dose of GDC-0214 was active in the lung. For this, they measured FeNO in asthma patients on this study.

FeNO was measured before the study started and at the end. Researchers found that 15 mg of GDC-0214 reduced FeNO. However, 1 mg and 4 mg doses of GDC-0214 were not effective.

After 10 days of treatment, patients who took 15 mg of GDC-0214 once a day saw 23% reduction in FeNO. Those who took two doses a day saw 43% reductions.

Therefore, GDC-0214 had some effect on mild asthma in patients who were given a dose of 15 mg daily or twice daily for 10 days.

## 5. What were the side effects?

Side effects are unwanted medical problems (such as a headache) that happen 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 medical problems related to the study medicine and are listed below.

| **Part A** (21 participants got the study medicine) | **Part B** (21 participants got the study medicine) | **Part C** (24 patients got the study medicine) |
|---|---|---|
| Sinus congestion (1 person)<br><br>Nausea (1 person) | Cough (1 person) | Thirst (1 patient) |

### 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.

## 6. How has this study helped research?

This study was the first time that the study medicine, GDC-0214, was given to any human. This study helped researchers learn that the study medicine was safe for humans when inhaled at doses up to 15 mg twice daily for 14 days.

Researchers also learned that it took about 6 days for the study medicine to reach stable levels in the blood and 40 hours for GDC-0214 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.

Researchers found out that 15 mg daily for 10 days was effective. That means this dose reduced inflammation in the lung in asthma patients. Getting the medicine twice a day was more effective than once a day. This was the highest dose tested in this study.

## 7. Are there plans for other studies?

Based on the results of this study, researchers plan to continue working with this type of study medicine to see if it can become an effective treatment for patients with mild asthma.

## 8. Where can I find more information?

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

**Australian New Zealand Clinical Trial Registry**
Registration number: ACTRN12617001227381

https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=373446&isReview=true

### Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Please contact a representative at your local Roche office.
- Visit the ForPatient portal on the web and fill out a form https://forpatients.roche.com/en/About.html

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 I study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of inhaled GDC-0214 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 GA39846.