Summary of Clinical Trial Results

A study to find out how safe is it to give people a new medicine called "GDC-8264" – including the effect of food on GDC-8264, and the effect of combining GDC-8264 with other medicines

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 January 2020 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.**

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 medicine studied – "GDC-8264".

Key information about this study

- This study was done to find out if it was safe to give single and multiple doses of a study medicine to people.
- In this study, people were given either the medicine being studied (GDC-8264) or a placebo (that did not contain any medicine). It was decided by chance which treatment each person was given.
- This study included 68 people in one country.
- The main finding was that single and multiple doses of GDC-8264 taken by mouth were safe and well tolerated by healthy people at the doses used in this study.
- Taking GDC-8264 with food slowed the absorption of GDC-8264, but did not affect the overall exposure to GDC-8264.
- When GDC-8264 was taken with another medicine – one type of measurement indicated a drug-drug interaction, while other measurements did not.
- No one in this study got any serious side effects.

1. General information about this study

Why was this study done?

GDC-8264 is a new medicine that may be used for the treatment of inflammatory bowel disease (IBD). IBD includes two main conditions: Ulcerative colitis and Crohn's disease.

Patients with IBD have long-lasting inflammation and increased cell death in parts of the intestines. The gastrointestinal tract can no longer work normally in patients with IBD.

Patients with IBD can have abdominal pain, diarrhea and may not feel hungry (reduced appetite). Many of these patients need to be hospitalized and undergo surgery. In the Netherlands, approximately 1 in 200 people suffer from this disease.

GDC-8264 works by preventing cell death and inflammation, by blocking a protein from performing its action. GDC-8264 may be able to reduce inflammation.

This study was done to find out how safe was it for healthy people to get GDC-8264 and how well GDC-8264 was tolerated. This was the first study where GDC-8264 was given to humans.

What were the study medicines?

A medicine called “GDC-8264” was the focus of this study.

- GDC-8264 works by preventing cell death and inflammation – by blocking a protein from performing its action.
- This means that GDC-8264 may be able to reduce inflammation in patients with IBD.

GDC-8264 was compared to a “placebo”.

- The placebo looked similar to GDC-8264. However, the placebo did not contain any real medicine. This means it had no medicine-related effect on the body.

Researchers compared the medicine being studied (GDC-8264) to the placebo. This way, they could compare the effects of the treatment with medicine to the effects of the treatment without any real medicine.

What did researchers want to find out?

The main question that researchers wanted to answer was:

1. Was GDC-8264 safe and tolerable when given to people as single and multiple doses?

Other questions that researchers wanted to answer included:

2. Was there a difference when GDC-8264 was taken with or without food?
3. Did GDC-8264 cause any drug-drug interaction?

What kind of study was this?

- **Phase 1 study**
  This study was a “Phase 1” study, which means that this was one of the first studies for GDC-8264. A small number of healthy people (without IBD) got treatments. Researchers did medical tests on the people to find out more about the treatments.
- **Randomized study**
  A computer randomly decided which person got GDC-8264 and who got placebo. Researchers and people had no control over this.
- **Double-blind study**
  The researchers and people in the study did not know who was getting GDC-8264 and who was getting the placebo. That made it a double-blind study.
- **Placebo-controlled study**
  Some people got GDC-8264 while others got a placebo. This was done so that the treatment with GDC-8264 could be compared to the treatment with placebo – to find out the real effect of GDC-8264.

When and where did the study take place?

The study started in January 2020 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 – The Netherlands.

2. Who took part in this study?

Sixty-eight healthy people took part in this study, including 40 (59%) men and 28 (41%) women. They were between 18 and 55 years old. They joined 3 different study groups:

	SAD Study Single ascending dose study	**MAD Study** Multiple ascending dose study	**DDI Study** Drug-drug interaction study
Number of people who joined the study group	38	15	15
Number of women	14 (37%)	8 (53%)	6 (40%)
Number of men	24 (63%)	7 (47%)	9 (60%)
Youngest age (years)	18	19	19
Oldest age (years)	55	54	53

People could take part in the study if:

- They were between 18 to 55 years old.
- They met the height-to-weight ratio (BMI between 18 to 30 kg/m^2).
- They agreed to use birth control during the study.
- They signed a consent form to agree to participate in the study.

People could not take part in the study if:

- They received an experimental medicine within the last 90 days.
- They participated in four other studies within a year prior to this study.
- They had recent treatments with certain medicines, had been recently hospitalized, or had surgery planned to occur while still on this study.
- They did not meet other health criteria.
- They had drug or alcohol problems within the last 12 months.
- They consumed alcohol, caffeine, or any other listed food or drink within 2 days prior to starting this study.
- Women could not take part if they were pregnant or breastfeeding. They couldn't take part if they intended to become pregnant during or soon after the study.

3. What happened during the study?

Healthy volunteers joined the SAD, MAD, and DDI study groups.

Randomized and double-blind study
For SAD and MAD studies, study treatments (GDC-8264 or placebo) were selected for each person at random by a computer. It was a double-blind study because doctors and people in the study did not know which treatment (GDC-8264 or placebo) the people were getting.

Open-label study
The DDI study was open-label because the doctors and people in the study knew which treatment they were getting.

What were the treatments?

Everyone got GDC-8264 or placebo treatments. Group 10 got GDC-8264 and midazolam.

SAD Study Single ascending dose groups	**MAD Study** Multiple ascending dose groups	**DDI Study** Drug-drug interaction group
Group 1 Participants = 6	**Group 8** Participants = 7	**Group 10** GDC-8264 and midazolam Participants = 15
Group 2 Participants = 6	**Group 9** Participants = 5	
Group 3 Participants = 5		
Group 4 Participants = 5		
Group 5 Participants = 6		
Placebo Pills with no medicine (10 participants)	**Placebo** Pills with no medicine (3 participants)	

How was the treatment given?

- The treatment (GDC-8264 or placebo) was given by mouth as a liquid suspension in water for some doses.
- For other doses, treatment was given as tablets taken with water.
- All participants got their treatment after an 8 hour overnight fast.
- After getting their treatment,
    - People in the SAD study continued to fast for another 4 hours before eating lunch. They skipped breakfast.
    - People in the MAD study continued to fast for another 4 hours before eating lunch on days 1, 7, and 14. On other days, they received breakfast 1 hour after treatment.
    - People in the DDI study continued to fast for another 4 hours before eating lunch on days 1 and 10. On other days, they received breakfast with their treatment.
- The length of the study was different for each group:
    - SAD – people got a single dose.
    - MAD – people got a single dose daily for 14 days.
    - DDI – this was a 10-day study (see below).

Studying the effect of food

- Group 3 in the SAD study got a single treatment after an overnight fast as above. After waiting for the medicine to be cleared from their bodies (washout period), they were given another dose. This second dose was given after eating a high-fat breakfast. Doctors wanted to know if taking GDC-8264 with food was any different than taking it without food (overnight fast).

Studying the effect of another medicine

- There is a group of medicines known to increase or decrease liver enzymes. There is another group of medicines that are processed by these liver enzymes.
- This means that the first group of medicines can affect the concentration of the second group of medicines in the body – if medicines from the two groups are taken together. This is called “drug-drug interaction” or “DDI”.
- In the DDI study group, people were treated with GDC-8264 from Day 3 until Day 10. On Day 1 and Day 10, they also took “midazolam” a medicine that is processed by liver enzymes. Doctors looked at the concentration of this midazolam taken alone (Day 1) and when taken with GDC-8264 (Day 10) – to find out if GDC-8264 had any drug-drug interaction.

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.

4. What were the results of the study?

Question 1: Was GDC-8264 safe and tolerable when given to people as single and multiple doses?

Researchers found that single and multiple doses of GDC-8264 taken by mouth were safe and well tolerated at the doses studied.

Question 2: Was there a difference when GDC-8264 was taken with or without food?

Researchers found out that taking GDC-8264 with food delayed the absorption of GDC-8264. However, people were exposed to the same amount of GDC-8264 over time. It would not make a difference if patients took GDC-8264 with or without food.

Question 3: Did GDC-8264 cause any drug-drug interaction?

When a medicine that is processed by liver enzymes (midazolam) was taken together with GDC-8264, one type of measurement indicated drug-drug interaction, while other measurements did not.

5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happened during the study.

- They will be described in this summary if the study doctor believes the side effects were related to the treatments in the study.
- Not everyone in any study gets 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 and no deaths reported in SAD, MAD, and DDI groups in this study.

Most common side effects

Some people had side effects that were not considered serious but were thought to be related to GDC-8264.

Here is a list of common side effects thought to be caused by GDC-8264 – seen in two or more of people in the entire study of 68 people.

- If someone got side effects with placebo treatment, they are indicated in **blue**.
- Counts are for **number of people** with that side effect, followed its percentage for that study group – SAD, MAD, or DDI.
- Among the total number of side effects
    - Some people got more than one type of side effect.
    - Some people got the same side effect more than once

	SAD Study	MAD Study	DDI Study
All the people in group	38	15	15
All the people with side effects	5 (13%)	10 (67%)	11 (73%)
Total number of side effects	5	27	25
Number of people with common side effects (Numbers for placebo treatment are in **blue**)			
Diarrhea		3 (20%)	3 (20%)
Feeling dizzy		2 (13%)	4 (27%)
Headache	1 (3%)	2 (13%)	2 (13%)
Feeling drowsy (somnolence)		1 (7%)	2 (13%)
Feeling sick to stomach (nausea)	2 (5%)	1 (7%)	
Frequent urination (pollakiuria)			3 (20%)
Funny sounds in stomach (abnormal gastrointestinal sounds)	1 (3%)	1	
Gum inflammation (gingivitis)		2 (13%)	
Indigestion (dyspepsia)		1 (7%) **1 (7%)**	
Stomach ache		1 (7%) **1 (7%)**	

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 68 healthy people who did not have IBD. These results helped researchers learn more about GDC-8264, the effect of food on GDC-8264, and the effect of GDC-8264 when taken in combination with a certain class of medicines.

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.

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7. Are there plans for other studies?

At the time of writing this summary, there were no other ongoing studies looking at GDC-8264, although studies looking at GDC-8264 may be planned in the future.

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/autoimmune-disorder/ibd/a-study-to-find-out-how-safe-is-it-to-give-people-a-new-medicine.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, randomized, double-blinded, placebo-controlled study to evaluate the safety, tolerability, and pharmacokinetics of single- and multiple-ascending doses of oral GDC-8264 and the effect of food on the pharmacokinetics of GDC-8264 in healthy volunteers.

The protocol number for this study is GP41678.