Summary of Clinical Trial Results

Investigating side effects of a new medicine (migoprotafib) and whether it can be tolerated by people

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 November 2022. This summary was written after the study had ended.

A single study cannot tell us all there is to know about the risks and benefits of a medicine. It takes many people in several 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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Contents of the summary

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 cancer and the study medicine (migoprotafib).

Key information about this study

- This study was done to investigate the side effects of a new medicine (migoprotafib) to find out if it can be tolerated by people.
- People with advanced or metastatic cancer could join this study.
- The study included 56 people in one country, the USA.
- People took one daily dose of the study medicine until they decided to stop or doctors asked them to.
- The main finding was that the side effects (safety profile) of migoprotafib could be managed with "supportive care" and changing the dose. Supportive care included treatments to prevent or treat side effects as early as possible.
- Seven people (13%) in the study experienced serious side effects thought to be caused by migoprotafib. Fifty-one people (91%) experienced side effects that were not serious but were thought to be caused by migoprotafib.

1. General information about this study

Why was this study done?

"**SHP2**" is a type of protein, a "protein phosphatase," present throughout the body.

A protein phosphatase can act like a switch in cell signaling pathways. A "signaling pathway" is a group of molecules in a cell that work together to control a cell function, and when turned on, they can tell cells to grow, divide, or survive.

One signaling pathway that SHP2 is active in is the "RAS/MAPK pathway." This pathway controls several cell functions, including cellular growth.

In healthy cells, SHP2 can switch on the RAS/MAPK pathway when it is necessary for cell growth to occur. SHP2 becomes inactive when cell growth is not needed.

In certain cancers, SHP2 can become overactive, leading to uncontrolled cell growth through the RAS/MAPK pathway. Here, SHP2 may be slightly different (mutated), or it may be present at higher levels (high expression).

Several kinds of medicines are available for treating cancer. While they are useful, patients eventually become unresponsive (develop resistance) to these therapies, and cancer ends up taking a person's life. This highlights the need for new cancer therapies that provide more options for patients and doctors.

Researchers are hopeful that a medicine that blocks (inhibits) SHP2 activity could prove beneficial for multiple cancer types that signal through the RAS/MAPK pathway. This study was done to test migoprotafib, a new cancer medicine which is an "SHP2 inhibitor."

What was the study medicine?

The study medicine was called "**migoprotafib**." It is also known by other names:

- SHP2 inhibitor
- GDC-1971
- RO7517834
- RLY-1971

Migoprotafib belongs to a class of medicines known as “small molecule inhibitors.” Migoprotafib may be useful for people who have certain types of cancers.

What did researchers want to find out?

The main questions that researchers wanted to answer were:

- What were the side effects of migoprotafib?
- Was migoprotafib safe and could it be tolerated by people based on side effects?

What kind of study was this?

Here are some ways to describe this study.

Phase 1 study: A Phase 1 study is carried out with a small group of people who have a disease of interest. People in the study may benefit from the medicine being tested. The main goal of a Phase 1 study is to figure out the ideal dose of medicine that can be safely given to people. This decision is made after looking at side effects of the medicine at different doses.

Open-label study: This is a type of clinical trial in which both the researchers and the patients participating in the study are aware of the treatment being administered. In the current study, everyone received migoprotafib and nobody received a placebo. (A placebo looks like the real medicine but does not have any active medicinal ingredient.)

Dose-escalation study: In a dose-escalation study, the first group of people gets the lowest dose of the medicine. When a dose is found to be safe based on the side effects seen for that dose, the next group gets a higher dose. This gets repeated, and each new group gets a higher dose than what was given to the previous group. The goal is to find the highest dose that can be given to patients without causing unacceptable side effects. Sometimes, the dose must be reduced to get to a dose where the side effects are better tolerated.

Dose-expansion study: After a dose-escalation study, researchers may decide on one dose that they think could be safe and perhaps beneficial for people with the disease. In a dose-expansion study, a larger group of people receive this one dose. This allows researchers to gather more information about the medicine given to people at that one dose. The expansion dose is typically higher than several of the doses tested during dose escalation.

Safety study: A safety study is designed to look at the side effects – to decide if a new medicine is safe to give to patients at the doses tested in the study.

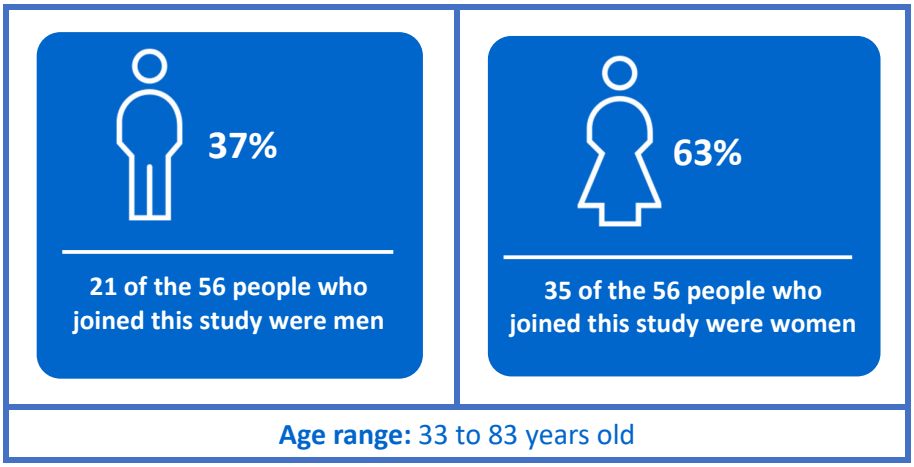
When and where did the study take place?

The study started in January 2020 and finished in November 2022. This summary was written after the study had ended.

The study took place at six study centers in one country – the USA.

2. Who took part in this study?

Fifty-six people joined this study. They had advanced cancer, or cancer that had spread (metastasized). The cancer was unresponsive (refractory) to approved therapies, or no suitable therapy was available.



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

- Signed the informed consent form for the study
- At least 18 years old
- Still physically active with only minor restrictions to their daily activities
- Tumors could be measured with imaging equipment at the clinic
- Recovered from side effects of prior therapies
- Sufficient kidney, bone marrow, and liver function
- Agreed to use birth control if pregnancy was a possibility

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

- Their cancer type would not benefit from the therapy being tested
- Not enough time had passed since their last cancer therapy or radiotherapy
- Not enough time had passed since their last surgery
- People with certain types of brain tumors
- People with certain types of eye, stomach (gastrointestinal), or heart disease
- People with any other serious medical condition

3. What happened during the study?

Screening

People interested in the study visited the clinic. The study doctor asked questions, collected blood and urine samples, and performed several medical tests to learn about each person's health.

Treatment

People who met study conditions were able to start the experimental treatment. They took their medicine daily, at about the same time, with a glass of water, one hour before or two hours after a meal or snack.

Eight different doses were tested in this dose escalation study. Researchers picked one dose for the expansion study. Three to seven people were in each dose-escalation group. Twenty people joined the dose-expansion group.

The average length that people remained on treatment was 61 days.

What happened during the study
Every 3 weeks of treatment was called a "cycle." During each cycle, people visited the study center anywhere from 1 to up to 4 days.

When did the treatment end
People stopped their treatment if they wanted to, if the disease became worse, or if the decision was made by the study doctor or sponsor.

People visited the study center within 7 days of stopping treatment. They also visited 30 days after stopping treatment.

What happened at the study center during visits
The study doctor asked questions, collected blood and urine samples, and performed several medical tests to learn about each person's health.

4. What were the results of the study?

Question: What were the side effects of migoprotafib? Was migoprotafib safe and could it be tolerated by people based on side effects?

Researchers looked at blood test results, physical exams, medical tests, images of the cancer, and notes about how patients were feeling. They noted what kinds of side effects were seen, how soon after treatment they happened, how often they happened, and how severe they were.

During dose escalation, researchers decided the highest dose that was reached had too many side effects which made that dose intolerable. They then tested lower doses.

The dose selected for expansion study was lower than the highest dose tested in this study. Researchers believed this lower dose could be tolerated by people over long treatment periods. This lower dose was to be used in future studies of migoprotafib.

Side effects were reported in this study and are discussed in Section 5. Seven people (13%) in the study experienced serious side effects thought to be caused by migoprotafib. Fifty-one people (91%) experienced side effects that were not serious but were thought to be caused by migoprotafib.

Based on the data collected in this study, researchers decided that side effects (safety profile) of migoprotafib could be managed with "supportive care" and changing the dose. Supportive care included treatments to prevent or treat side effects as early as possible.

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.

- If they were seen in this study, they are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Everybody in a study will not have all 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.
- If serious and common side effects were seen in this study, they will be 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.

Seven people (13%) out of 56 in the study had at least one serious side effect that study doctors thought was caused by migoprotafib. These serious side effects were:

- Six people (19%) out of 31 treated at the escalation dose had at least one serious side effect. (Some people had more than one side effect).
    - Red blood cells lower than normal (anemia), 2 people (6%)
    - Low level of platelets in the blood (thrombocytopenia), 2 people (6%)
    - Swelling of the belly area (abdominal distension), 1 person (3%)
    - Diarrhea, 1 person (2%)
    - Higher than normal levels of a protein from the heart, brain, and muscle (blood creatine phosphokinase increased), 1 person (3%)
    - An increase in weight, 1 person (3%)
    - Lung infection caused by inhaling saliva, food, drink, or vomit (pneumonia aspiration), 1 person (3%)
    - Sleeping for unusually long periods or having a strong desire for sleep (somnolence), 1 person (3%)
- One person (4%) out of 25 treated at the expansion dose had a serious side effect.
    - Swelling, inflammation of the large intestine (colitis)

Doctors thought that one death, due to an infection, was caused by migoprotafib. The affected person died of aspiration pneumonia during the 30-day period after stopping migoprotafib treatment. "Aspiration pneumonia" occurs when food or liquid is breathed into the airways or lungs, instead of being swallowed.

During the study, 8 people (14%) decided to stop taking their medicine because of side effects. In addition, 31 people (55%) delayed their dose to deal with side effects (dose interruption) and 7 people (13%) had their doses reduced.

Most common side effects

Fifty-one people (91%) out of 56 in this study had a side effect that was not serious but was thought to be caused by the study medicine. This included:

- Twenty-seven people (87%) out of 31 treated at the escalation doses
- Twenty-four people (96%) out of 25 treated at the expansion dose

Here are the side effects thought to be caused by the study medicine and seen in ten percent or more people in the study:

- Diarrhea, 25 people (45%)
- Swelling of the hands, ankles, or feet (edema peripheral), 16 people (29%)
- Low level of platelets in the blood (thrombocytopenia), 9 people (16%)
- High levels of liver enzyme present in blood (ALT increased), 8 people (14%)
- High levels of liver enzyme present in blood (AST increased), 8 people (14%)
- Low levels of platelets in blood which help blood to clot, 8 people (14%)
- Red blood cells lower than normal (anemia), 7 people (13%)
- Feeling tired or weak (fatigue), 6 people (11%)
- Swelling in a part of the body (localized edema), 6 people (11%)

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 56 people with cancer. These results helped researchers learn more about cancer and migoprotafib.

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7. Are there plans for other studies?

At the time of writing this summary, other studies testing migoprotafib in people were in progress.

8. Where can I find more information?

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

- https://clinicaltrials.gov/study/NCT04252339?tab=results
- https://forpatients.roche.com/en/trials/cancer/solid-tumors/rly-1971-in-subjects-with-advanced-or-metastatic-solid--45813.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, dose escalation and expansion study of RLY-1971, a highly potent and selective SHP2 inhibitor, in subjects with advanced or metastatic solid tumors

- The protocol number for this study is GO43242.
- The ClinicalTrials.gov identifier for this study is NCT04252339.