Summary of Clinical Trial Results

What happens to a medicine (entrectinib) when given to people in different forms

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 July 2022 and finished in October 2022. 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 study 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 different forms of a medicine called "entrectinib."

Key information about this study

- Researchers wanted to know how much medicine was absorbed into the body – when taken in different forms, or with another medicine.
- In this study, people got a medicine called "entrectinib" – in different forms (formulations), or with another medicine.
- Thirty-two people took part in this study at one study center in USA.
- The main finding was that four different ways of taking the medicine were comparable to the hard capsule. Taking entrectinib with a medicine that lowers the amount of acid in the stomach – did not change the amount of entrectinib in the body.
- There were differences in some of the measurements, but these did not impact the effect of the medicine on people – the differences were not "clinically relevant".
- There were no serious side effects in this study.
- Five people (16%) had side effects that were not serious but were thought to be caused by the study medicine.
- One person (3%) stopped the study (discontinued) because of a side effect that was not serious but was thought to be caused by the study medicine.

1. General information about this study

Why was this study done?

Entrectinib is a medicine that has been approved for use in several countries. This medicine is prescribed to patients with certain types of cancers – if they meet other conditions (criteria).

A capsule form of entrectinib (hard capsule **formulation**) – can be used by adults and children – who are able to swallow capsules.

Another formulation – coated granules formulation – is under development for children unable to swallow capsules – but who are able to swallow smaller bits (granules) mixed with soft food.

For people unable to swallow capsules or soft foods, an alternative formulation is needed.

This study was done to look at different formulations of entrectinib – how they compared to the hard capsules when given to adults.

This study also looked at the effect of taking entrectinib with a medicine that lowers the amount of acid in the stomach.

What was the study medicine?

This study looked at a medicine called "**entrectinib**."

- Entrectinib is also known as: Rozlytrek, RO7102122, and RXDX-101.
- Entrectinib is a medicine known as a "**tyrosine kinase inhibitor**". This medicine interferes with "cell signaling" to disrupt the growth of cancer cells.

Some people took a medicine called “lansoprazole” before taking entrectinib.

- Lansoprazole belongs to a class of medicines that are called “**proton pump inhibitors**” (**PPIs**).
- PPI lower the amount of acid in the stomach.
- Researchers wanted to know if taking PPI would affect how much entrectinib was absorbed into the body.

What did researchers want to find out?

Researchers wanted to gather information about how people’s bodies processed entrectinib when it was given using different formulations, or when taken with a PPI.

The main questions that researchers wanted to answer were:

1. How much medicine was available in the body – the “bioavailability” of entrectinib – when taken in different formulations?
2. Did taking a PPI interfere with how much medicine was available in the body?

What kind of study was this?

There are several ways to describe this study.

Phase 1 study
This was a “Phase 1” study to gather information about the study medicine. A small number of healthy people were given the study medicine. Information from this study may be used in other studies with more people.

Open-label study
Researchers and people in the study knew which medicine the people were getting. That made it an “open-label” study.

Randomized study
A computer randomly decided who joined which treatment group. Researchers and people in the study had no control over this.

Three-period crossover study
There were 3 groups in Part A, and they got 3 treatments (A, B, C) in different orders. That made it a “three-period crossover study.”

- Group 1 got A→B→C.
- Group 2 got B→C→A.
- Group 3 got C→A→B.

In Part B, there were another 2 groups, and they got treatments (C, D, E).

- Group 4 got C→D.
- Group 5 got D→C.
- Both groups got E as the third treatment.

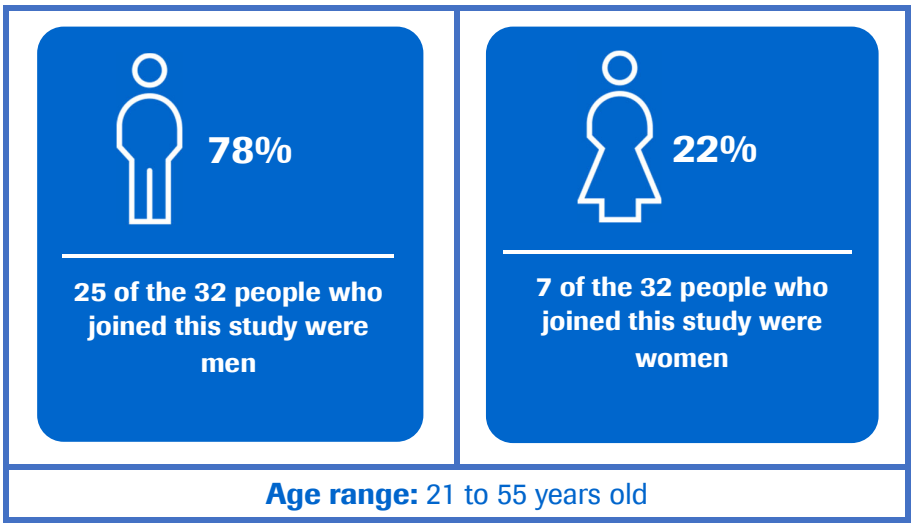
When and where did the study take place?

The study started in July 2022 and finished in October 2022. This summary was written after the study had ended.

The study took place at one study center – in one country – USA.

2. Who took part in this study?

Thirty-two healthy people took part in this study.



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

- Males who agreed to use birth control and not donate sperm for a required period
- Females who were not pregnant, could not get pregnant, and agreed not to donate eggs for a required period
- Met the height to weight ratio (BMI 18.0 to 32.0 kg/m^2)
- Weighed at least 50 kg
- In good health – doctors asked questions, did medical exams, and blood tests
- Tested negative for illegal drugs
- Agreed to follow the study restrictions
- Understood and signed the informed consent form

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

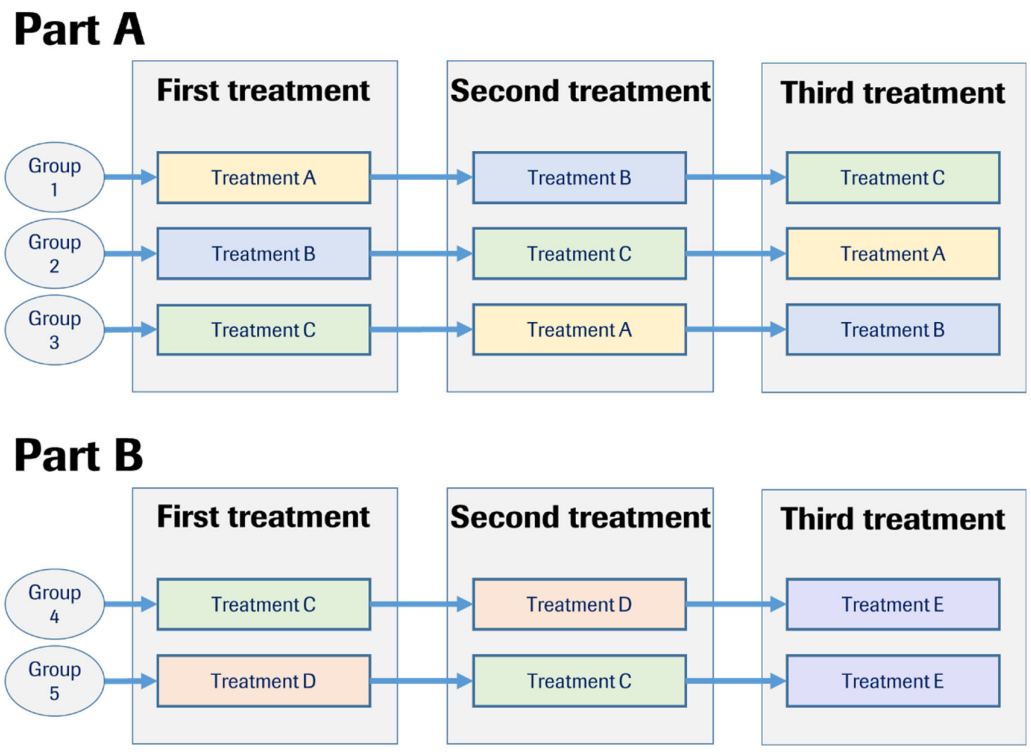
- Females who were pregnant, breast feeding, or intended to become pregnant during the study or shortly thereafter
- Males who had a pregnant partner
- They did not meet a list of health requirements – doctors asked questions, did medical exams, and blood tests
- Use of over-the-counter and prescription medicines that were not allowed
- Recently received the COVID-19 vaccine
- Recently participated in another study with another study medicine

- Recent history or current use of products – prescription medicines and over-the-counter non-prescription items - that were not allowed
- Recent history of drug or alcohol abuse or addiction
- Current use of more than the allowed amount of alcohol
- Recent history or current use of tobacco or nicotine products
- Recent history of donating blood
- Recent history of using food and drinks not allowed in the study
- Recently participated in strenuous exercise

3. What happened during the study?

Screening
Study staff asked questions and did medical tests to find out if people interested in the study met the study requirements. This happened up to 28 days before starting the study.

Treatment
People were randomly assigned to one of six treatment groups.



The entrectinib treatments were given five different ways – to people on an empty stomach who had not eaten overnight for 8 hours:

A. Mixed into water and given in a tube through the nose into the stomach.
B. Mixed into milk and taken by mouth.
C. Hard capsules taken by mouth with water.
D. Mixed into water and taken by mouth.
E. People got daily doses of the PPI medicine for five days. On the fifth day, they also got entrectinib that was mixed into water and taken by mouth.

People checked into the study center one day before each treatment (Day -1). They got their treatment on Day 1. They went home on Day 5 after the first and second treatments. They went home on Day 9 after the third treatment.

At least 14 days passed from one dose to the next. This was called a "**washout period**". It was enough time to allow entrectinib to leave the body before the next dose.

People in the study received a follow-up telephone call about 12-14 days after the last treatment. Study staff asked questions to gather further information about the treatments.

4. What were the results of the study?

Question 1: How much medicine was available – the "bioavailability" of entrectinib – when taken in different formulations?

Researchers looked at how much medicine (entrectinib) – was available in the body when taken in different formulations – according to Treatments A, B, C, D, and E.

- Treatment C included taking entrectinib in hard capsule form by mouth with water.
- Treatment C was the reference – the other treatments were compared to Treatment C.
- The main finding was Treatments A, B, D, and E – gave similar (but not the same) amounts of medicine in the body – when compared to the hard capsule.
- Researchers took measurements of different factors related to taking a dose of medicine. There were differences in some of the measurements for different treatments, but these did not impact the effect of the medicine on people – the differences were **not** "**clinically relevant**."

Question 2: Did taking a PPI interfere with how much medicine was available in the body?

Another piece of information that researchers collected was – whether taking a PPI medicine had any effect on the amount of entrectinib absorbed into the body.

- Treatment D was the reference. People took entrectinib – mixed into water and taken by mouth.
- Treatment E was the test. People got daily doses of the PPI medicine for five days. On the fifth day, they also got entrectinib that was mixed into water and taken by mouth.
- Taking entrectinib with a PPI – a medicine that lowers the amount of acid in the stomach – did slightly change the amount of entrectinib in the body.
- Researchers took measurements of different factors related to taking a dose of medicine. There were differences in some of the measurements for the different treatments, but these did not impact the effect of the medicine on people – the differences were **not** "**clinically relevant**."

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 happened 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.
- Every person in a single study – does not get 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 if they happened this study.

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 seen in this study.

There were no deaths seen in this study.

Most common side effects

During this study, five people (16%) had at least one side effect that was not considered serious – but study doctors believed they were caused by the study treatments.

- In Part 1, one person had two side effects and another person had one side effect. The side effects were:
    - Having a difficult bowel movement (constipation)
    - Feeling numb in the mouth (hypoesthesia oral)
    - Having an abnormal feeling in the mouth (paresthesia oral)
- In Part 2, three people had one side effect each:
    - Stomach ache (abdominal pain upper)
    - Feeling like throwing up (nausea)
    - Feeling sick to the stomach (vomiting)

One person in Part 2 stopped study treatments – because of a side effect that the study doctors believed was caused by the study treatment. This person was vomiting.

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 32 healthy people. These results helped researchers learn more about different formulations of entrectinib.

No single study can tell us everything 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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7. Are there plans for other studies?

Other studies with entrectinib are still happening.

8. Where can I find more information?

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

https://www.isrctn.com/ISRCTN57815030

https://forpatients.roche.com/en/trials/healthy-volunteers/a-two-part--open-label--comparative--single-dose--randomized--fi.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 two-part, open-label, comparative, single-dose, randomized, five-treatment, three-way crossover sequential study to assess the relative bioavailability of entrectinib capsule compared to nasogastric and oral administration of suspension in healthy subjects

- The protocol number for this study is GP44192.
- The ISRCTN number for this study is 57815030.