Summary of Clinical Trial Results

A study to look at a new medicine called "UTTR1147A" – how safe are different doses for healthy people and patients to take – and how is this medicine processed through 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 – the "**study participants**".

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

The study started in April 2016 and finished in February 2020. 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 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 have helped researchers to answer important questions about ulcerative colitis and Crohn's disease, and the study medicine called, "UTTR1147A".

Key information about this study

- This study was done to investigate a new medicine and find out how safe was it at different doses.
- People participating in this study got a study medicine (UTTR1147A) or a placebo (which did not contain any medicine). It was decided by chance which treatment each person was given.
- This study included 69 people in two countries. Some people were healthy volunteers while others were patients with ulcerative colitis (UC) or Crohn's disease (CD).
- The main finding was that UTTR1147A was safe for patients with UC and CD at all the doses tested in this study. Knowledge learned from this study has been used to launch other studies for UTTR1147A.
- There were no serious side effects thought to be caused by the treatment (UTTR1147A or placebo) in people who participated in this study.

1. General information about this study

Why was this study done?

Ulcerative colitis (UC) affects the colon, and Crohn's disease (CD) affects the gastrointestinal (GI) tract. These diseases are caused by inflammation that lasts long-term.

UC is associated with bleeding through the rectum, stomachache, diarrhea, and bloody diarrhea. Patients with CD can experience feeling sick to the stomach (nausea), vomiting, stomachache, and diarrhea.

Many medicines are available for treating UC and CD. These include corticosteroids, immuno-suppressants (azathioprine, 6-mercaptopurine, and methotrexate), anti-tumor necrosis factor (TNF), and anti-integrin therapy.

The available medicines do not always stop the progression of UC and CD, so that surgery can become necessary for some patients. In addition, these medicines can cause side effects.

Researchers are continuing to look for new medicines with fewer side effects. Medicines that can stop the disease from getting worse will be especially useful so that patients do not require surgery.

This study was done to investigate an experimental (not approved) medicine that may be useful for patients with UC and CD.

What was the study medicine?

A medicine called "**UTTR1147A**" was the focus of this study.

- UTTR1147A is a medicine which is a protein – made by connecting (fusing) two different proteins – one of which is **IL-22** and the other one is the tail region of an antibody.
- There are receptors for IL-22 present on cells in the GI tract. Receptors are structures on cells where another protein can dock – just like a lock on a house where a key can go in.
- IL-22 has an effect on cells when it attaches to the **IL-22 receptor**.
- These effects include activities in cells to repair and heal the GI tract.
- It is possible that UTTR1147A will have the same effect on cells in the GI tract as IL-22. Therefore, UTTR1147A could be useful for patients with UC and CD.

UTTR1147A was compared to a "**placebo**".

- In this study, some people got UTTR1147A while others got a placebo.
- The placebo looked the same as UTTR1147A but did not contain any real medicine.
- Having the placebo allowed researchers to find out if the effect of the treatment was really due to the medicine.

What did researchers want to find out?

Researchers did this study to compare side effects from UTTR1147A and the placebo.

The main question that researchers wanted to answer was :

1. Was UTTR1147A safe for people?

Another question that researchers wanted to answer was:

2. What happens to UTTR1147A inside the body?

What kind of study was this?

This was a "**multiple-ascending, dose-escalation study**". Patients received several doses of their treatment, described as "multiple doses". Each new group of patients received a higher dose of the treatment, described as "ascending dose". The decision to administer the next higher dose level – "dose-escalation" – was made after reviewing results from all previously dosed people at the lower dose levels.

This was a "**placebo-controlled study**", which means that researchers could compare results for patients who received the study medicine with those who received a treatment without any medicine.

The study was "**observer-blinded**". This means that the researchers who were collecting results did not know who was getting the medicine and who was getting the placebo. This was another way to reduce unfairness (bias) in the study.

When and where did the study take place?

The study started in April 2016 and finished in February 2020. This summary was written after the study had ended.

The study took place at 2 study centers in Germany and the United Kingdom.

2. Who took part in this study?

There were 69 people who took part in this study:

	Healthy volunteers	Patients with UC	Patients with CD
Number of people in this group	38	24	7
Half of the people in this group were below this age (median age)	37 years	39 years	28 years
The youngest person and oldest person in this group (age range)	33 years and 47 years	37 years and 47 years	25 years and 60 years
Men and Women	38 men (100%) No women (0%)	17 men (71%) 7 women (29%)	4 men (57%) 3 women (43%)

People could take part in the study if:

- They agreed to sign a consent form.
- They agreed to use birth control methods while on the study.
- Other requirements form healthy volunteers:
  - Be between 18-50 years old.
  - Body mass index between 18-32 kg/m^2.
  - Weight between 40-120 kg.
  - In good health.
- Other requirements for patients with UC or CD:
  - Be between 18-80 years old.
  - Have moderate to severe UC or CD lasting at least 12 weeks.
  - Meet several requirements for types of medicines and doses taken in the past, as well as current doses.
  - Have had a recent colonoscopy or be willing to undergo one.

People could not take part in the study if:

- They had cancer or any of several other diseases.
- They had a history of allergic reactions to certain medicines.
- They had a history of drug or alcohol problems.
- They had recently lost or donated blood.
- They had recently used certain medicines before this study.
- They tested positive for certain blood tests.
- Healthy volunteers could not participate if they had participated in a prior study – GA29468.
- Patients with UC or CD could not participate if they had certain other medical conditions.

3. What happened during the study?

People were "randomized" to join groups. That means, it was decided by chance who could join which group and whether they received UTTR1147A or placebo.

Two people received placebo treatment in every group.

Study groups, treatment dose, and schedule of treatment:

Group	People	Dose	Treatment Day
A	8 healthy volunteers	30 µg/kg once every 4 weeks	Day 1, Day 29, Day 57
B	8 healthy volunteers	60 µg/kg once every 4 weeks	Day 1, Day 29, Day 57
C	8 patients with UC	60 µg/kg once every 4 weeks	Day 1, Day 29, Day 57
D	8 healthy volunteers	60 µg/kg once every 2 weeks	Day 1, Day 15, Day 29, Day 43, Day 57, Day 71
E	8 patients with UC	60 µg/kg once every 2 weeks	Day 1, Day 15, Day 29, Day 43, Day 57, Day 71
F	8 healthy volunteers	90 µg/kg once every 2 weeks	Day 1, Day 15, Day 29, Day 43, Day 57, Day 71
G	6 healthy volunteers	30 µg/kg **bolus** every 4 weeks	Day 1, Day 29, Day 57
H	7 patients with CD	60 µg/kg once every 4 weeks	Day 1, Day 29, Day 57
K	8 patients with UC	90 µg/kg once every 2 weeks	Day 1, Day 15, Day 29, Day 43, Day 57, Day 71

Having different groups allowed researchers to study the effects of:

- Health (healthy volunteers versus patients).
- Doses (30 µg/kg to 90 µg/kg).
- Treatment delivery time (1 minute versus 1 hour)
- Treatment frequency (every 2 weeks versus every 4 weeks)

How did people receive their treatments?

People in Group G received their dose all at once – a "**bolus injection**" – in their intravenous (IV) tube over a **1-minute** period.

People in all other groups received their IV treatment through a pump that delivered the entire dose over a period of approximately **1 hour**.

What happened after treatment started?

Study participants received treatments up Day 57 or Day 71, according to the group they had joined. They came to the clinic on certain days – before, during, and after receiving their treatments.

During each visit to the clinic, people gave blood samples and underwent other tests for the study. They answered questions so researchers could learn about effects of the treatments. Doctors managed any side effects that people experienced.

4. What were the results of the study?

Many people completed the study, including 23 of 38 healthy volunteers (61%), 17 of 24 patients with UC (71%), and 5 of 7 patients with CD (71%).

Question 1: Was UTTR1147A safe for people?

Healthy volunteers could tolerate UTTR1147A up to 60 µg/kg when administered slowly. The bolus injection was not tolerable.

Patients with UC tolerated every dose they received – "90 µg/kg once every 2 weeks" was the highest dose they received.

Patients with CD tolerated every dose that they received – 60 µg/kg once every 4 weeks.

Question 2: What happens to UTTR1147A inside the body?

Researchers found that UTTR1147A behaved differently in the body of healthy volunteers versus patients.

UTTR1147A stayed in the body of healthy volunteers for a longer duration than it did in the body of patients with UC.

Patients with UC or CD had lower medicine concentrations in their body in comparison to healthy volunteers – when comparing the same dose groups.

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.

- 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.

During this study, there were no serious side effects thought to be caused by the study treatment.

There were no deaths on this study.

Most common side effects

There were several side effects thought to be caused by the study treatment that were not serious. The most common side effects are shown in the following table. Some people had more than one side effect – this means that they are included in more than one row in the table:

	Healthy volunteers	Patients with UC	Patients with CD
People with side effects thought to be caused by the study treatment	29 people (76%)	24 people (100%)	5 people (71%)
Total number of side effects	124	114	25
Most common side effects caused by the study treatment:			
Dry skin	21 people (55%)	17 people (71%)	5 people (71%)
Dry lip	19 people (50%)	14 people (58%)	5 people (71%)
Redness of the skin (erythema)	12 people (32%)	8 people (33%)	1 person (14%)
Skin discomfort	9 people (24%)	7 people (29%)	1 person (14%)
Skin peeling (exfoliation)	9 people (24%)	3 people (13%)	1 person (14%)
People who stopped treatment because of side effects	4 people (11%)	1 person (4%)	None (0%)

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 69 people.

This study provided researchers with information about UC and CD, and UTTR1147A.

Results from this study led to the launch of another study (Phase 2) to further assess the effectiveness of UTTR1147A in patients with UC or CD.

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7. Are there plans for other studies?

At the time of writing this summary, other studies investigating UTTR1147A were underway.

8. Where can I find more information?

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

https://clinicaltrials.gov/ct2/show/results/NCT02749630

https://forpatients.roche.com/en/trials/autoimmune-disorder/ulcerative-colitis/a-safety-study-of-intravenously-administered-uttr1147a-in-health.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:

> "An observer-blinded, placebo-controlled, multiple ascending, dose-escalation study to explore the safety, tolerability, pharmacokinetics, and pharmacodynamics of repeat intravenous administrations of UTTR1147A in healthy volunteers and patients with ulcerative colitis, and patients with Crohn's Disease".

- The protocol number for this study is **GA29469**.
- The ClinicalTrials.gov identifier for this study is **NCT02749630**.
- The EudraCT number for this study is **2015-002512-32**.