Clinical Trial Results – Layperson Summary

A study to compare the safety and effectiveness of etrolizumab with infliximab in people with "ulcerative colitis," a long-term illness where the lower part of the gut is inflamed

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), written for:

- Members of the public, and
- People who took part in the study.

This summary is based on information known at the time of writing (October 2021). More information may now be known.

The study started in December 2014 and finished in June 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 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 study medicine and a long-term illness called ulcerative colitis, an inflammatory bowel disease where the lower part of the gut is inflamed.

Key information about this study

Key methods	Key findings
• This study was done to compare the study medicine, called etrolizumab, with another medicine, called infliximab, in people with ulcerative colitis. • In this study, people received either a combination of etrolizumab and a placebo, or a combination of infliximab and a placebo—it was decided by chance using a computer which treatment each person was given. • This study included 397 people in 20 countries.	• The main finding was that in people with ulcerative colitis, etrolizumab did not reduce inflammation in the gut or symptoms of ulcerative colitis significantly better than infliximab. • Around 2% of people who received etrolizumab had serious side effects that the study doctor considered to be related to the treatment, compared with around 4% of people who received infliximab. • At the time of writing this summary, the study has concluded. No new information is being collected.

1. General information about this study

Why was this study done?

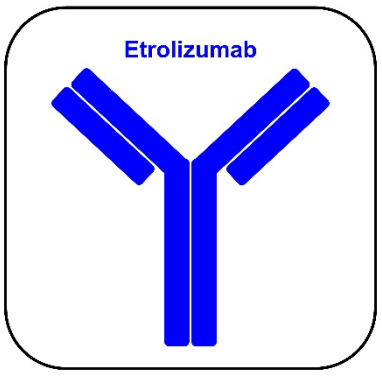
Ulcerative colitis is a long-term illness where the lower part of the gut becomes inflamed, causing ulcers to form. People with ulcerative colitis often experience diarrhea with blood, stomach cramps, and the urgent need to have a bowel movement. These painful and debilitating symptoms can get in the way of sleep, social activities, and other daily activities.

There are different types of medicines available to help treat ulcerative colitis and its symptoms. These medicines often do not work for everyone, or don't work for a long time in some people with ulcerative colitis, so researchers are looking at new medicines that work in other ways.

This study looked at etrolizumab, which works differently in the body than existing medicines, such as infliximab. The study doctors wanted to find out if etrolizumab was more effective at reducing inflammation and symptoms of ulcerative colitis than infliximab. They also wanted to find out how safe etrolizumab was.

What were the study medicines?

A medicine called etrolizumab was the focus of this study.



It works in a different way than infliximab.

- You say this as "et – roe – liz – oo – mab."
- Etrolizumab is a type of protein called an antibody. It works by sticking to and blocking a second protein, called β7. You say this as "bay-tuh seh-ven."
    - This prevents the movement of inflammatory cells into the gut and decreases inflammatory processes in the gut.
        - Etrolizumab is given as an injection under the skin.

"Infliximab" is an existing medicine given to people with ulcerative colitis.

- You say this as "in – flick – sih – mab."
- Infliximab works by attaching to a protein in the body called tumor necrosis factor alpha (or TNF-alpha for short).
    - TNF-alpha helps the body fight infections, but too much TNF-alpha can damage the gut. Some researchers think that people with ulcerative colitis produce too much TNF-alpha in their bodies.
    - Infliximab attaches to TNF-alpha and stops TNF-alpha from damaging the gut.
- In this study, infliximab was given as an injection into the vein.

What did researchers want to find out?

Researchers did this study to compare etrolizumab with an existing medicine called infliximab to see how well the study medicine worked (see section 4, "What were the results of the study?").

They also wanted to find out how safe the medicine was, by checking how many people had side effects when taking each of the medicines during this study (see section 5, "What were the side effects?").

The main questions that researchers wanted to answer were:

1. Was etrolizumab more effective in reducing inflammation and symptoms of ulcerative colitis than infliximab?
2. Did people who received etrolizumab have any side effects, and if so, what were they? Were there any differences in side effects between people who received etrolizumab and infliximab?

What kind of study was this?

This study was a “phase 3” study. This means that etrolizumab had been tested in a smaller number of people with ulcerative colitis before this study (called a “phase 2” study). In this phase 3 study, a larger number of people with ulcerative colitis received either etrolizumab or infliximab (a standard treatment for ulcerative colitis). This was to find out about the side effects of etrolizumab and to see if etrolizumab was more effective in reducing inflammation and symptoms of ulcerative colitis than infliximab.

The study was “randomized.” This means that it was decided by chance, like tossing a coin, which of the two treatments, either etrolizumab and placebo or infliximab and placebo, people in the study would receive. This was done by a computer.

The was a “double-blind” study. This means that neither the people taking part in the study, nor the study doctors, knew which of the study medicines people were taking. “Blinding” of a study is done so that the person does not know which treatment they are receiving and what effect of the treatment to expect.

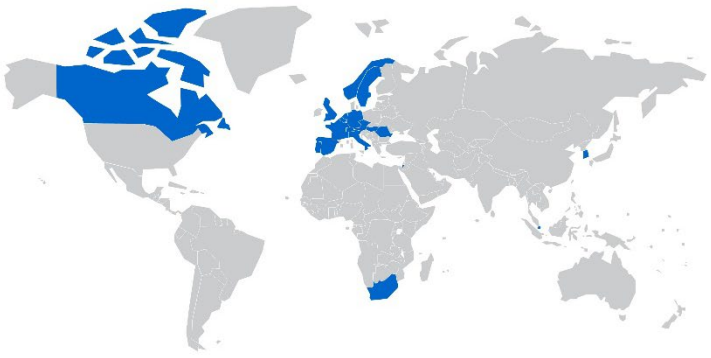
This was also a “double-dummy” study, which compares treatments that have a different appearance or look different. This is done so people do not know which treatment they are receiving based on what it looks like or how they receive it. In this study, each person received two treatments that look similar: an injection under the skin and an injection into a vein—one of these had the active treatment and the other had no medicine (placebo).

When and where did the study take place?

The study started in December 2014 and finished in June 2020. This summary was written after the study had ended.

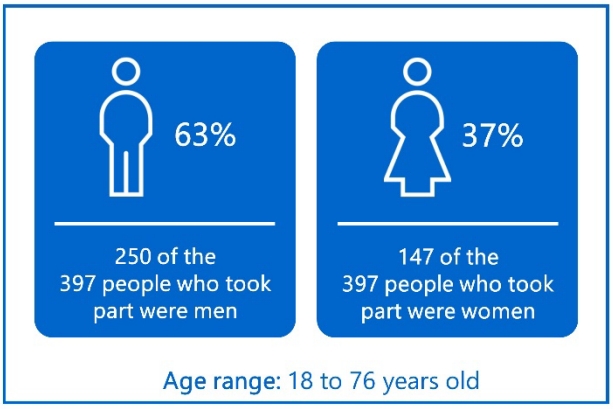
The study took place at 119 study centers worldwide, across 20 countries in Africa, Asia, Europe, the Middle East, and North America. The following map shows the countries where this study took place.

- Austria
- Belgium
- Canada
- Czech Republic
- France
- Germany
- Hungary
- Israel
- Italy
- Korea
- Netherlands
- Norway
- Portugal
- Romania
- Singapore
- South Africa
- Spain
- Sweden
- Switzerland
- United Kingdom



2. Who took part in this study?

More information on the 397 people with ulcerative colitis who participated in this study is given below.



People **could** take part in the study if they:

- Were adults aged 18 to 80 years old
- Had been diagnosed with moderate to severe ulcerative colitis more than 3 months before starting the study
- Had received treatments for ulcerative colitis that didn't work—or that were not well tolerated.

People **could not** take part in the study if they had:

- A history of certain stomach and gut problems, such as a past or present abnormal connection between two parts of the gut (called a fistula) or a painful collection of pus (called an abscess) in their abdomen, colon polyps that appear to be cancerous (colonic mucosal dysplasia), or a narrowed large intestine, or infections such as HIV, hepatitis B or C, or tuberculosis (to avoid potential safety issues)
- Previously taken certain medicines, such as corticosteroid enemas or suppositories, 5-aminosalicylate rectal preparations, or anti-TNF therapy (including infliximab) or anti-integrin therapy (including vedolizumab or natalizumab)
- Surgery to treat their ulcerative colitis or other stomach or gut problems, including surgery to remove part of the colon to remove cancer (colonic resection or colectomy), or surgery to divert part of the intestine through the abdomen wall (ileostomy or colostomy).

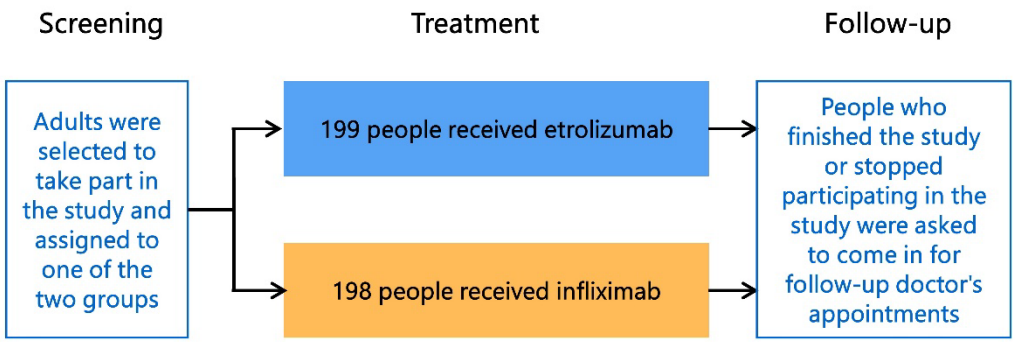
3. What happened during the study?

During the study, people were selected by chance to receive one of two active treatments and a placebo of the other treatment. The treatments were selected at random by a computer.

The treatment groups were:

- **Etrolizumab (the study medicine) group:** 105 milligrams of etrolizumab injected just under the skin once every 4 weeks and placebo by drip (infusion) at weeks 0, 2, and 6, and then every 8 weeks. People received both treatments so that they would not be able to tell if they received etrolizumab or infliximab.
    - 199 people were randomly assigned to this group.
- **Infliximab (existing medicine) group:** 5 milligrams for each kilogram of body weight of infliximab given by drip (infusion) at weeks 0, 2, and 6, and then every 8 weeks, and placebo was injected under the skin once every 4 weeks so people in the infliximab group would not be able to tell if they were receiving etrolizumab or infliximab.
    - 198 people were randomly assigned to this group.

People in the study attended the study center to receive the treatments for up to 52 weeks. When the study finished, the people who took part were asked to go back to their study center for transfer to another study, called an open-label study, where they continued to receive etrolizumab or had follow-up visits to check their overall health. Look below to see more information about what happened in the study.



4. What were the results of the study?

Was etrolizumab more effective in reducing inflammation and symptoms of ulcerative colitis than infliximab?

Researchers looked at whether people who received etrolizumab had inflammation and symptoms that improved at 10 weeks and if the improvement in those people was also observed at week 54. They compared the improvement in people who received etrolizumab to the improvement in the people who received infliximab, to see if etrolizumab improved symptoms significantly more than infliximab. About 2 in 10 people (19%) who received the combination of etrolizumab and placebo had improved symptoms of ulcerative colitis at 10 weeks and continued to have no symptoms after around 1 year (54 weeks). This was compared with 2 in 10 people (20%) who received the combination of infliximab and placebo who had the same improvements. This suggests that etrolizumab did not improve symptoms significantly more than infliximab.

On average, the number of people who received etrolizumab whose ulcerative colitis symptoms improved was not higher than those who received infliximab.

5. What were the side effects?

Side effects (also known as "adverse reactions") are unwanted medical problems (such as a headache) that happen during a study.

- Only side effects that the study doctor believed were related to the study treatments are described below.

Serious and common side effects are listed in the following sections.

Serious side effects that the study doctor believed were related to the treatment

A side effect is considered "serious" if it is life-threatening, needs hospital care, or causes lasting problems.

During this study, 2 out of 100 people (2%) who received etrolizumab had at least one serious side effect, compared with 4 out of 100 people (4%) who received infliximab. The most common serious side effects in people who received etrolizumab were a collection of pus (called an "abscess") in the anus, inflammation of the colon due to viral infection, inflammation of the testicles, pneumonia, and serious reaction to an infection, sometimes called "blood poisoning" or "sepsis." The most common serious side effects in the infliximab group were meningitis, allergic reaction, blood clot in the back of the eye, increased inflammation and symptoms of ulcerative colitis, and reddening of the skin.

During the study, some people decided to stop taking their medicine because of side effects that the study doctor believed were related to the study treatment.

- In the etrolizumab group, 2 out of 100 people (2%) stopped receiving treatment for related side effects.
- In the infliximab group, 8 out of 100 people (8%) stopped receiving treatment for related side effects.

Most common side effects that the study doctor believed were related to study treatment

During this study, around 18 out of every 100 people (18%) who received etrolizumab had a side effect that was not considered serious, compared with 23 out of every 100 people (23%) who received infliximab. In the etrolizumab group, the most common side effects were headache, rash, and increased inflammation and symptoms of ulcerative colitis. In the infliximab group, the most common side effects were a cold, reaction to receiving the treatment, increased inflammation and symptoms of ulcerative colitis, joint pain, allergic reaction, and respiratory tract infection.

Other side effects

You can find information about other side effects (not shown in the sections above, such as side effects that doctors did not consider to be related to etrolizumab) on the websites listed at the end of this summary – see section 8 (Where can I find more information?).

6. How has this study helped research?

The information presented here is from a single study of 397 people with ulcerative colitis. These results helped researchers learn more about ulcerative colitis and etrolizumab.

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 than those 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.

7. Are there plans for other studies?

At the time of writing this summary (October 2021), the study has been completed and no more information is being collected. The main finding of this study was that in people with ulcerative colitis, etrolizumab did not significantly reduce inflammation in the gut or symptoms of ulcerative colitis compared with infliximab. Around 2% of people who received etrolizumab had serious side effects that the study doctor considered to be related to the treatment, compared with around 4% of people who received infliximab.

Other phase 3 studies looking at the safety and effects of etrolizumab in people with ulcerative colitis who have not received TNF inhibitors (such as infliximab) have taken place.

Currently, etrolizumab is being studied in adults with Crohn’s disease.

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/NCT02136069
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2013-004282-14/results
- https://forpatients.roche.com/en/trials/autoimmune-disorder/ulcerative-colitis/a-study-comparing-the-efficacy-and-safety-of-etrolizumab-to-infl.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/trials/autoimmune-disorder/ulcerative-colitis/a-study-comparing-the-efficacy-and-safety-of-etrolizumab-to-infl.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 F. Hoffmann-La Roche Ltd., which has its headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: “A study comparing the efficacy and safety of etrolizumab to infliximab in participants with moderate to severe ulcerative colitis who are naïve to tumor necrosis factor (TNF) inhibitors.”

The study is known as “GARDENIA.”

- The protocol number for this study is: GA29103.
- The ClinicalTrials.gov identifier for this study is: NCT02136069.
- The EudraCT number for this study is: 2013-004282-14.