# Clinical Trial Results – Layperson Summary

## A study to compare etrolizumab with placebo in people with "ulcerative colitis," a long-term illness where the lower part of the gut is inflamed, who have been treated with tumor necrosis factor inhibitors

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 May 2014 and finished in April 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

- This study was done to compare the study medicine, called "etrolizumab," with a placebo, which looked the same as the study medicine, but did not contain any real medicine. The study looked at people with ulcerative colitis after they had received treatment with one or more tumor necrosis factor (or TNF for short) inhibitors drugs.
- In this study, people received either etrolizumab or a placebo. It was decided by chance using a computer which treatment each person was given.
- This study included 609 people in 24 countries.

### Key findings

- The main finding was that more people who received etrolizumab (2 out of 10 people) had reduced inflammation of their gut and symptoms of ulcerative colitis after 14 weeks of treatment than those who received placebo (1 out of 10 people).
- Of those people who originally had improved inflammation and symptoms after etrolizumab treatment, a similar number of people treated with etrolizumab or placebo had improved inflammation and symptoms after 16 months of treatment (about 2 out of 10 people).
- In the first part of the study, less than 1% of people (fewer than 1 out of 100 people) who received etrolizumab had serious side effects that the study doctor considered to be related to the treatment, compared with 0% of people who received placebo.
- In the second part of the study, the number of people whose ulcerative colitis symptoms and inflammation were reduced after longer treatment was similar between those who received etrolizumab and placebo.
- 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.

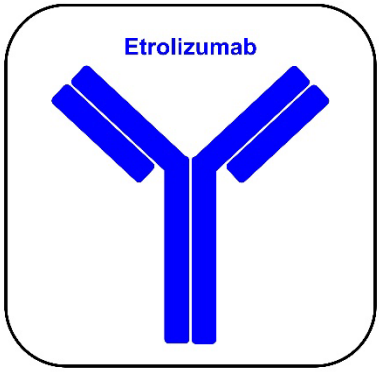
There are several treatments available for ulcerative colitis:

- Medicines that reduce inflammation ("corticosteroids")
- Medicines that reduce the general activity of the immune system ("immunosuppressants")
- Medicines that affect only the immune cells thought to cause ulcerative colitis so there is less damage to healthy cells ("targeted therapies")
- In people with ulcerative colitis, these medicines may work in the short term, but in some patients might stop working, so researchers are looking at new medicines that work in other ways and for longer.

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

## What is the study medicine?

A medicine called etrolizumab was the focus of this study.




- 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.

Etrolizumab was compared with a "placebo."

- You say this as "plah – see – bo."
- The placebo looked the same as etrolizumab but did not contain any real medicine. This means it had no medicine-related effect on the body.
- Researchers compared etrolizumab with a placebo so they could show which benefits or side effects are actually caused by the medicine.

For the purpose of this study, etrolizumab and placebo are both referred to as "treatments."

## What did researchers want to find out?

Researchers did this study to compare etrolizumab with a placebo – 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. How many people had their ulcerative colitis inflammation and symptoms reduced after receiving etrolizumab or placebo for 14 weeks?
2. How many people had their ulcerative colitis inflammation and symptoms reduced after longer treatment during Part 2 of the study
3. Did people who received etrolizumab have any side effects, and if so, what were they?

## 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 a placebo. This was to find out about the side effects of etrolizumab and if etrolizumab reduced inflammation and symptoms after short-term or long-term treatment.

The study was "randomized." This means that it was decided by chance, like tossing a coin, whether people in the study would receive etrolizumab or placebo. This was done by a computer.

This was a "double-blind" study. This means that neither the people taking part in the study, nor the study doctors, knew whether people received etrolizumab or placebo. "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.

## When and where did the study take place?

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

The study took place at 184 study centers, across 24 countries in Africa, Asia, Europe, the Middle East, North America, and South America. The following map shows the countries where this study took place.

- Argentina
- Australia
- Austria
- Belgium
- Brazil
- Canada
- Czech Republic
- Denmark
- France
- Germany
- Greece
- Hungary
- Israel
- Italy
- Korea
- Lithuania
- Mexico
- Netherlands
- Poland
- Romania
- Spain
- Switzerland
- United Kingdom
- United States

## 2. Who took part in this study?

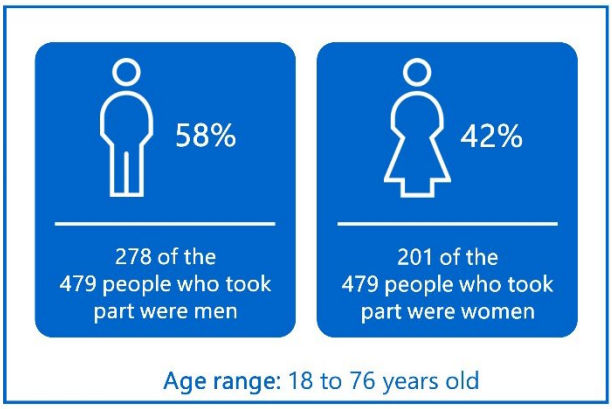
There were two parts to this study (see section 3, "What happened during the study?").

In the first part, there were two groups of people with ulcerative colitis.

- Group 1 consisted of 130 people with ulcerative colitis. All of the people knew that they received etrolizumab.
- Group 2 consisted of 479 people who were "blinded." This means that they did not know if they received etrolizumab or placebo.

The results reported here focus on Group 2.

People who took part in the study were between 18 and 76 years old. 278 of the 479 people (58%) were men and 201 of the 479 people (42%) were women.




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

- Were 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 anti-TNF drugs within 5 years of starting the study.

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, anti-integrin therapy (including vedolizumab or natalizumab), or anti-adhesion molecule therapy
- 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 treatments. The treatments were selected at random by a computer. People received the treatments at the study center.

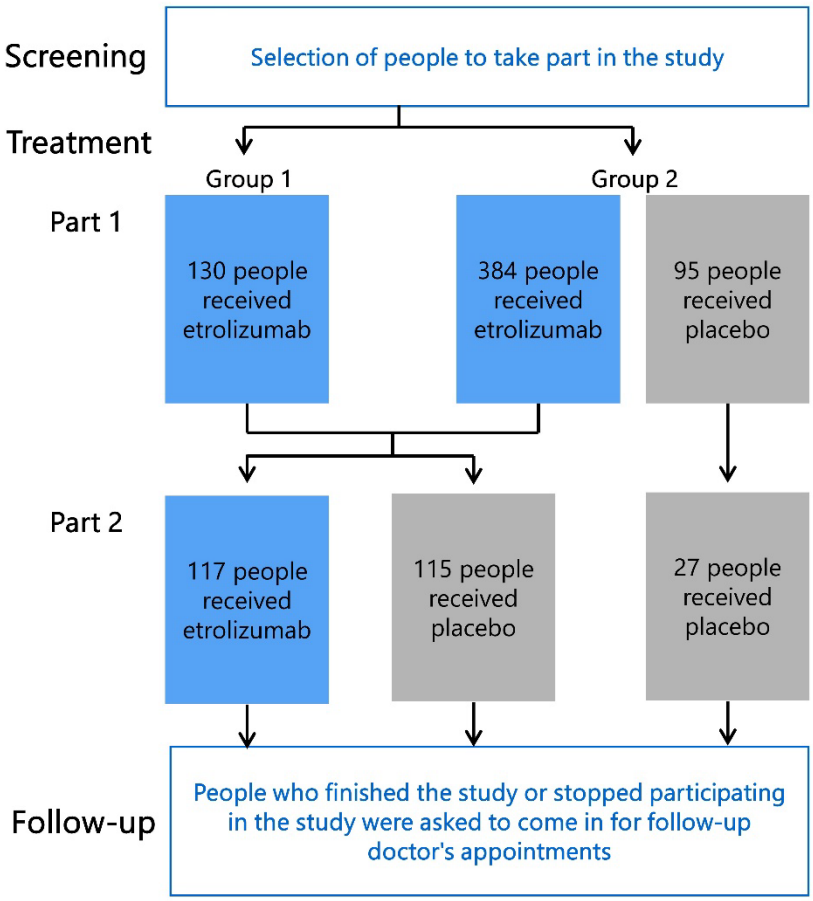
The treatment groups were:

- **Etrolizumab (the study medicine) group:** 105 milligrams injected just under the skin once every 4 weeks
- **Placebo group:** injected under the skin every 4 weeks.

There were two parts to this study:

- **Part 1: this lasted about 3 months (14 weeks)**
  - People received etrolizumab (Group 1)
  - People received either etrolizumab or placebo (Group 2)
- **Part 2: this lasted about 12 months (52 weeks)**
  - People from Group 1 and Group 2 who received etrolizumab and had their inflammation and symptoms reduced by the end of Part 1 received either etrolizumab or a placebo in Part 2 of the study
  - People from Group 2 who received placebo and had their inflammation and symptoms reduced by the end of Part 1 received placebo in Part 2 of the study.

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?

### Question 1: How many people had their ulcerative colitis inflammation and symptoms reduced after receiving etrolizumab or placebo for 14 weeks?

In the first part of the study, researchers looked at how many people had their ulcerative colitis inflammation and symptoms significantly reduced after the start of treatment (about 3 months after treatment started). About 2 in 10 people (19%) who received etrolizumab had their symptoms significantly reduced after the start of treatment. This compares with less than 1 in 10 people (6%) who received placebo.

**In the first part of the study, more people who received etrolizumab had less inflammation and improved symptoms compared with those who received placebo.**

### Question 2: How many people had their ulcerative colitis inflammation and symptoms reduced after longer treatment during Part 2 of the study?

In the second part of the study, researchers also looked at how many people had reduced inflammation and symptoms of ulcerative colitis after 16 months of treatment with etrolizumab. People who received etrolizumab in the first part of the study and saw improvement in symptoms were randomized to either etrolizumab or placebo. About 2 in 10 people (24%) who received etrolizumab in both parts of the study had their ulcerative colitis inflammation and symptoms reduced after longer treatment. This compares with 2 in 10 people (20%) who received etrolizumab in the first part of the study and placebo in the second part.

**In the second part of the study, the number of people whose ulcerative colitis symptoms and inflammation were reduced after longer treatment was similar between those who received etrolizumab or placebo.**

## 5. What were the side effects?

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

- Only the 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 the first part of this study, less than 1 out of 100 people (less than 1%) in Group 2 who received etrolizumab had at least one serious side effect compared with 0 out of 100 (0%) people who received placebo. The only serious side effects in people who received etrolizumab were swollen lips and unspecified viral infection.

During the first part of 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, less than 1 out of 100 people (less than 1%) in Group 2 stopped receiving etrolizumab due to related side effects.
- In the placebo group, there were no people in Group 2 who stopped receiving treatment due to related side effects.

During the second part of this study, less than 1 out of 100 people (less than 1%) who received etrolizumab in both parts of the study experienced a serious side effect. The serious side effect was pneumonia.

In people who received etrolizumab in the first part of the study and placebo in the second part, around 3 out of 100 people (3%) had a serious side effect. These side effects were a bacterial gastrointestinal infection known as *Clostridium difficile*, a viral infection known as cytomegalovirus, pneumonia, and swelling of the legs or hands.

There were no people who received placebo in both parts of the study who had a serious side effect.

During the second part of 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 people who received etrolizumab in both parts of the study, less than 1 out of 100 people (less than 1%) stopped receiving etrolizumab due to related side effects.
- In the people who received etrolizumab in the first part of the study and placebo in the second part, no one stopped receiving treatment due to related side effects.
- In the people who received placebo in both parts of the study, 1 out of 27 people (4%) stopped receiving treatment due to related side effects.

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

In the first part of this study, around 15 out of every 100 people (15%) who received etrolizumab in Group 2 had a side effect that was not considered serious compared with around 16 out of 100 (16%) of people who received placebo.

The most common side effects in people who received etrolizumab in Group 2 were headache, dizziness, joint pain, redness at the injection site, itchy skin, and nausea. The most common side effects in people who received placebo in Group 2 were redness at the injection site and headache.

In the second part of this study, around 21 out of every 100 people (21%) who received etrolizumab in both parts of the study had at least one side effect that was not considered serious. The most common side effects in this group were redness at the injection site and rash.

In people who received etrolizumab in the first part of the study and placebo in the second part, around 19 out of 100 people (19%) had at least one side effect that was not considered serious. The most common side effect in this group was itchy skin, chest pain that was not related to heart problems, redness at the injection site, cold, and headache.

In people who received placebo in both parts of the study, around 22 out of 100 people (22%) had at least one side effect that was not considered serious. The most common side effects in this group were headache and redness at the injection site.

## 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 609 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 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, the study has been completed and no more information is being collected. The main finding of this study was that more people who received etrolizumab (2 out of 10 people) had reduced inflammation of their gut and symptoms after 14 weeks of treatment than those who received placebo (1 out of 10 people). Of those people who originally had improved inflammation and symptoms after etrolizumab treatment, a similar number of people treated with etrolizumab or placebo had improved inflammation and symptoms after 16 months of treatment (about 2 out of 10 people).

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, researchers are studying etrolizumab 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/NCT02100696
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2013-004278-88/results
- https://forpatients.roche.com/en/trials/autoimmune-disorder/ulcerative-colitis/a-study-of-the-efficacy-and-safety-of-etrolizumab-in-ulcerative-.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-of-the-efficacy-and-safety-of-etrolizumab-in-ulcerative-.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 of the efficacy and safety of etrolizumab in participants with ulcerative colitis who have been previously exposed to tumor necrosis factor (TNF) inhibitors.”

The study is known as “HICKORY.”

- The protocol number for this study is: GA28950.
- The ClinicalTrials.gov identifier for this study is: NCT02100696.
- The EudraCT number for this study is: 2013-004278-88