

## Summary of Clinical Trial Results

### A study that looked at the long-term safety and effectiveness of treatment with etrolizumab 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 (March 2024).

The study started in September 2014 and stopped early – in October 2023 – after the sponsor decided not to apply for regulatory approval for etrolizumab in adults with ulcerative colitis because the medicine did not work as well as expected across primary studies.

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.**

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#### Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about a long-term illness called “ulcerative colitis,” an inflammatory bowel disease where the lower part of the gut is inflamed, and the medicine studied – ‘etrolizumab’.

## Key information about this study

- This study was done to find out how well long-term treatment with etrolizumab worked in people with ulcerative colitis and how safe long-term treatment with etrolizumab was in these people.
- This was an 'open label extension' study, which means that people who had taken etrolizumab or a different treatment as part of a previous study were given long-term treatment with etrolizumab in this study.
- This study was conducted in 2 parts. In Part 1, people were given long-term treatment with etrolizumab for up to 9 years. In Part 2, people were followed to monitor for side effects for 92 weeks after they stopped taking etrolizumab.
- The main finding was that around 6 in every 10 people (58%) who completed 108 weeks of the study in Part 1 had remission (ie, no symptoms) of ulcerative colitis at 108 weeks.
- Around 2 in every 10 people (21%) had at least one serious side effect during long-term etrolizumab treatment in Part 1. Fewer than 1 in every 100 people (<1%) had at least one serious side effect after stopping etrolizumab in Part 2.
- This study stopped early after the sponsor decided not to apply for regulatory approval for etrolizumab in adults with ulcerative colitis because the medicine did not work as well as expected across primary studies.

## 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 (the colon) becomes inflamed, causing ulcers to form. People with ulcerative colitis often experience diarrhoea 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. Researchers wanted to find out how well etrolizumab worked in the long term in people with ulcerative colitis. They also wanted to find out how safe etrolizumab was in the long term in these people.

## What was the medicine being studied?

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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  $\beta 7$ . 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.

## What did researchers want to find out?

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- Researchers had previously done multiple studies to compare etrolizumab with a placebo (which looked like the study medicine but did not contain any real medicine) or other medicines.
- In this study, some of the people who had taken part in one of the previous studies continued taking etrolizumab on a long-term basis. People who had received a placebo or a different medicine in one of the previous studies could start treatment with etrolizumab in this study.
- Researchers wanted to gather long-term information on etrolizumab:
  - How well etrolizumab worked in the long term
  - How safe etrolizumab was in the long term
  - Whether any people had side effects after stopping etrolizumab.

### **The main questions that researchers wanted to answer were:**

1. How many people had remission (ie, no symptoms) of ulcerative colitis after 108 weeks of treatment with etrolizumab?
2. How many people had side effects during long-term treatment with etrolizumab, and how many of these side effects were serious?
3. How many people had side effects after stopping etrolizumab?

## What kind of study was this?

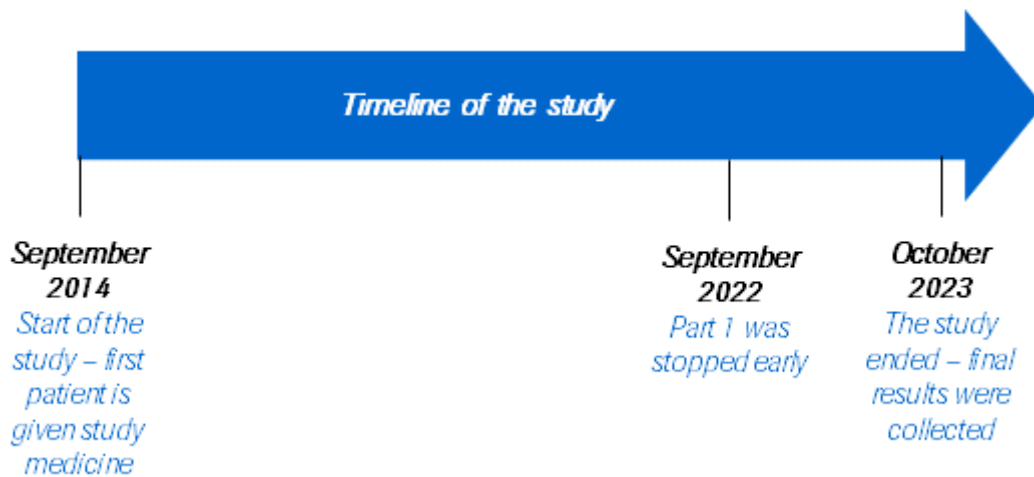
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This was a Phase 3 ‘open-label extension’ study. This means that people who had taken part in a previous study of etrolizumab compared with a placebo or a different medicine continued or started receiving etrolizumab in this study. Both the people taking part and the study doctors knew that the medicine people were receiving was etrolizumab.

## When and where did the study take place?

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The study started in September 2014 and stopped early after the sponsor decided not to apply for regulatory approval for etrolizumab in adults with ulcerative colitis because the medicine did not work as well as expected across primary studies. This summary presents the results of the study up until it was stopped in October 2023.



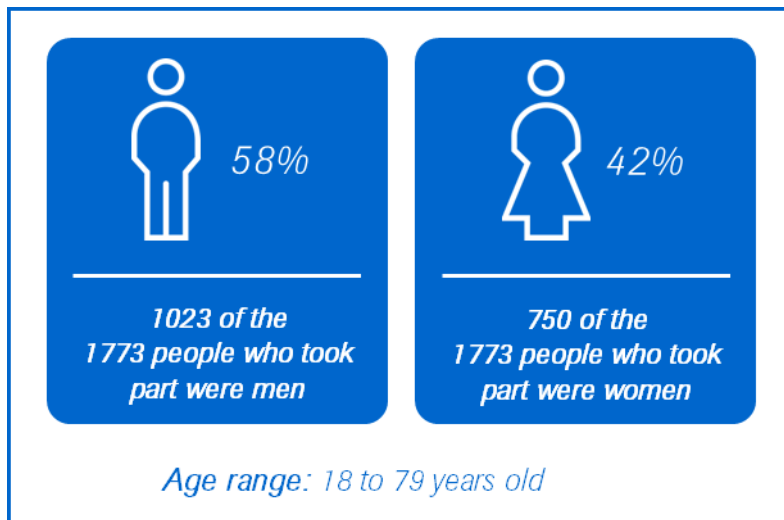
The study took place at 409 study centres – across 42 countries worldwide. The following map shows the countries where this study took place.



## 2. Who took part in this study?

In this study, 1822 people with ulcerative colitis took part. 1773 people took part in Part 1 and 796 people took part in Part 2.

More information on the people who took part is given below.



People could take part in the study if:

- They had been diagnosed with moderately to severe ulcerative colitis
- They had participated in a previous study investigating etrolizumab
  - To participate in Part 1, people had to have finished treatment in the previous study, or had not responded well or had worsening of disease symptoms during treatment in the previous study
  - To participate in Part 2, people had to have participated in Part 1, or were not eligible for or chose not to participate in Part 1

People could not take part in the study if:

- They left the previous study earlier than Week 10

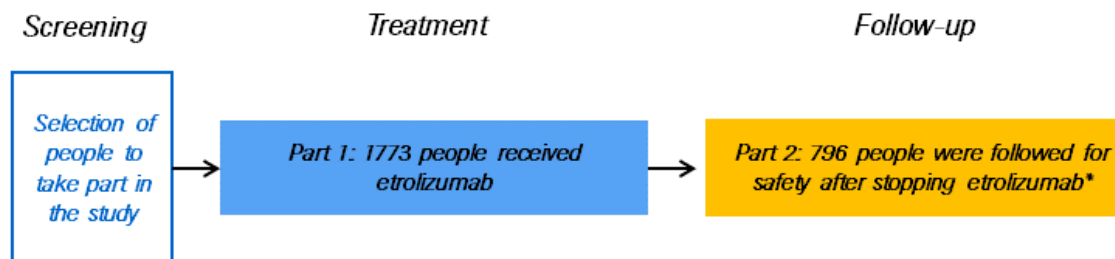
### 3. What happened during the study?

There were two parts to this study. People in Part 1 were treated with etrolizumab every 4 weeks for up to 9 years, regardless of the treatment they received when they took part in 1 of the original studies, and were then monitored for side effects for a further 12 weeks. People who participated in Part 1 were encouraged to participate in Part 2, during which no etrolizumab was given. People in Part 2 were monitored for side effects for 92 weeks.

- In Part 1, people received etrolizumab 105 mg injected subcutaneously (ie, under the skin) every 4 weeks.
- In Part 2, people did not receive treatment with etrolizumab.

The total length of the study was initially planned to be approximately 9 years. However, the study was discontinued early because the sponsor decided not to apply for regulatory approval for etrolizumab in adults with ulcerative colitis. Part 1 was approximately 8 years long and continued until September 2022. Following Part 1, people entered Part 2 for a period of 92 weeks. Part 2 was also discontinued early, and the last patient had their last follow-up visit in October 2023.

More information about what happened in the study is described below.



\*Including 747 people who participated in Part 1, and 49 people who entered Part 2 without participating in Part 1.

## 4. What were the results of the study?

**Question 1:** How many people had remission (ie, no symptoms) of ulcerative colitis after 108 weeks of treatment with etrolizumab?

In Part 1, researchers looked at the number of people who experienced remission of ulcerative colitis symptoms after 108 weeks of treatment with etrolizumab. Among people who completed 108 weeks of the study, 362 of 623 people (58%) had remission of ulcerative colitis symptoms.



*Around 6 in every 10 people (58%) in Part 1 had remission of ulcerative colitis symptoms at 108 weeks*

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 happen during 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.
- 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, around 2 in every 10 people (21%) had at least one serious side effect during long-term etrolizumab treatment in Part 1. Fewer than 1 in every 100 people (less than 1%) had serious side effects after stopping etrolizumab in Part 2.

The six most common serious 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.

<b>Serious side effects reported in this study</b>	<b>Part 1: people taking etrolizumab</b> (1773 people total)	<b>Part 2: people who had stopped etrolizumab</b> (796 people total)
Ulcerative colitis flare-up	7% (131 out of 1773)	Less than 1% (1 out of 796)
Low number of red blood cells	1% (17 out of 1773)	0% (0 out of 796)
COVID-19	< 1% (14 out of 1773)	Less than 1% (1 out of 796)
Inflammation of the appendix	< 1% (11 out of 1773)	0% (0 out of 796)
Lung infection (pneumonia)	< 1% (10 out of 1773)	0% (0 out of 796)
Kidney stones	< 1% (10 out of 1773)	0% (0 out of 796)

In studies, people may die due to side effects that may be related to the study:

- In Part 1, 9 out of 1773 people (less than 1%) died. However, no people died because of side effects thought to be related to the study medicine.
- In Part 2, 1 out of 796 people (less than 1%) died. However, no people died because of side effects thought to be related to the study medicine.

During the study, some people decided to stop taking their medicine because of side effects:

- In Part 1, 234 out of 1773 people (13%) stopped taking their medicine because of side effects.

### **Most common side effects**

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During this study, around 8 out of every 10 people (81%) in Part 1 had at least one side effect (including serious side effects and side effects that were not considered serious) during treatment with etrolizumab. Side effects were thought to be related to the study medicine in around 2 out of every 10 people (15%) in Part 1. Fewer than 1 out of every 100 people (less than 1%) in Part 2 had at least one side effect after stopping etrolizumab. However, no people had side effects that were thought to be related to the study medicine in Part 2.

The five 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.

<b>Most common side effects reported in this study</b>	<b>Part 1: people taking etrolizumab</b> (1773 people total)	<b>Part 2: people who had stopped etrolizumab</b> (796 people total)
Ulcerative colitis	38% (676 out of 1773)	Less than 1% (3 out of 796)
Sore throat and runny nose	13% (226 out of 1773)	0% (0 out of 796)
COVID-19	10% (180 out of 1773)	Less than 1% (1 out of 796)
Low number of red blood cells	8% (141 out of 1773)	0% (0 out of 796)
Headache	8% (135 out of 1773)	0% (0 out of 796)

## 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 1822 people with ulcerative colitis. These results helped researchers learn more about the long-term effects of etrolizumab in people with ulcerative colitis.

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, no more studies looking at etrolizumab are planned at the current time.



## 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/NCT02118584>
- <https://www.clinicaltrialsregister.eu/ctr-search/search?query=2013-004435-72>
- <https://forpatients.roche.com/en/trials/autoimmune-disorder/ulcerative-colitis/study-for-participants-with-ulcerative-colitis-previously-enroll.html>

### Who can I contact if I have questions about this study?

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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/study-for-participants-with-ulcerative-colitis-previously-enroll.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 organised and paid for this study?

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This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.

### Full title of the study and other identifying information

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The full title of this study is: “An Open-Label Extension and Safety Monitoring Study of Moderate to Severe Ulcerative Colitis Patients Previously Enrolled in Etrolizumab Phase II/III Studies”.

The study is known as ‘COTTONWOOD’.

- The protocol number for this study is: GA28951.
- The ClinicalTrials.gov identifier for this study is: NCT02118584.
- The EudraCT number for this study is: 2013-004435-72.