Summary of Clinical Trial Results

A study that looked at the long-term safety and effectiveness of continued treatment with etrolizumab for people with "Crohn's disease," a long-term illness where the gut is inflammed

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 June 2015 and stopped early – in October 2023 – after the sponsor decided not to apply for regulatory approval for etrolizumab in adults with Crohn's disease 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.**

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 a long-term illness called "Crohn's disease," a type of inflammatory bowel disease, 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 Crohn's disease 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 placebo 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 treatment with etrolizumab for up to 10 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, for people who remained in the study and continued etrolizumab, the number of people with remission (ie, no symptoms of Crohn's disease) increased at first and then the number of people with remission stayed mostly the same over time. However, assuming that people who left the study did not have remission, the number of people with remission slowly decreased over time.
- Around 3 in every 10 people (28%) had at least one serious side effect during etrolizumab treatment in Part 1. Fewer than 1 in every 100 people (less than 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 Crohn's disease because the medicine did not work as well as expected across primary studies.

1. General information about this study

Why was this study done?

Crohn's disease is a long-term illness where the gut (intestines) becomes inflamed. People with Crohn's disease often experience abdominal pain, diarrhoea, constipation, tiredness, fever, and the urgent need to have a bowel movement. These painful and debilitating symptoms can get in the way of sleep, social activities, work or school attendance, and other daily activities.

There are different types of medicines available to help treat Crohn's disease and its symptoms. Unfortunately, these medicines often do not work for everyone or may stop working in some people with Crohn's disease. Because of this, 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 Crohn's disease. They also wanted to find out how safe etrolizumab was in the long term in these people.

What was the medicine being studied?

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.”
    - The β7 protein is located on the outside of certain cells and allows them to stick to the gut, where they can contribute to inflammation and symptoms of Crohn’s disease.
- Etrolizumab is given as an injection under the skin.

What did researchers want to find out?

- Researchers had previously done a study to compare etrolizumab with a placebo which looked like the study medicine but did not contain any real medicine.
- In this study, some of the people who had taken part in the previous study continued taking etrolizumab on a long-term basis. People who had been given placebo in the previous study could start treatment with etrolizumab in this study.
- Researchers wanted to gather long-term information on etrolizumab:
    - How well etrolizumab worked over time
    - 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:

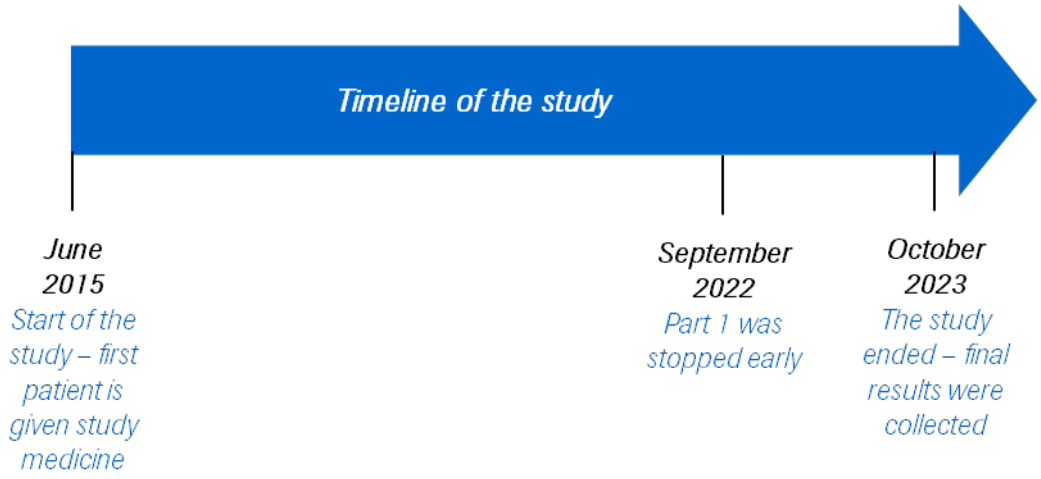
1. How many people had remission (ie, no symptoms) of Crohn’s disease over time during long-term treatment with etrolizumab?
2. How many people had side effects during long-term treatment with etrolizumab, and how many of these side effects were serious?
3. How many people had side effects after stopping etrolizumab?

What kind of study was this?

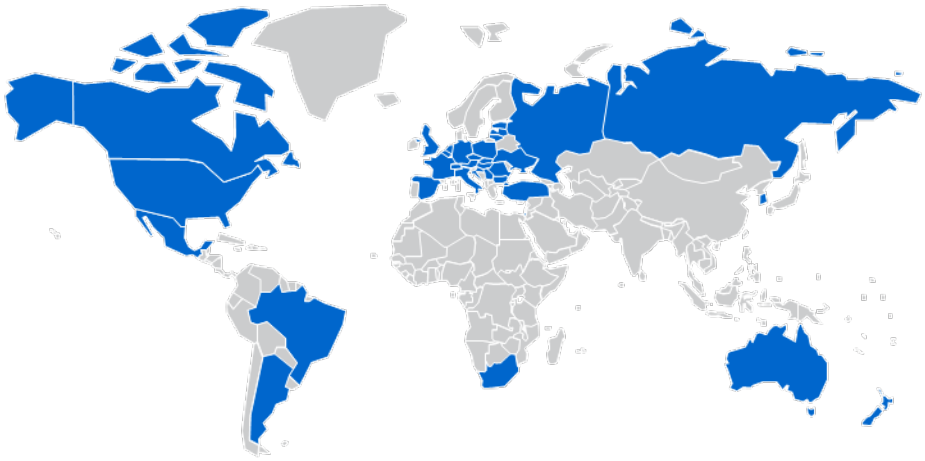
This was a Phase 3 ‘open-label extension’ study. This means that people who had taken part in a previous study and received either etrolizumab or placebo continued or started receiving etrolizumab in this study. Both the people taking part and the study doctors knew that the medicine people were receiving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

When and where did the study take place?

The study started in June 2015 and stopped early after the sponsor decided not to apply for regulatory approval for etrolizumab in adults with Crohn’s disease 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 291 study centres – across 33 countries worldwide. The following map shows the countries where this study took place.



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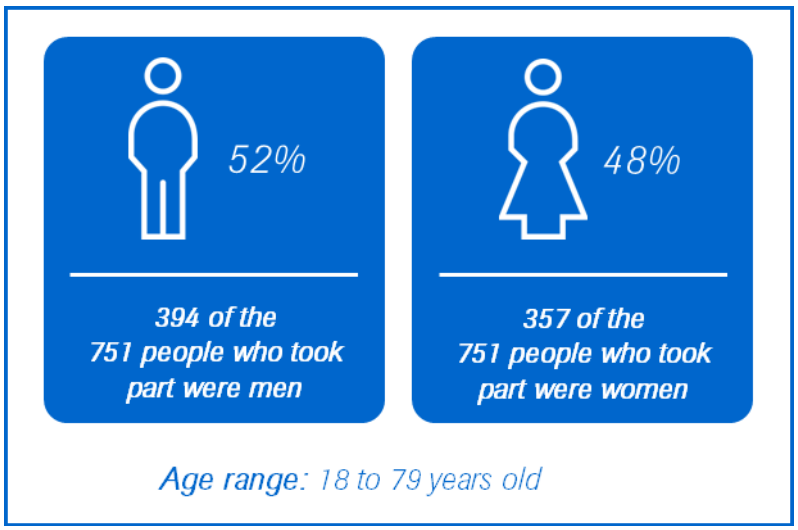
- Mexico
- Netherlands
- New Zealand
- Poland
- Romania
- Russia
- Serbia
- Slovakia
- South Africa
- South Korea
- Spain
- Switzerland
- Turkey
- Ukraine
- United Kingdom
- United States

2. Who took part in this study?

In this study, 790 people with Crohn's disease took part. 751 people took part in Part 1 and 359 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 severely active Crohn's disease
- To participate in Part 1, they had finished the previous study or had worsening of disease symptoms during treatment with etrolizumab or placebo in the previous study
- To participate in Part 2, they had participated in and completed 12 weeks of safety follow-up in Part 1, or were not eligible or chose not to participate in Part 1 and had completed 12 weeks of safety follow-up after the previous study

People could not take part in the study if:

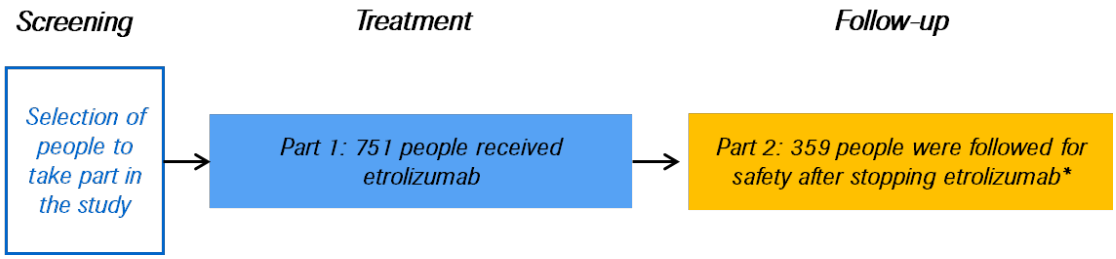
- They left the previous study earlier than Week 10

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 10 years 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 10 years. However, the study was discontinued early because the sponsor decided not to apply for regulatory approval for etrolizumab in adults with Crohn's disease. Part 1 was approximately 7 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 320 people who participated in Part 1, and 39 people who did not participate in Part 1.

4. What were the results of the study?

Question 1: How many people had remission (ie, no symptoms) of Crohn's disease over time during long-term treatment with etrolizumab?

In Part 1, researchers looked at the number of people who experienced remission of Crohn's disease symptoms every 12 weeks during continued treatment with etrolizumab. For people who remained in the study and continued treatment with etrolizumab, the number of people with remission (ie, no symptoms of Crohn's disease) increased at first and then the number of people with remission stayed mostly the same over time. However, assuming that people who left the study did not have remission, the number of people in remission slowly decreased over time.

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 3 in every 10 people (28%) had at least one serious side effect during etrolizumab treatment in Part 1. Fewer than 1 in every 100 people (less than 1%) had at least one serious side effect after stopping etrolizumab in Part 2.

The four 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.

Serious side effects reported in this study	**Part 1: people taking etrolizumab** (751 people total)	**Part 2: people who had stopped etrolizumab** (359 people total)
Crohn's disease flare-up	9% (69 out of 751)	0% (0 out of 359)
Abscess (pocket of infection) in the anus	2% (13 out of 751)	0% (0 out of 359)
Pain in the belly	1% (10 out of 751)	0% (0 out of 359)
Blockage in the small intestine	1% (10 out of 751)	0% (0 out of 359)

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

- In Part 1, 5 out of 751 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 359 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, 112 out of 751 people (15%) stopped taking their medicine because of side effects.

Most common side effects

During this study, around 8 out of every 10 people (83%) 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 (16%) in Part 1. Around 1 out of every 100 people (1%) in Part 2 had at least one side effect after stopping etrolizumab. However, no people had side effects thought to be related to the study medicine in Part 2.

The six 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.

Most common side effects reported in this study	**Part 1: people taking etrolizumab** (751 people total)	**Part 2: people who had stopped etrolizumab** (359 people total)
Crohn's disease	30% (229 out of 751)	Less than 1% (1 out of 359)
Pain in the belly	12% (92 out of 751)	Less than 1% (1 out of 359)
Pain in the joints	12% (87 out of 751)	0% (0 out of 359)
COVID-19	11% (86 out of 751)	0% (0 out of 359)
Sore throat and runny nose	11% (80 out of 751)	0% (0 out of 359)
Headache	10% (76 out of 751)	0% (0 out of 359)

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 790 people with Crohn's disease. These results helped researchers learn more about the long-term effects of etrolizumab in people with Crohn's disease.

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/NCT02403323
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=2014-003855-76
- https://forpatients.roche.com/en/trials/autoimmune-disorder/crohn-s-disease/open-label-extension-and-safety-study-for-patients-with-crohn-s-.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/crohn-s-disease/open-label-extension-and-safety-study-for-patients-with-crohn-s-.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?

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

The full title of this study is: “An Open-Label Extension and Safety Monitoring Study of Patients With Moderately to Severely Active Crohn's Disease Previously Enrolled in the Etrolizumab Phase III Protocol GA29144”.

The study is known as ‘JUNIPER’.

- The protocol number for this study is: GA29145.
- The ClinicalTrials.gov identifier for this study is: NCT02403323.
- The EudraCT number for this study is: 2014-003855-76.