# Clinical Trial Results – Layperson

## A study to look at how safe different doses of etrolizumab were for children with inflammatory bowel disease – and how this medicine was processed in 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), written for:

- Members of the public; and
- Children who took part in the study or their caregivers.

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

The primary study started in March 2018 and ended in December 2019 and the open label extension phase is ongoing This summary was written after the primary study had ended.

No single study can tell us everything about the risks and benefits of a medicine. It takes many 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 children who took part in this study

The children who took part in this study have helped researchers to answer important questions about the study medicine and inflammatory bowel disease, which is long-term inflammation of the gastrointestinal tract.

## Key information about this study

| Key Methods | Key Findings |
|---|---|
| • This study was done to find out how safe different doses of the study medicine (called etrolizumab) were for children with inflammatory bowel disease.<br>• The study also looked at how etrolizumab was processed in the body.<br>• Researchers wanted to see how giving less medicine more frequently (called the "more frequent lower dose" group) compared with higher doses of medicine given less frequently (called the "less frequent higher dose" group). It was decided by chance which treatment each person was given.<br>• This study included 24 children aged between 4 and 18 years old in 4 countries. | • The main finding was that, on average, the children in the less frequent higher dose group had slightly more medicine in their bodies than the children in the more frequent lower dose group.<br>• Around 17% of children (4 out of 24) taking etrolizumab had serious side effects, including diarrhea, gastritis, vomiting, anemia, anxiety disorder, or worsening of their inflammatory bowel disease.<br>• At the time of writing this summary, the primary study has concluded, but the open label extension phase is ongoing . |

## 1. General information about this study

### Why was this study done?

Children with inflammatory bowel disease, including ulcerative colitis and Crohn's disease, often have more severe symptoms than adults. Children may have difficulty absorbing nutrients from their food, causing reduced growth and development. It is important that children with inflammatory bowel disease receive enough medicine to treat their disease properly. Most studies of treatments for inflammatory bowel disease only involve adults. The results may not be the same as in children. Some studies have shown that a larger dose of medicine is needed to treat inflammatory bowel disease in children.

This study looked at different doses of etrolizumab in children with inflammatory bowel disease to see how the medicine was processed in the body, and to find out if the medicine was safe.

## 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.”
    - 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 inflammatory bowel disease.
- Etrolizumab is given as an injection under the skin. Part of this study was to find out how much medicine is needed, and how often it should be given.

## What did researchers want to find out?

Researchers did this study to look at how etrolizumab is processed in children, and how well different doses treated inflammatory bowel disease. They wanted to see how giving less medicine more frequently (called the “more frequent lower dose” group) compared with higher doses of medicine given less frequently (called the “less frequent higher dose” group).

Researchers also wanted to find out how safe etrolizumab is for children by checking whether, and how many, children had side effects when taking the medicine (see section 5 – “What were the side effects?”).

The main questions that researchers wanted to answer were:

1. How was etrolizumab processed in children’s bodies in the more frequent lower dose group and the less frequent higher dose group?
2. Did children’s body weight and age affect how long etrolizumab stayed in their bodies?
3. How effective was etrolizumab at blocking the protein that contributes to inflammation in inflammatory bowel disease?
4. What dose of etrolizumab was given to children with inflammatory bowel disease?
5. Did children who received etrolizumab have any side effects, and if so, what were they? Were there any differences in side effects between children in the more frequent lower dose group and the less frequent higher dose group?

## What kind of study was this?

This study was a ‘phase 1’ study, which means that it was a study designed to test the safety of etrolizumab and how the body processed this medicine. A small number of children with inflammatory bowel disease took etrolizumab. Researchers carried out medical tests on the children who took part in the study to find out more about etrolizumab.

The study was ‘randomized.’ This means that it was decided by chance, like tossing a coin, which of the doses of etrolizumab children in the study would receive.

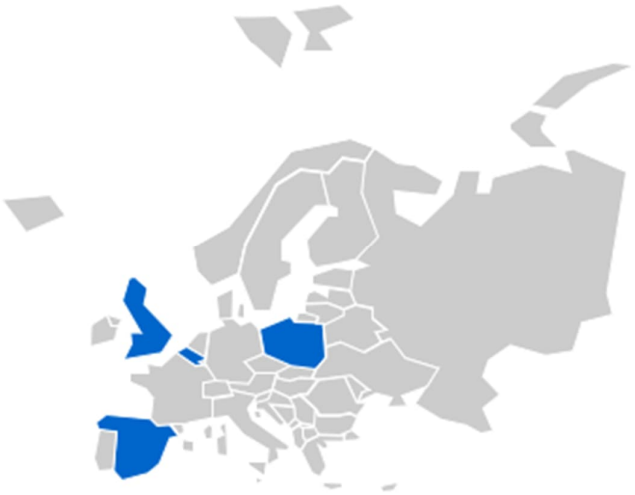
This was an ‘open-label’ study, which means that the children taking part in the study, their caregivers, and the study doctors knew that the children were receiving etrolizumab.

## When and where did the study take place?

The primary study started in March 2018 and ended in December 2019. This summary was written after the primary study ended. The open label extension phase is ongoing.

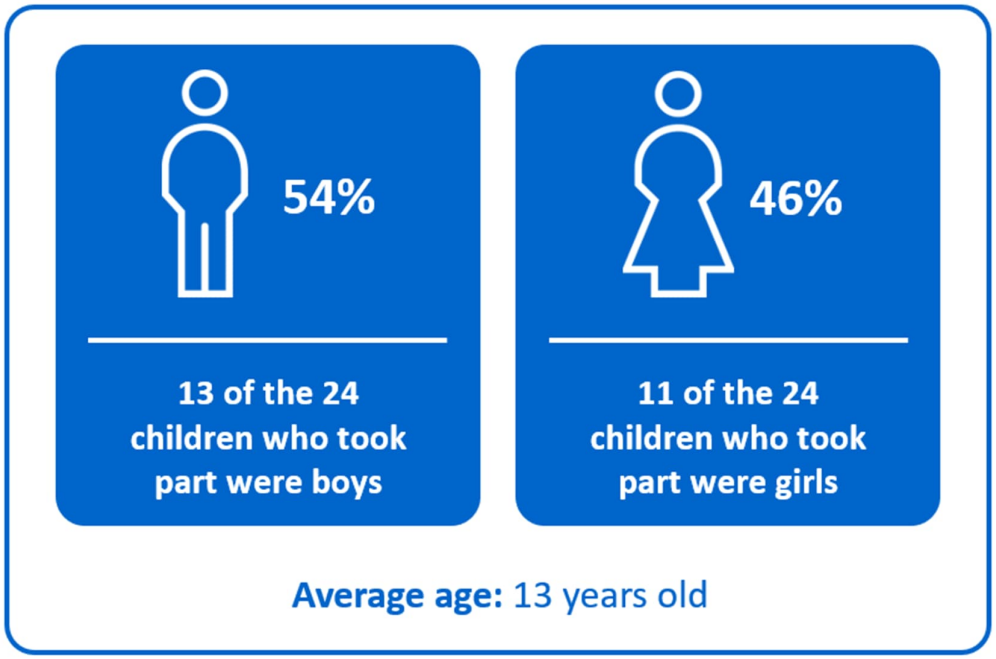
The study took place at 5 study centers across 4 countries in Europe. The following map shows the countries where this study took place.

- Poland
- Spain
- Belgium
- United Kingdom



## 2. Who took part in this study?

More information on the 24 children with inflammatory bowel disease who took part in this study is given below.



Children could take part in the study if they:

- Were children or adolescents aged 4 to less than 18 years old
- Weighed at least 13 kilograms (kg)
- Had been diagnosed with ulcerative colitis or Crohn's disease more than 3 months before starting the study
- Had certain previous treatments for their inflammatory bowel disease that did not work.

Children could not take part in the study if they had any of the following:

- A history of certain gastrointestinal disorders or infections, neurological disorders or diseases, or tuberculosis (to avoid potential safety issues)
- Previously taken certain medicines or had surgery to treat their inflammatory bowel disease.

## 3. What happened during the study?

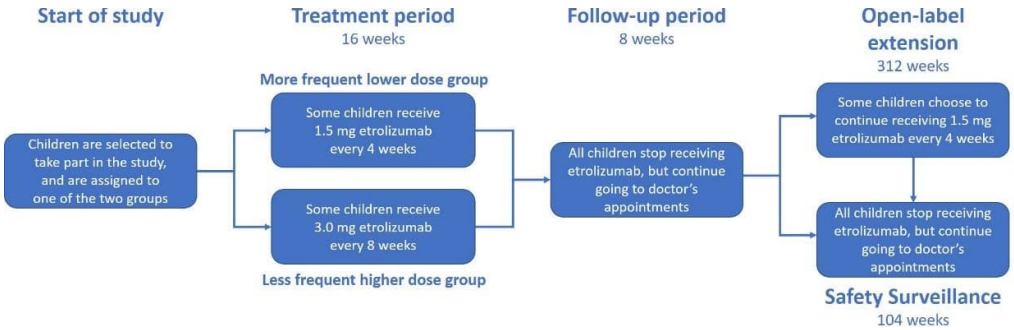
During the study, children were selected by chance to receive different doses of etrolizumab. The treatment groups were selected at random – by a computer.

The treatment groups were:

- More frequent lower dose group: 1.5 milligrams (mg) of etrolizumab for every kg that a person weighed every 4 weeks
    - 12 children were randomly assigned to this group
- Less frequent higher dose group: 3.0 mg of etrolizumab for every kg that a person weighed every 8 weeks
    - 12 children were randomly assigned to this group

Children received etrolizumab as an injection under the skin of the stomach or thigh. If a person's disease got worse during the study, researchers were allowed to give them other medicines to help them get better. Children who received the other medicines also continued to receive etrolizumab.

Children in the study received etrolizumab for 16 weeks. When the study finished, the children who took part were asked to go back to their study center for more visits for another 8 weeks to check their overall health. Look below to see more information about what happened in the study.




The primary study was completed in December 2019, but the open label extension phase is ongoing. This summary reports the results from the primary study.

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

### Question 1: How was etrolizumab processed in children's bodies in the more frequent lower dose group and the less frequent higher dose group?

Researchers looked at levels of etrolizumab in children's bodies during the study to compare the more frequent lower dose group and the less frequent higher dose group. They wanted to see if the medicine remained in the body for longer in children who received more frequent injections or less frequent injections.

On average, children who received less frequent injections at a higher dose had slightly more medicine in their bodies during the study compared with those who had more frequent injections at a lower dose. At the point in the study when children had the greatest levels of etrolizumab in their body, children who received less frequent injections at a higher dose had greater levels than those who received more frequent injections at a lower dose.

On average, children who received less frequent injections at a higher dose had
more medicine in their bodies during the study compared with children who had more frequent injections at a lower dose.

### Question 2: Did children's body weight and age affect how long etrolizumab stayed in their bodies?

Researchers looked at whether children's body weight and age affected how fast etrolizumab was cleared from their bodies. This helps researchers to find out how much medicine children should receive. In this experiment, researchers looked at everyone taking part in the study, regardless of whether they were in the more frequent lower dose group or the less frequent higher dose group.

On average, etrolizumab was cleared away from the body slower in children with lower body weights than those with higher body weights.

Researchers then looked at whether age had an impact on how fast etrolizumab was cleared away from the body. On average, etrolizumab was cleared away from the body slower in younger children's bodies than in those of children aged 12 or older.

Overall, etrolizumab was cleared slower from the bodies of children who weighed less, and who were younger, compared with heavier or older children.

### Question 3: How effective was etrolizumab at blocking the protein that contributes to inflammation in inflammatory bowel disease?

The inflammation associated with inflammatory bowel disease can be caused by certain types of cells in a person's gut called T and B cells. The β7 protein on the outside of these cells allows them to stick to the gut, where they contribute to inflammation. Etrolizumab blocks the β7 protein on these cells, which prevents them from sticking to the gut where they can cause damage.

Researchers looked at how many of these cells in children etrolizumab had blocked β7 protein to find out how effective less frequent higher dose injections and more frequent lower dose injections were.

On average, the β7 protein was blocked on most cells that researchers looked at during the treatment period. Similar blocking was seen in both the more frequent lower dose group and the less frequent higher dose groups.

Once children stopped receiving their medicine in the follow-up period, researchers saw fewer cells with blocked β7 protein. But, at the end of the study, the amount of unblocked β7 protein in children was still lower than before they started their medicine.

Nearly 100% of **β**7 protein (which contributes to inflammation) was blocked by etrolizumab in both the more frequent lower dose group and the less frequent higher dose group.

### Question 4: What dose of etrolizumab was given to children with inflammatory bowel disease?

Researchers also wanted to find out how much etrolizumab children need in their bodies to treat inflammatory bowel disease. They compared the number of cells with blocked β7 protein with the amount of medicine in their bodies. This helped them to find out how much medicine was needed to block most of the β7 protein.

Researchers found that between 1 and 3 micrograms (or µg) of medicine for every milliliter (or mL) of blood in a person's body was enough to block most of the β7 protein. If children have less than 1 to 3 µg of medicine for every mL of blood, not enough β7 protein is blocked to treat their disease.

Overall, researchers found that between 1 and 3 µg of medicine for every mL of blood in a person's body is enough medicine to block the **β**7 protein on most cells.

## 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.

- They are described in this summary because the study doctor believes the side effects were related to the treatment in the study.
- Not all of the children in this study had all of the side effects.

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, 1 out of 12 children (8%) in the more frequent lower dose group had a serious side effect (anxiety disorder) related to the treatment. This person stopped taking the medicine because of this side effect. No one in the less frequent higher dose group had any serious side effects related to the treatment. This means that in the entire study, 1 out of the 24 children (4%) had at least one serious side effect related to the treatment.

### Most common side effects

In the more frequent lower dose group, the most common side effects were low levels of red blood cells, fever, and pain in the stomach area. In the less frequent higher dose, the most common side effects were worse Crohn's disease symptoms and headache.

### 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.

## 6. How has this study helped research?

The information presented here is from a single study of 24 children with inflammatory bowel disease. The results helped researchers learn more about inflammatory bowel disease and etrolizumab, and also about how these learnings could help children with inflammatory bowel disease in the future.

No single study can tell us everything about the risks and benefits of a medicine. It takes many 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 study only looked at 24 children, and was designed to inform researchers so they can design additional larger studies correctly for the safety and benefit of children with inflammatory bowel disease.

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 other studies taking place or planned?

At the time of writing this summary (October 2021), the primary study has been completed and the open-label extension phase is ongoing.

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/NCT03478956
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2017-003649-10/results
- https://forpatients.roche.com/en/trials/autoimmune-disorder/ulcerative-colitis/a-phase-i-study-of-etrolizumab-followed-by-open-label-extension-.html

### Whom 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-phase-i-study-of-etrolizumab-followed-by-open-label-extension-.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 who have their headquarters in Basel, Switzerland.

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

The full title of this study is: “A phase I, open-label, randomized, pharmacokinetic, pharmacodynamic, and safety study of etrolizumab followed by open-label extension and safety monitoring in pediatric patients from 4 Years to less than 18 years of age with moderate to severe ulcerative colitis or moderate to severe Crohn's disease”

The study is known as “FENNEL.”

- The protocol number for this study is: CA40192.
- The ClinicalTrials.gov identifier for this study is: NCT03478956.
- The EudraCT number for this study is: 2017-003649-10.