Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medication works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor:	Arena Pharmaceuticals Inc. (a wholly owned subsidiary of Pfizer Inc.)
Medicine(s) Studied:	Velsipity™ (etrasimod)
Protocol Number:	C5041011 (APD334-210)
Dates of Study:	12 April 2021 to 19 June 2024
Title of this Study:	A Study on Etrasimod in Adults With Ulcerative Colitis [A Randomized, Double-Blind, Placebo-Controlled, 52-Week Study to Assess the Efficacy and Safety of Etrasimod in Subjects with Moderately Active Ulcerative Colitis]
Date(s) of this Report:	22 April 2025

– Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

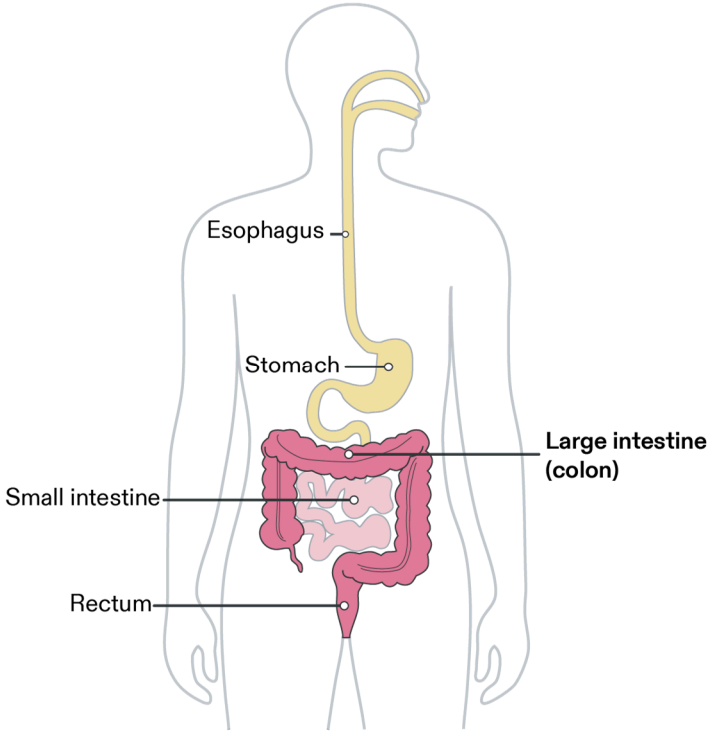
This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is ulcerative colitis (UC)?

UC is a disease that affects the lower part of the body system that helps you digest food. This lower part of the digestive system is called the large intestine. Figure 1 shows where the large intestine is located in the body. The large intestine has several parts, including the colon.

Figure 1 The digestive system



Lymphocytes are white blood cells in the body that protect against infection. In people with UC, the lymphocytes attack the colon causing redness and swelling of the colon, which is known as inflammation. This

attack damages the colon causing symptoms such as diarrhea, bloody stool, and belly pain.

What is etrasimod?

Etrasimod (et – ras' – i – mod) is a medication already approved in people with moderately to severely active UC. Etrasimod is taken as a tablet by mouth once a day. It helps by stopping lymphocytes from going to the inflamed areas in the colon. In past studies, etrasimod helped participants with moderately to severely active UC to have remission. "Remission" is defined as disappearance of blood in the stool, a normal or reduced number of stools, and healing of the colon.

What was the purpose of this study?

In this study, etrasimod 2 mg was the study medication being tested to treat less active UC. Researchers compared etrasimod with placebo to see if more study participants who took etrasimod had remission of UC after 52 weeks and to see what medical problems occurred. A study participant is someone who agrees to take part in the study. A placebo is a tablet that does not have any medicine in it, but looks exactly like the study medication.

Researchers wanted to know:

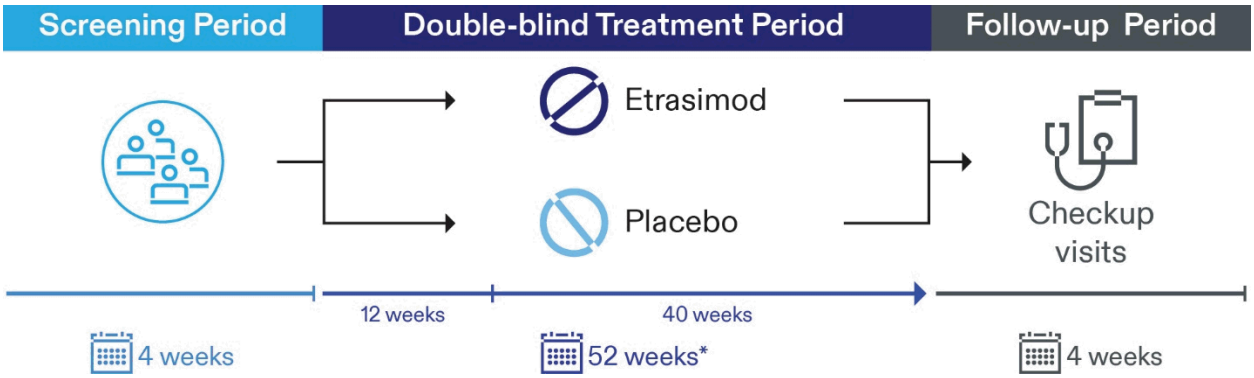
Did more participants taking etrasimod have remission of UC compared to participants taking placebo?

What happened during the study?

How was the study done?

Researchers performed the study across 3 study periods. Figure 2 shows what happened in the study.

Figure 2 What happened in the study?



* During study visits Researchers asked participants about their UC. Starting with Week 12, participants who had any improvement continued in the study. Participants who did not improve or had worsening of UC could leave the Double-blind study and could join a new study to take etrasimod.

The 3 study periods were:

1. Screening Period: Within up to 4 weeks, researchers checked each participant and did medical tests to see if the participant met the study rules for entry. Study rules included the age of participants, how long they had UC, their prior UC therapy, and severity of their UC.

2. Double-blind (DB) Treatment Period: The Treatment Period lasted up to 52 weeks and included a 12-week and a 40-week treatment period. At the start, participants were placed in either the etrasimod 2 mg or placebo treatment group by chance. During the first 12 weeks of the Treatment Period, participants took the study treatment (etrasimod 2 mg or placebo) once a day.

Also, the study participants, study doctors and the researchers did not know who took etrasimod and who took placebo. This is known as a “double-blind” study.

At the end of 12 weeks of treatment, the researchers did medical tests and asked participants questions about their UC. The researchers reviewed the test results and then decided if a participant had any improvement of UC. If a participant had some improvement of UC, the participant could continue in the double-blind treatment period for another 40 weeks. If a participant did not improve of had worsening of UC, the participant could leave the study and join a new study to take etrasimod.

3. Follow-up Period: This period started after participants stopped their DB treatment. The researchers and study doctors checked each participant’s health in 2 visits over 4 weeks.

Where did this study take place?

The company who ran the study is called the Sponsor. The Sponsor included participants in this study from 78 study sites in 18 countries around the world.

When did this study take place?

The study began on 12 April 2021 and ended on 19 June 2024.

Who participated in this study?

There were 233 participants who took at least 1 tablet of the study treatment. This group was called the "Safety Analysis Set" and was used to see what medical problems participants had during the study.

Out of these 233 participants, 187 had specific results from medical tests describing how active their UC was when they joined the study. This

smaller group of 187 participants was called the “Primary Analysis Set” and was used to see if etrasimod reduced UC signs and symptoms. There were 127 participants in the etrasimod group and 60 participants in the placebo group.

In the etrasimod group, 51 out of 127 participants in the Primary Analysis Set did not finish the study treatment. In the placebo group, 32 out of 60 participants did not finish the study treatment. The most common reasons participants did not complete the study treatment were:

- participant’s UC got worse
- participant decided not to stay in the study
- participant had a medical problem.

Table 1 shows a summary of the participants in the Safety Analysis Set and Primary Analysis Set.

Table 1 Summary of Safety Set and Primary Analysis Set

Safety Analysis Set	Primary Analysis Set
• 233 participants • these participants took at least 1 tablet of study treatment during the DB treatment period • these participants were used to see what medical problems these participants had during study	• 187 of the 233 participants from the Safety Analysis Set • these participants had specific results from medical tests for UC • these participants were used to see if etrasimod reduced UC signs and symptoms

In the Primary Analysis Set for this study:

- There was a total of 104 men and 83 women
- Participants were 18 to 74 years of age
- Most participants were White (167 out of 187 participants).

How long did the study last?

Study participants could have stayed in the study for up to 60 weeks for Screening, DB Treatment, and Follow-up periods. Study participants could have received study treatment for up to 52 weeks. The entire study took 38 months to complete. The study completed as planned.

The Sponsor began reviewing the information collected when the study ended in June 2024. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

What percentage of participants taking etrasimod had remission of UC compared to participants taking placebo?

Researchers looked at the participants' medical test results and reported the percentage of participants who had remission of UC at Week 52.

There were 187 participants in the Primary Analysis Set (127 in the etrasimod group and 60 in the placebo group). In the etrasimod group, 33 out of 127 (26.0%) of participants had remission of UC. In the placebo group, 11 out of 60 (18.3%) of participants had remission of UC.

Based on these results, the researchers have decided that the results are likely due to chance. This means the study results did not show that etrasimod was better than placebo for causing remission of UC.

This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies may have different results.

What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by a different disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medication might have on a participant.

There were 150 out of 233 participants (64.3%) in the Safety Analysis Set who had at least 1 medical problem. There were 11 out of 233 participants (4.7%) who stopped study treatment because of medical problems. Table 2 shows the medical problems reported by more than 11 out of 233 of study participants (5%). Compared with previous studies, no new health concerns with etrasimod were found in the current study.

Below Are Instructions on How to Read Table 2.

- The **1st** column of Table 2 lists medical problems that were commonly reported during the study. All medical problems reported by more than or equal to 5% of participants are listed.
- The **2nd** column tells how many of the 154 participants taking the study medication reported each medical problem. Next to this number is the percentage of the 154 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 79 participants taking a placebo reported each medical problem. Next to this number is the percentage of the 79 participants taking a placebo who reported the medical problem.
- Using these instructions, you can see that 101 out of 154 (65.6%) participants taking study medication had 1 or more medical problems during the study. In the placebo group, 49 out of 79 (62.0%) participants had 1 or more medical problems during the study.

Table 2. Commonly reported medical problems by study participants

Medical Problem	Etrasimod (154 Participants)	Placebo (79 Participants)
One or more medical problems	101 out of 154 participants (65.6%)	49 out of 79 participants (62.0%)
Ulcerative colitis[a]	20 out of 154 participants (13.0%)	8 out of 79 participants (10.1%)

Table 2. Commonly reported medical problems by study participants		
Medical Problem	**Etrasimod (154 Participants)**	**Placebo (79 Participants)**
COVID-19 (a type of infection)	15 out of 154 participants (9.7%)	7 out of 79 participants (8.9%)
Increased alanine aminotransferase (a liver enzyme in the blood)	13 out of 154 participants (8.4%)	1 out of 79 participants (1.3%)
Increased gamma-glutamyltransferase (a liver enzyme in the blood)	13 out of 154 participants (8.4%)	2 out of 79 participants (2.5%)
Headache	9 out of 154 participants (5.8%)	3 out of 79 participants (3.8%)
Increased aspartate aminotransferase (a liver enzyme in the blood)	8 out of 154 participants (5.2%)	1 out of 79 participants (1.3%)
Increased blood triglycerides (a type of fat in the blood)	8 out of 154 participants (5.2%)	1 out of 79 participants (1.3%)
Anemia (low levels of red blood cells)	4 out of 154 participants (2.6%)	6 out of 79 participants (7.6%)
Upper respiratory tract infection (a type of infection)	3 out of 154 participants (1.9%)	4 out of 79 participants (5.1%)

Table 2. Commonly reported medical problems by study participants		
Medical Problem	Etrasimod (154 Participants)	Placebo (79 Participants)

a. This is a worsening of the participants existing ulcerative colitis.

Did study participants have any serious medical problems?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

- 6.5% of participants (10 out of 154) in the etrasimod group had a serious medical problem. UC was the only serious medical problem that occurred in more than 1 participant.
- 1.3% of participants (1 out of 79) in the placebo group had a serious medical problem.

No participants died during in the study.

Where can I learn more about this study?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number C5041011

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier **NCT04607837**
https://euclinicaltrials.eu	Use the study identifier **2020-003507-34**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!