Plain Language Clinical Study
Summary

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 medicine 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 Studied: Velsipity™ (etrasimod, also known as PF-07915503)

Protocol Number: C5041006 SS1-P2b (APD334-202 or CULTIVATE)

Dates of Study: 06 January 2020 to 27 November 2024

Title of this Study: A Study of Etrasimod in Adults With Crohn's Disease – Substudy 1

[A Multicenter, Randomized, Double-Blind, Parallel-Group Study to Assess the Efficacy and Safety of Oral Etrasimod as Induction and Maintenance Therapy for Moderately to Severely Active Crohn's Disease – Substudy 1]

Date of this Report: 21 November 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. Do you have any questions about the study or the results? If so, please contact the doctor or staff at your study site.

Why was this study done?

What is Crohn's disease?

Crohn's disease (or CD) is a condition caused by inflammation (pain, swelling, and redness) in the gut. CD can affect any part of the gut from the mouth to the anus. This inflammation can lead to symptoms like diarrhea, abdominal pain, blood in the stool, weight loss, and tiredness. Signs of damage caused by CD include narrowing of the gut or sores in its lining.

What is etrasimod?

Etrasimod (et –ras' – i – mod), also called Velsipity™, is a medicine in tablet form that is swallowed. It is approved for adults with moderately to severely active ulcerative colitis, a disease that causes inflammation in the colon (large intestine). In this study, etrasimod is considered investigational because it is not approved for the treatment of CD outside of research studies.

Etrasimod is designed to partially block the movement of certain groups of lymphocytes to areas of inflammation in the gut. Lymphocytes are a type of white blood cell that are a part of the immune system (the body's defense system against infection). Studies show that certain lymphocytes may be involved in causing CD. Researchers think that blocking these certain lymphocytes may reduce inflammation and help with CD symptoms.

What was the purpose of this study?

The main purpose of Substudy 1 was to learn whether 2 milligrams (mg) or 3 mg etrasimod could help improve inflammation of the intestines in adult participants with moderately to severely active CD. To check if inflammation in the small and large intestines had improved, study doctors used a thin tube with a small camera. This procedure is called an endoscopy.

The other purpose of Substudy 1 was to learn whether etrasimod can improve other symptoms of CD and if etrasimod is safe when given to participants with moderately to severely active CD.

Researchers wanted to know:

- **How many participants had improved inflammation of the intestines after 14 weeks of treatment?**
- **What medical problems did participants have during this study?**

What happened during the study?

How was the study done?

Researchers tested 2 doses of etrasimod to find out which could improve inflammation of the intestines caused by CD. Researchers then compared those results with those taking a placebo. A placebo does not have any medicine in it, but it looks just like the study medicine. The study participants and researchers did not know who took etrasimod and who took the placebo. This is known as a "blinded" study.

The treatment phase was divided into 2 parts: Initial Treatment Phase (called Induction Phase) and Extended Induction Phase.

During the **Induction Phase**, participants were assigned to 1 of 3 treatment groups by chance alone: etrasimod 2 mg, etrasimod 3 mg, or a placebo. Participants took their assigned treatment once per day for 14 weeks.

After 14 weeks, researchers checked whether participants were considered responders or not.

- Eligible participants who were **responders** could take part in another etrasimod study.
- Participants who were **not responders** took part in the Extended Induction Phase.

Participants must meet at least 1 of the following response criteria to be considered a clinical or endoscopic responder:

Clinical Responder

Participant must have a **Crohn's Disease Activity Index (CDAI)** score of less than 150 points or the score went down by 100 points or more from before the treatment began.

CDAI measures CD symptoms based on how a person is feeling (like if they have diarrhea), medicines taken for CD symptoms, and certain laboratory test results.

Endoscopic Responder

Participant must have a **Simple Endoscopic Score for Crohn's Disease (SES-CD)** of 4 points or lower, and the score went down by 2 points or more, with no single area of the intestines scoring higher than 1, or the score went down by at least 50% from before the treatment began.

SES-CD is a test that doctors use during an endoscopy to measure the inflammation in the small and large intestines caused by CD.

During the **Extended Induction Phase**, participants continued to take their assigned dose of etrasimod, while those who took placebo were randomly assigned to take etrasimod 2 mg or 3 mg. The Extended Induction Phase lasted for 6 weeks.

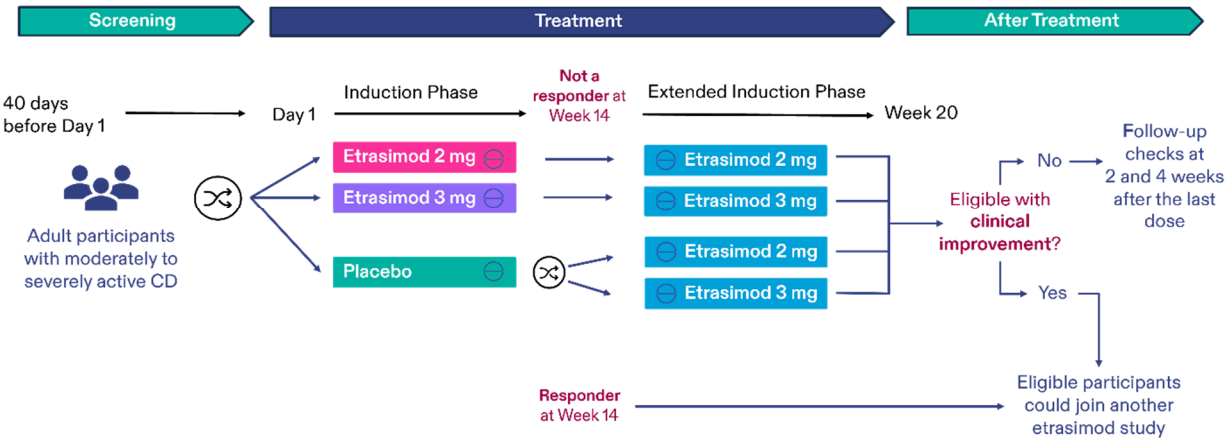
After 6 weeks, researchers checked whether participants showed clinical improvements based on the study doctor's assessment. Eligible participants who had clinical improvements could take part in another etrasimod study.

Throughout the study, study doctors checked on the participants' health and asked them how they were feeling.

Pfizer

Figure 1 shows how the study was done.

Figure 1. How was the study done?



Where did this study take place?

The Sponsor ran this study at 197 locations in 38 countries worldwide.

When did this study take place?

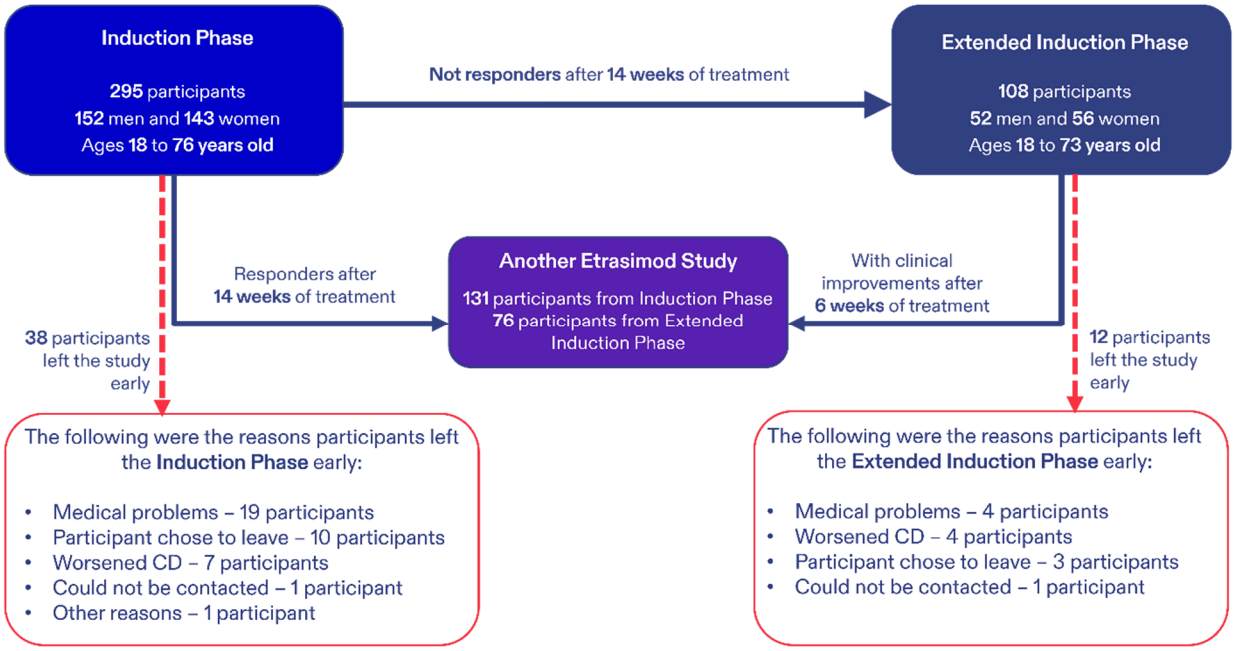
It began on 06 January 2020 and ended on 27 November 2024.

Who participated in this study?

The study included adult participants who had moderately to severely active CD. These participants had also tried other CD treatments. But, they could not tolerate the treatment, or the treatments either did not work for them, or worked at first but stopped working after some time.

Figure 2 shows the number of participants who took part in this study.

Figure 2. How many participants took part in this study?



How long did the study last?

Study participants were in Substudy 1 for up to 30 weeks (about 7 months). The entire Substudy 1 took around 4 years and 10 months to complete.

When Substudy 1 ended in November 2024, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

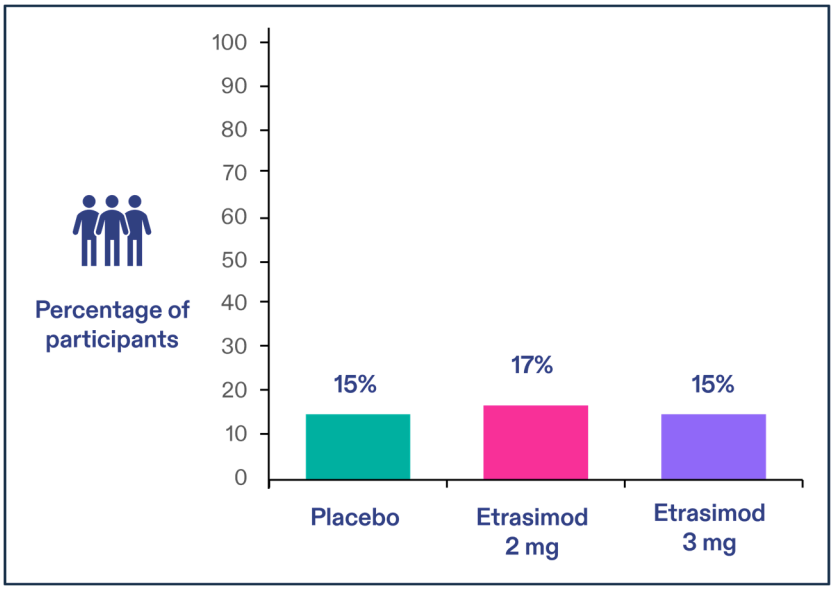
How many participants had improved inflammation of the intestines after 14 weeks of treatment?

To answer this question, researchers checked the number of participants who had met 1 of the Endoscopic Responder criteria during the Induction Phase.

Figure 3 shows the percentage of participants who were endoscopic responders after 14 weeks of treatment:

- 15% of participants who took placebo
- 17% of participants who took etrasimod 2 mg
- 15% of participants who took etrasimod 3 mg

Figure 3. How many participants were endoscopic responders after 14 weeks of treatment?



Based on these results, the researchers found that taking etrasimod 2 mg or 3 mg did not work better than the placebo in improving inflammation of the intestines of participants with moderately to severely active CD.

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 an underlying 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 medicine might have on a participant.

Induction Phase

Figure 4 shows the number of participants who had at least 1 medical problem.

Figure 4. How many participants had medical problems – Induction Phase?

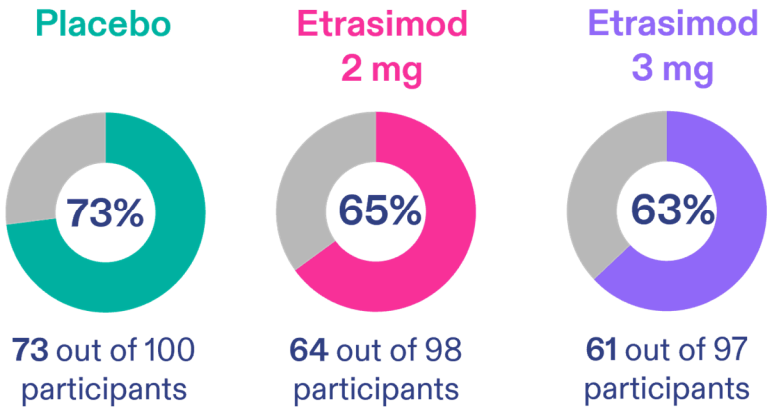


Figure 5 shows the number of participants who stopped taking the study treatment because of medical problems during the **Induction Phase**.

Figure 5. How many participants stopped taking the study treatment because of medical problems – Induction Phase?

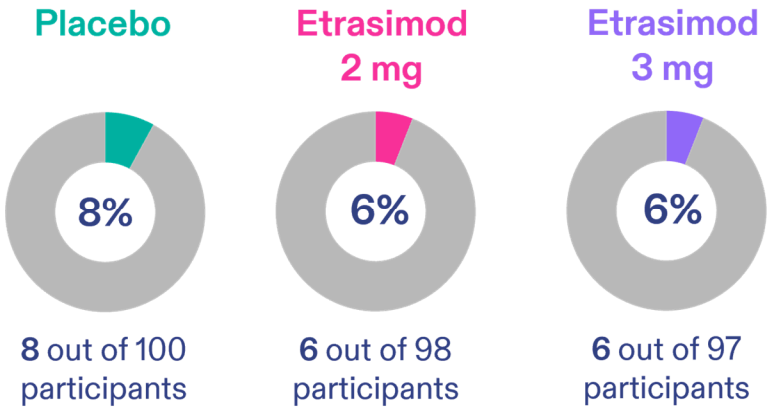


Table 1 lists the most common medical problems during the **Induction Phase**.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column lists the top 5 medical problems that were commonly reported during the **Induction Phase**.
- The **2nd** column tells the number and percentage of participants who took **placebo** and reported a medical problem.
- The **3rd** column tells the number and percentage of participants who took **etrasimod 2 mg** and reported a medical problem.
- The **4th** column tells the number and percentage of participants who took **etrasimod 3 mg** and reported a medical problem.
- Using these instructions, you can see that 8 out of the 100 participants (8%) who took placebo, 7 out of 98 participants (7%) who took etrasimod 2 mg, and 8 out of 97 participants (8%) who took etrasimod 3 mg reported nausea.

Table 1. Commonly reported medical problems by study participants – Induction Phase

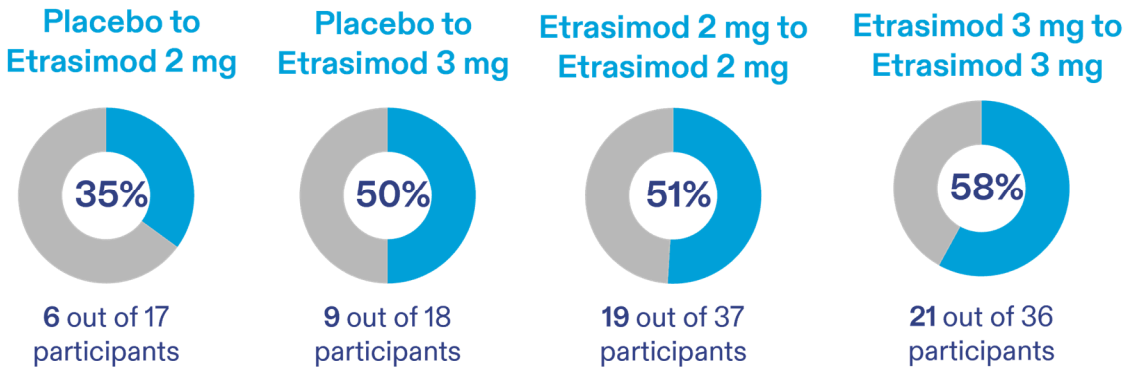
Medical Problem	Placebo (100 Participants)	Etrasimod 2 mg (98 Participants)	Etrasimod 3 mg (97 Participants)
Nausea	8 out of 100 participants (8%)	7 out of 98 participants (7%)	8 out of 97 participants (8%)

Table 1. Commonly reported medical problems by study participants – Induction Phase			
Medical Problem	**Placebo (100 Participants)**	**Etrasimod 2 mg (98 Participants)**	**Etrasimod 3 mg (97 Participants)**
Abdominal pain	9 out of 100 participants (9%)	13 out of 98 participants (13%)	1 out of 97 participants (1%)
Crohn's disease	9 out of 100 participants (9%)	7 out of 98 participants (7%)	6 out of 97 participants (6%)
Joint pain (arthralgia)	3 out of 100 participants (3%)	9 out of 98 participants (9%)	9 out of 97 participants (9%)
Headache	8 out of 100 participants (8%)	6 out of 98 participants (6%)	7 out of 97 participants (7%)

Extended Induction Phase

Figure 6 shows the number of participants who had at least 1 medical problem.

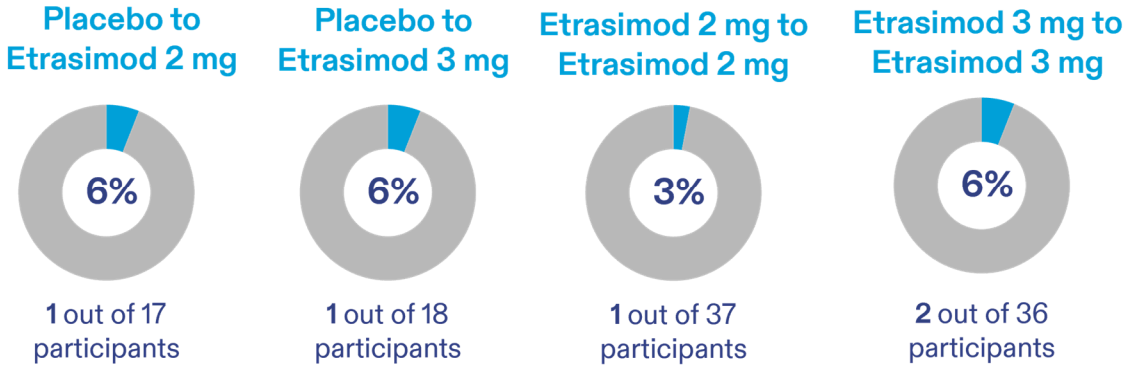
Figure 6. How many participants had medical problems – Extended Induction Phase?



The most common medical problem – reported by at least 1 participant in each group during the **Extended Induction Phase** – was Crohn's disease.

Figure 7 shows the number of participants who stopped taking the study treatment because of medical problems during the **Extended Induction Phase**.

Figure 7. How many participants stopped taking the study treatment because of medical problems – Extended Induction Phase?



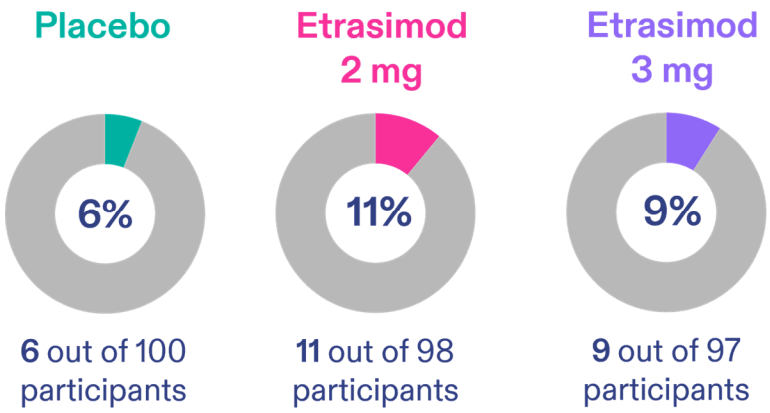
Did study participants have any serious medical problems?

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

Induction Phase

Figure 8 shows the number of participants who had at least 1 serious medical problem.

Figure 8. How many participants had serious medical problems – Induction Phase?



The most common serious medical problems – reported by at least 2 participants in any group during the **Induction Phase** – were:

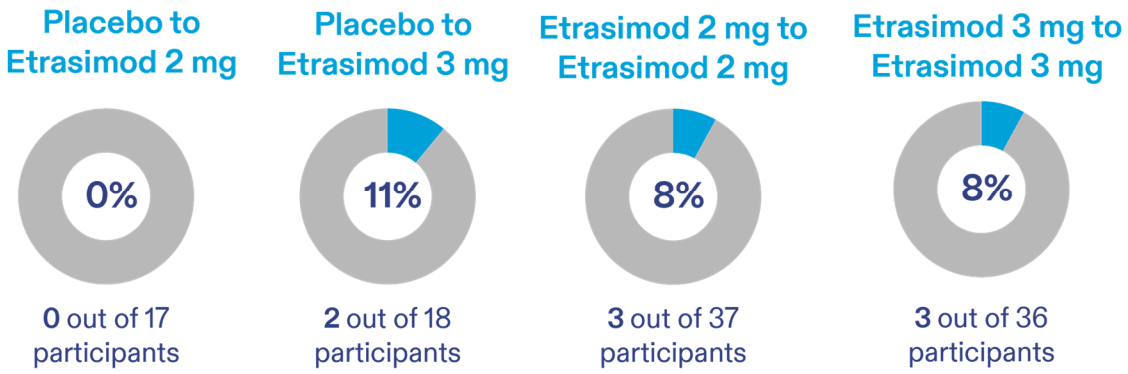
- Crohn’s disease (total of 8 participants)
- A blockage that stops stool from passing through the intestines (intestinal obstruction – total of 3 participants)
- Diarrhea and vomiting (gastroenteritis – total of 2 participants)

No participants died during the **Induction Phase**.

Extended Induction Phase

Figure 9 below shows the number of participants who had at least 1 serious medical problem.

Figure 9. How many participants had serious medical problems – Extended Induction Phase?



The most common serious medical problem – reported by at least 2 participants in any group during the **Extended Induction Phase** – was Crohn's disease.

No participants died during the **Extended Induction Phase**.

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 **C5041006 SS1-P2b**

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

www.clinicaltrials.gov	Use the study identifier **NCT04173273**
https://euclinicaltrials.eu	Use the study identifier **2020-004775-40**

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!

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