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 SS3-M (APD334-202 or CULTIVATE)

Dates of Study: 24 March 2022 to 23 April 2025

Title of this Study: A Study of Etrasimod in Adults With Crohn's Disease – SubStudy 3 Maintenance

[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 3 Maintenance]

Date of this Report: 04 February 2026

– Thank You –

Pfizer

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, as checked via a thin tube with a small camera. This procedure is called endoscopy.

What is etrasimod?

Etrasimod (et –ras' – i – mod), also called Velsipity™, is a medicine in tablet form that is swallowed. It is approved for adult participants 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 lymphocytes may reduce inflammation and help with CD symptoms.

What was the purpose of this study?

The main purpose of the Substudy 3 was to learn if the continuing treatment of 2 milligrams (mg) or 3 mg etrasimod could help improve CD symptoms in adult participants with moderately to severely active CD. Participants in this study took part in an earlier etrasimod study.

Researchers wanted to know:

- **How many participants had improved CD symptoms after 52 weeks of treatment?**
- **What medical problems did participants have during this study?**

This study was stopped early and was not completed as planned. This was because results from an earlier etrasimod study showed that it did not work in improving CD symptoms. This was not because of safety concerns or a request from health authorities.

What happened during the study?

How was the study done?

Researchers tested the 2 continuing doses of etrasimod to find out whether it could improve CD symptoms. Researchers then compared the 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.

In Substudy 3, participants were divided into 2 groups: responder group or non-responder group. To be a responder, a participant must meet at least 1 of the following response criteria in the earlier etrasimod study:

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.

Responder Group

Participants who were considered **responders** during the earlier etrasimod study were included in this group.

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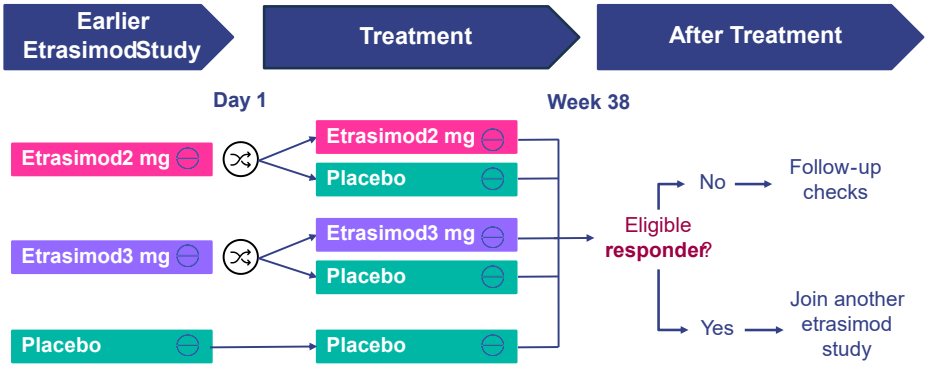
- Participants who took **etrasimod** in the earlier etrasimod study were randomly divided (like flipping a coin) into 2 treatment groups: etrasimod or placebo. Participants assigned to the etrasimod group continued with the same etrasimod dose (2 mg or 3 mg) they had taken during the earlier etrasimod study.
- Participants who took **placebo** in the earlier etrasimod study continued to take placebo in this study.

Participants took their assigned treatment once per day for 38 weeks (about 9 months). After 38 weeks, researchers checked whether participants were considered clinical or endoscopic responders.

After 6 weeks of treatment, participants in the responder group could be tested to see whether their CD had worsened. Those whose CD worsened could be transferred to the non-responder group.

Figure 1 shows how the study was done for the responder group.

Figure 1. How was the study done – Responder group?



Non-responder Group

Participants who were considered **non-responders** but had clinical improvement of CD symptoms during the earlier etrasimod study were included in this group.

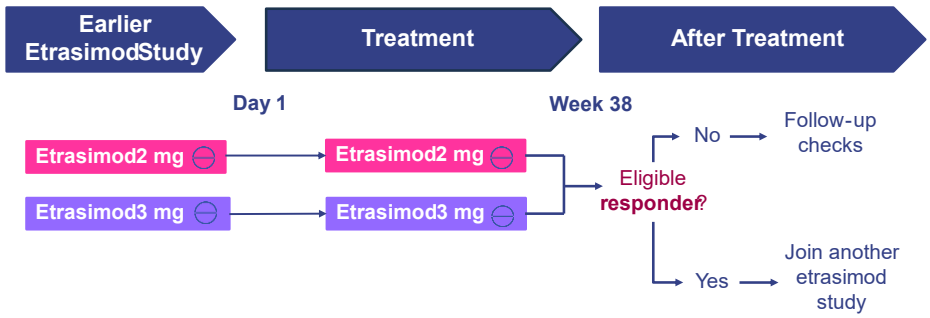
Participants continued with the same etrasimod dose (2 mg or 3 mg) they had taken during the earlier etrasimod study for 38 weeks. After 38 weeks, researchers checked whether participants were considered clinical or endoscopic responders.

Participants in the **etrasimod responder** group, whose CD got worse after 6 weeks of treatment, could be transferred to the non-responder group and continued to take the same etrasimod dose in a "blinded" manner. Participants in the **placebo responder** group who transferred to the non-responder group were switched to take etrasimod at either 2 mg or 3 mg. After the transfer, these participants would be counted in the non-responder group, as well as the medical problems they experienced.

Participants in this group, who still did not show clinical improvement, were asked to stop the study early.

Figure 2 shows how the study was done for the non-responder group.

Figure 2. How was the study done – Non-responder group?



Where did this study take place?

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

When did this study take place?

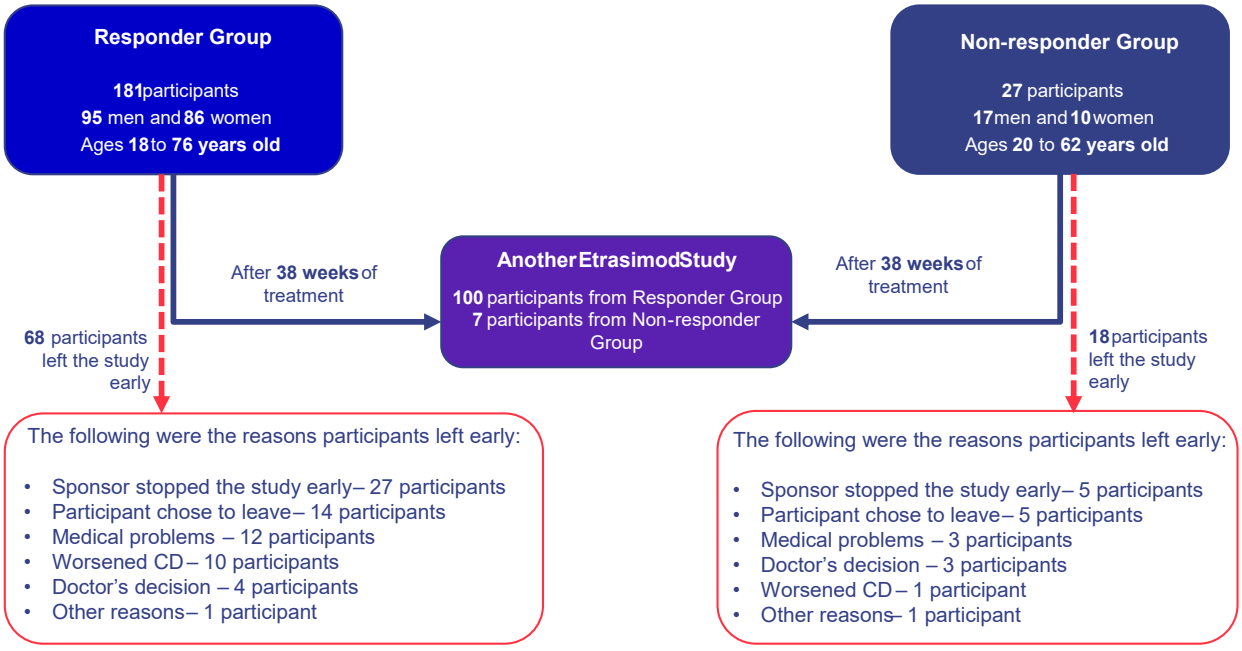
It began on 24 March 2022 and ended on 23 April 2025.

Who participated in this study?

The study included adult participants who had moderately to severely active CD. These participants had also completed at least 14 weeks of treatment in the earlier etrasimod study.

Figure 3 shows the number of participants who took part in this study.

Figure 3. How many participants took part in this study?



How long did the study last?

Participants were planned to take etrasimod for a total of 52 weeks (about 1 year). This included at least 14 weeks from an earlier etrasimod study and 38 weeks in this substudy. Substudy 3 ran for about 3 years before the Sponsor stopped the substudy early and was not completed as planned.

The Sponsor decided to stop Substudy 3 early after learning that etrasimod did not work in improving CD symptoms in an earlier study of etrasimod. This decision was not due to safety concerns reported by other etrasimod studies or a request from health authorities.

When Substudy 3 ended in April 2025, 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 CD symptoms after 52 weeks of treatment?

To answer this question, researchers checked the number of participants who had met one of the Clinical or Endoscopic Response criteria after 52 weeks of treatment.

Substudy 3 was stopped early and was not completed as planned. There was not enough information to answer the main research question because the number of participants enrolled in this study was smaller than planned.

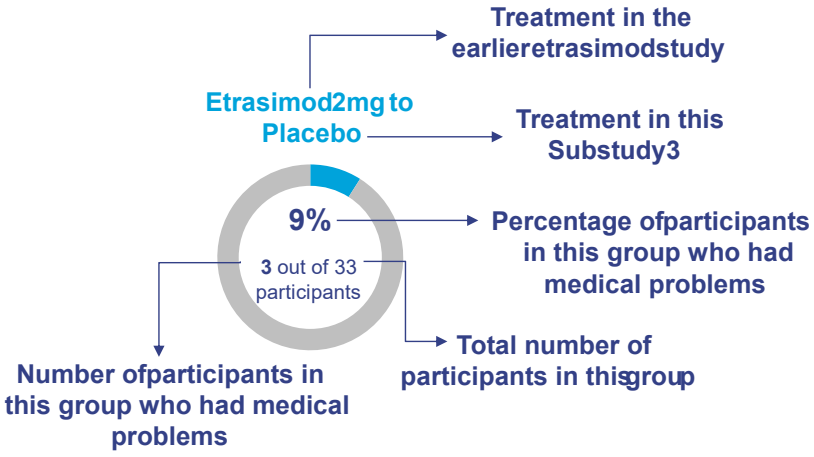
What medical problems did participants have during the study?

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.

Figure 4 shows how to read the groupings in the Responder group.

Figure 4. How to read the groupings – Responder group?



Using the figure above, you can see that 3 out of the 33 participants (9%) who took etrasimod 2 mg in the earlier study and placebo in this study reported a medical problem.

Responder Group

Figure 5 shows the number of participants who had at least 1 medical problem.

Figure 5. How many participants had medical problems – Responder group?

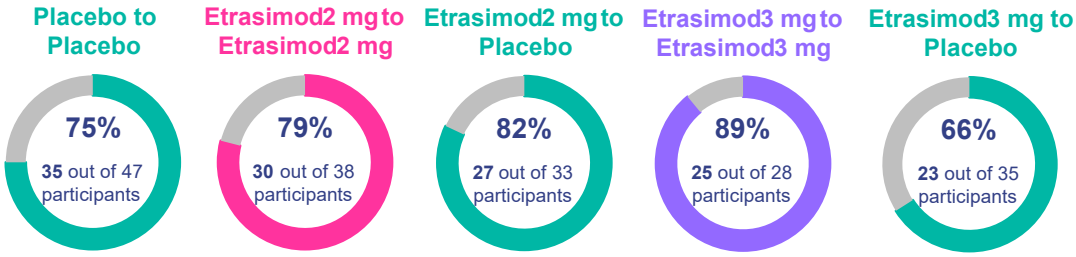
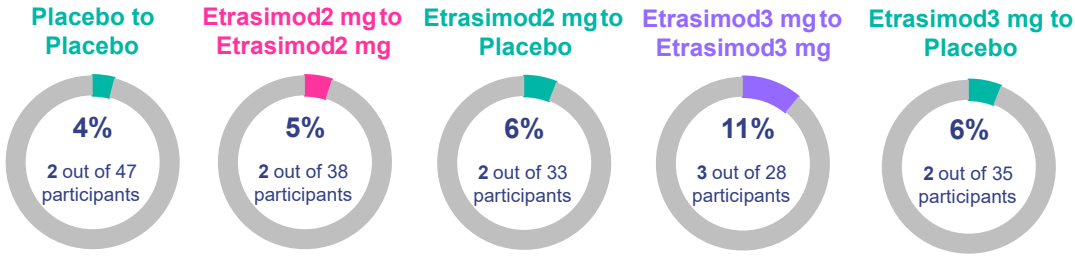


Figure 6 shows the number of participants who stopped taking the study treatment because of a medical problem.

Figure 6. How many participants stopped taking the study treatment because of a medical problem – Responder group?



Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The first row of the table shows the groups in the study and the number of participants in each group.
  - **First column**: participants who took **placebo** in the earlier study and in this study
  - **Second column**: participants who took **etrasimod 2 mg** in the earlier study and in this study
  - **Third column**: participants who took **etrasimod 2 mg** in the earlier study and **placebo** in this study
  - **Fourth column**: participants who took **etrasimod 3 mg** in the earlier study and in this study
  - **Fifth column**: participants who took **etrasimod 3 mg** in the earlier study and **placebo** in this study
- The rows that show individual medical problems were commonly reported medical problems by 10% of participants or more in the Responder Group.
- The subsequent rows show the number and percentage of participants in that group who had a medical problem.
- Using these instructions, you can see that 8 out of the 47 participants (17%) who took placebo in the earlier study and in this study reported a medical problem of CD.

Table 1. Commonly reported medical problems by study participants – Responder Group

Placebo to Placebo (47 participants)	Etrasimod 2 mg to Etrasimod 2 mg (38 participants)	Etrasimod 2 mg to Placebo (33 participants)	Etrasimod 3 mg to Etrasimod 3 mg (28 participants)	Etrasimod 3 mg to Placebo (35 participants)
Crohn's disease				
8 out of 47 participants (17%)	5 out of 38 participants (13%)	7 out of 33 participants (21%)	4 out of 28 participants (14%)	4 out of 35 participants (11%)
Joint pain (arthralgia)				
7 out of 47 participants (15%)	7 out of 38 participants (18%)	3 out of 33 participants (9%)	3 out of 28 participants (11%)	3 out of 35 participants (9%)
Abdominal pain				
4 out of 47 participants (9%)	4 out of 38 participants (11%)	2 out of 33 participants (6%)	3 out of 28 participants (11%)	5 out of 35 participants (14%)
Infection of the nose and throat (nasopharyngitis)				
1 out of 47 participants (2%)	2 out of 38 participants (5%)	2 out of 33 participants (6%)	3 out of 28 participants (11%)	1 out of 35 participants (3%)

Table 1. Commonly reported medical problems by study participants – Responder Group

Placebo to Placebo (47 participants)	Etrasimod 2 mg to Etrasimod 2 mg (38 participants)	Etrasimod 2 mg to Placebo (33 participants)	Etrasimod 3 mg to Etrasimod 3 mg (28 participants)	Etrasimod 3 mg to Placebo (35 participants)
Headache				
1 out of 47 participants (2%)	3 out of 38 participants (8%)	1 out of 33 participants (3%)	3 out of 28 participants (11%)	0 participants
Fever (pyrexia)				
5 out of 47 participants (11%)	0 participants	1 out of 33 participants (3%)	0 participants	1 out of 35 participants (3%)
Infection in the gut that causes diarrhea (*Clostridium difficile* infection)				
1 out of 47 participants (2%)	1 out of 38 participants (3%)	0 participants	3 out of 28 participants (11%)	1 out of 35 participants (3%)
Low levels of iron in the blood (iron deficiency)				
1 out of 47 participants (2%)	4 out of 38 participants (11%)	0 participants	0 participants	0 participants

Non-responder Group

Figure 7 shows the number of participants who had at least 1 medical problem.

Figure 7. How many participants had medical problems – Non-responder group?

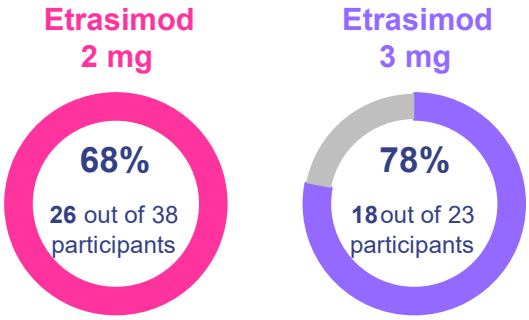
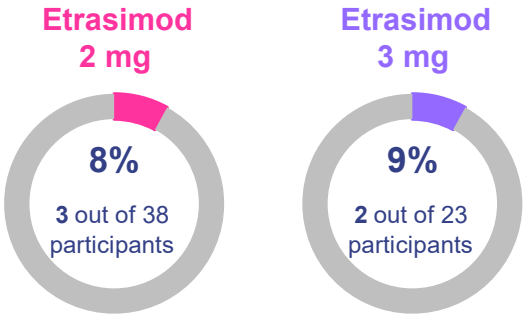


Figure 8 shows the number of participants who stopped taking the study treatment because of a medical problem.

Figure 8. How many participants stopped taking the study treatment because of a medical problem – Non-responder group?



Below are instructions on how to read Table 2.

Instructions for Understanding Table 2.

- The **1st** column lists the medical problems that were reported by 10% of participants or more in the **Non-responder Group**.
- The **2nd** column tells the number and percentage of participants who took **etrasimod 2 mg** and reported a medical problem.
- The **3rd** 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 11 out of 38 participants (29%) who took etrasimod 2 mg and 1 out of 23 participants (4%) who took etrasimod 3 mg reported CD.

Table 2. Commonly reported medical problems by study participants – Non-responder Group

Medical Problem	Etrasimod 2 mg (38 Participants)	Etrasimod 3 mg (23 Participants)
Crohn's disease	11 out of 38 participants (29%)	1 out of 23 participants (4%)
Abdominal pain	7 out of 38 participants (18%)	2 out of 23 participants (9%)

Table 2. Commonly reported medical problems by study participants – Non-responder Group		
Medical Problem	**Etrasimod 2 mg (38 Participants)**	**Etrasimod 3 mg (23 Participants)**
Increased level of liver enzyme (ALT increased)	0 participants	3 out of 23 participants (13%)
Condition caused by the coronavirus that often causes breathing problems (COVID-19)	0 participants	3 out of 23 participants (13%)

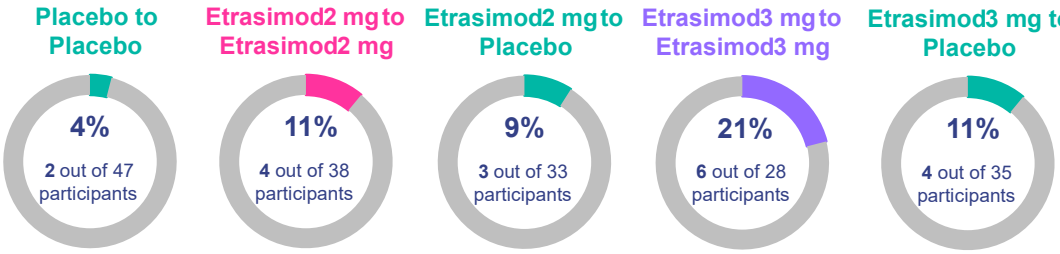
Did study participants have any serious medical problems?

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

Responder Group

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

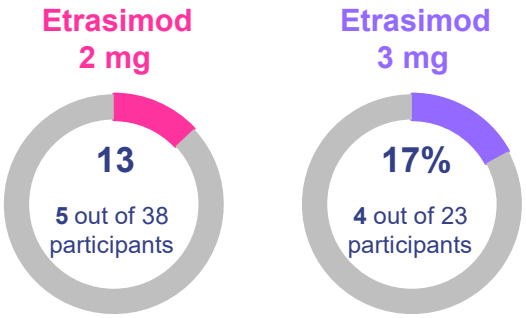
Figure 9. How many participants had serious medical problems – Responder group?



Non-responder Group

Figure 10 shows the number of participants who had at least 1 serious medical problem.

Figure 10. How many participants had serious medical problems – Non-responder group?



Responder and Non-responder Groups

The most common serious medical problems – reported by at least 2 participants overall in the Responder and Non-responder Groups – were abdominal pain and CD.

No participants died during 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 **C5041006 SS3-M**

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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