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 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, a wholly owned subsidiary of Pfizer

Medicine(s) Studied: Etrasimod

Protocol Number: APD334-301

Dates of Study: 13 June 2019 to 16 February 2022

Title of this Study: ELEVATE UC 52: Etrasimod Versus Placebo for the Treatment of Moderately to Severely Active Ulcerative Colitis

[A Phase 3, Randomized, Double-Blind, Placebo-Controlled, 52-Week Study to Assess the Efficacy and Safety of Etrasimod in Subjects with Moderately to Severely Active Ulcerative Colitis]

Date(s) of this Report: 5 August 2022

– Thank You –

If you participated in this study, Arena Pharmaceuticals, 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 moderately to severely active ulcerative colitis?

Ulcerative colitis, or UC, is an inflammatory bowel disease that affects the colon (large intestine). People with UC can have symptoms like abdominal pain, rectal bleeding (blood in stool), and loose stools.

The immune system is a network of white blood cells, tissues, and organs that help the body to fight infections. UC is a type of autoimmune disease. In autoimmune diseases, the immune system attacks its own tissues for unknown reasons, creating abnormal inflammation (redness and swelling). A group of white blood cells called lymphocytes play a crucial role in this immune reaction.

For this study, UC disease activity was determined based on frequency of stools, rectal bleeding, and endoscopy results (an imaging test of the colon and rectum). Participants in this study had UC that was determined to be moderately to severely active.

What is etrasimod?

Etrasimod is an investigational drug that is being studied for UC. It is believed that etrasimod works by reducing the number of lymphocytes in the blood and therefore reducing the abnormal inflammation in the gut in people with moderately to severely active UC.

What was the purpose of this study?

The main purpose of this study was to learn more about the safety and the effects of etrasimod on clinical remission in participants with moderately to severely active UC, compared to placebo. A placebo does not have any medicine in it, but it looks just like the investigational drug. Clinical remission means that the participant has a normal or almost normal frequency of stools, no rectal bleeding, and normal findings on endoscopy (no disease activity).

Researchers wanted to know:

How many participants achieved clinical remission after taking etrasimod or placebo for 12 weeks?

How many participants achieved clinical remission after taking etrasimod or placebo for 52 weeks?

What medical problems did participants have during the study?

What happened during the study?

How was the study done?

Researchers administered etrasimod or placebo to a group of participants who chose to join the study, to find out if they would achieve clinical remission.

Researchers compared the results of study participants taking etrasimod to the results of study participants taking placebo.

Participants received the following treatments during the study:

- Etrasimod group (289 participants): 2 milligram (mg) etrasimod tablet, once per day by mouth for up to 52 weeks
- Placebo group (144 participants): Placebo tablet, once per day by mouth for up to 52 weeks

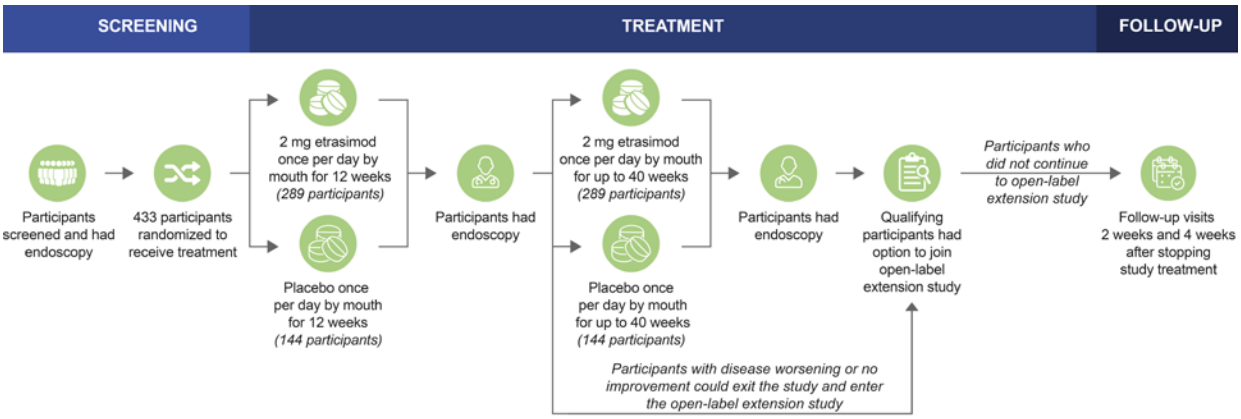
The study participants and researchers did not know who took etrasimod and who took the placebo. This is known as a "blinded" study. Study participants were assigned to each group by chance alone, which is known as "randomization".

Participants were first examined by a doctor to make sure they met the requirements to join the study. This was known as the screening period. There were 2 treatment

periods during this study: a 12-week "induction period" to determine if participants would achieve remission, followed by a 40-week "maintenance period" to determine how long participants would remain in remission. During the 52 weeks of treatment, participants were expected to attend 12 visits at the study center. At these visits, participants were checked by the study doctor and were monitored for any medical problems. Participants also had an endoscopy at the screening visit, Week 12 visit, and the last visit, to see if there was an improvement in their UC.

At the end of this study, qualifying participants had the option to enter an open-label extension study, which is a study that is sometimes done after a randomized study is completed, to gather additional data and to allow participants to continue receiving etrasimod. Open-label means that the study participants and researchers knew which treatment the participants received (in this case, all participants received etrasimod in the extension study). Participants who did not join the open-label extension study were expected to attend up to 2 visits after stopping study treatment to check whether they had any medical problems. These are called follow-up visits.

The figure below shows what happened during the study.



Where did this study take place?

The Sponsor ran this study at 185 locations in Africa, Asia-Pacific, Eastern Europe, Latin America, the Middle East, North America, and Western Europe.

When did this study take place?

The study began 13 June 2019 and ended 16 February 2022.

Who participated in this study?

This study included participants who:

- Were examined by the study doctor and determined to be appropriate for study participation
- Had been diagnosed with moderately to severely active UC
- Had an inadequate response, loss of response, or were unable to tolerate certain other marketed treatments for UC
- A total of 240 men (55%) participated in the study
- A total of 193 women (45%) participated in the study
- All participants were between the ages of 17 and 78 years

A total of 433 participants enrolled in this study, including 289 participants in the etrasimod group and 144 participants in the placebo group. 207 participants (48%) completed the study, including 161 participants (56%) in the etrasimod group and 46 participants (32%) in the placebo group. 226 participants (52%) left the study early.

In the etrasimod group, 128 participants (44%) left the study early due to:

- Ulcerative colitis worsened (79 participants, 27%)
- The participant's or parent/guardian's choice (24 participants, 8%)
- The participant had a medical problem (10 participants, 4%)
- The study treatment did not work for the participant (7 participants, 2%)

- A doctor decided it was best for a participant to stop being in the study (2 participants, 1%)
- The participant was "lost to follow-up" (unable to be contacted by the study staff) (1 participant, less than 1%)
- The participant became pregnant (2 participants, 1%)
- The study procedures were not followed (1 participant, less than 1%)
- Other reason (2 participants, 1%)

In the placebo group, 98 participants (68%) left the study early due to:

- Ulcerative colitis worsened (73 participants, 51%)
- The participant's or parent/guardian's choice (10 participants, 7%)
- The participant had a medical problem (5 participants, 4%)
- The study treatment did not work for the participant (4 participants, 3%)
- A doctor decided it was best for a participant to stop being in the study (2 participants, 1%)
- The participant was "lost to follow-up" (unable to be contacted by the study staff) (2 participants, 1%)
- Other reason (2 participants, 1%)

How long did the study last?

Study participants were in the study for up to 52 weeks, plus a screening period of up to 28 days and a follow-up period of up to 4 weeks (for those who did not join the open-label extension study). The entire study took about 2 ½ years to complete.

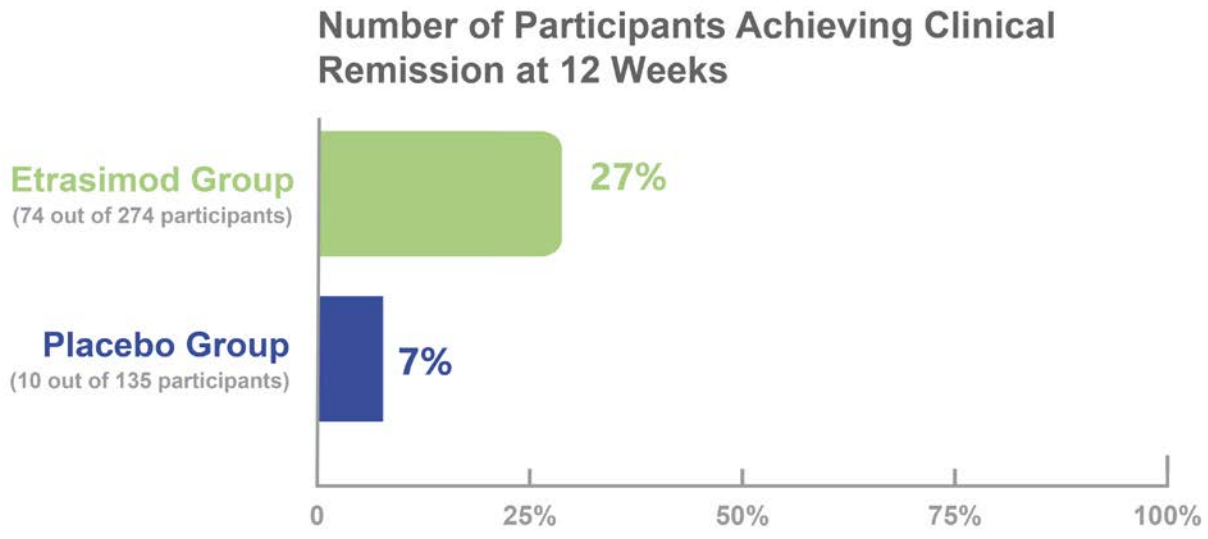
When the study ended in February 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

How many participants achieved clinical remission after taking etrasimod or placebo for 12 weeks?

To answer this question, researchers looked only at participants who had moderately to severely active UC at the beginning of the study, and who achieved clinical remission after taking etrasimod or placebo for 12 weeks. So, the number of participants varies from the total number of participants who joined the study. At Week 12, 74 out of 274 (27%) participants in the etrasimod group had achieved clinical remission. At Week 12, 10 out of 135 (7%) participants in the placebo group had achieved clinical remission. Based on these results, the researchers decided that the outcomes are not likely due to chance. Etrasimod may help people with moderately to severely active UC to achieve clinical remission.

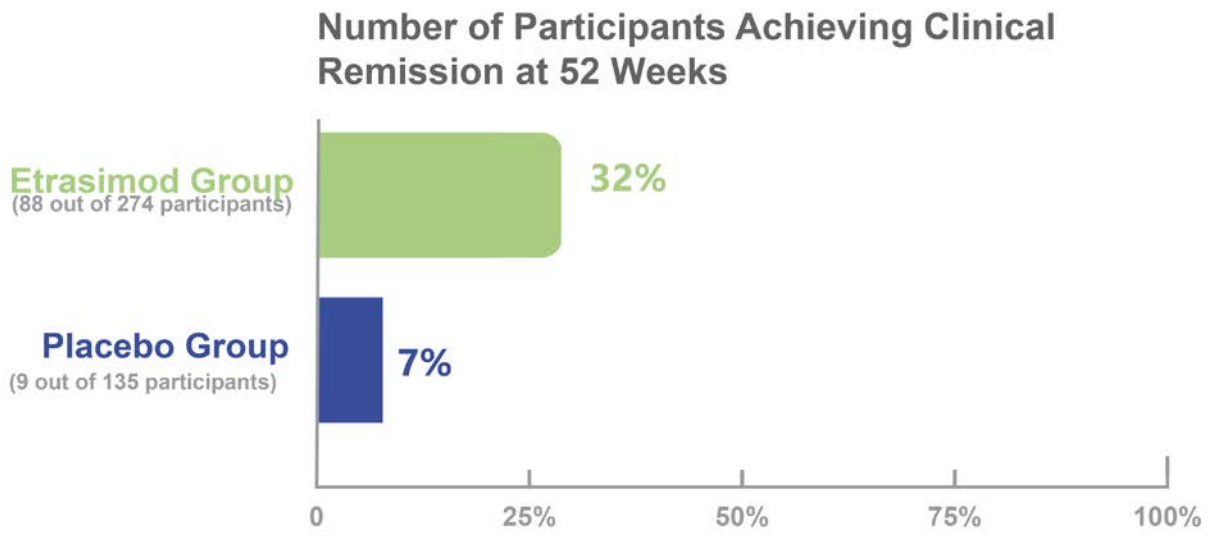
The figure below shows these results.



How many participants achieved clinical remission after taking etrasimod or placebo for 52 weeks?

To answer this question, researchers looked only at participants who had moderately to severely active UC at the beginning of the study, and who achieved clinical remission after taking etrasimod or placebo for 52 weeks. So, the number of participants varies from the total number of participants who joined the study. At Week 52, 88 out of 274 (32%) participants in the etrasimod group had achieved clinical remission. At Week 52, 9 out of 135 (7%) participants in the placebo group had achieved clinical remission. Based on these results, the researchers have decided that the outcomes are not likely due to chance. Etrasimod may help people with moderately to severely active UC to achieve and maintain clinical remission.

The figure below shows these results.



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 that are done with etrasimod 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 medication might have on a participant.

287 out of 433 (66%) participants in this study had at least 1 medical problem, including 206 out of 289 (71%) participants in the etrasimod group and 81 out of 144 (56%) participants in the placebo group. A total of 19 (4%) participants stopped taking study treatment because of medical problems. The most common medical problems – those reported by more than 3% of participants – are described below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by more than 3% of participants are listed.
- The **2nd** column shows how many of the 289 participants treated with etrasimod reported each medical problem. Next to this number is the percentage of the 289 participants treated with etrasimod who reported the medical problem.
- The **3rd** column shows how many of the 144 participants treated with placebo reported each medical problem. Next to this number is the percentage of the 144 participants treated with placebo who reported the medical problem.
- Using these instructions, you can see that 24 out of 289 (8%) participants in the etrasimod group reported headache, and 7 out of 144 (5%) participants in the placebo group reported headache.

Table 1. Commonly reported medical problems by study participants		
Medical Problem	Etrasimod Group (289 Participants)	Placebo (144 Participants)
Low number of red blood cells	24 out of 289 participants (8%)	14 out of 144 participants (10%)
Headache	24 out of 289 participants (8%)	7 out of 144 participants (5%)
Ulcerative colitis flare-up	22 out of 289 participants (8%)	13 out of 144 participants (9%)
COVID-19	20 out of 289 participants (7%)	9 out of 144 participants (6%)
Dizziness	15 out of 289 participants (5%)	1 out of 144 participants (1%)
Fever	14 out of 289 participants (5%)	6 out of 144 participants (4%)
Joint pain	13 out of 289 participants (5%)	3 out of 144 participants (2%)
Abdominal pain	11 out of 289 participants (4%)	5 out of 144 participants (4%)
Nausea	9 out of 289 participants (3%)	2 out of 144 participants (1%)
Increased level of enzyme in blood that could indicate liver damage	8 out of 289 participants (3%)	2 out of 144 participants (1%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	Etrasimod Group (289 Participants)	Placebo (144 Participants)
High blood pressure	8 out of 289 participants (3%)	1 out of 144 participants (1%)

Did study participants have any serious medical problems?

A medical problem is considered "serious" when it is life-threatening, the participant needs hospital care, or the participant has lasting problems.

A total of 29 (7%) participants had serious medical problems.

- 20 (7%) participants in the etrasimod group had serious medical problems.
- 9 (6%) participants in the placebo group had serious medical problems.

UC flare-up was the most common serious medical problem, which happened in 6 (2%) participants from the etrasimod group and 3 (2%) participants from the placebo group. A total of 2 participants had serious medical problems that the study doctor considered to be related to study treatment: 1 participant in the etrasimod group had a blighted ovum (early pregnancy that never fully develops and typically leads to miscarriage) and 1 participant in the placebo group had a serious skin infection called cellulitis. In clinical studies it is standard practice to record if any deaths took place. No participants died during this 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.clinicaltrials.gov	Use the study identifier **NCT03945188**
www.clinicaltrialsregister.eu	Use the study identifier **2018-003987-29**

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!