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 Studied:	Etrasimod
Protocol Number:	C5041008 (APD334-205)
Dates of Study:	29 July 2020 to 07 June 2023
Title of this Study:	A Study on Etrasimod in Adults With Patchy Hair Loss [A Multicenter, Randomized, Double-Blind, Placebo-Controlled, 24-Week Study, With a 28-Week Open-Label Extension, to Assess the Safety and Efficacy of Etrasimod in Subjects With Moderate-to-Severe Alopecia Areata]
Date of this Report:	01 February 2024

– 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 alopecia areata (AA)?

AA is a disease that is also known as patchy hair loss. AA happens when the immune system attacks hair follicles, which may cause hair loss on the scalp, face, and sometimes on other body areas. This attack happens because the immune system mistakenly thinks the hair follicles are harmful invaders.

Hair follicles are structures within the skin that grow hair.

What is etrasimod?

Etrasimod (et – ras' – i – mod) is a tablet taken by mouth. The use of etrasimod in this study is investigational because it is not approved for the treatment of AA outside of this research study. Etrasimod is approved to treat of ulcerative colitis, an inflammatory bowel disease that affects the colon (large intestine).

Etrasimod is designed to block the movement of white blood cells called lymphocytes, which are part of the immune system. Etrasimod helps to stop these cells from moving to areas of inflammation. Since hair follicles represent sites of inflammation in people with AA, researchers think etrasimod can help treat AA.

What was the purpose of this study?

The main purposes of the study were:

- To learn if etrasimod can help participants with AA reduce how much of the scalp has hair loss.
- To learn if etrasimod is safe when given to participants with AA.

Researchers wanted to know:

- **Did taking etrasimod for 24 weeks reduce how much of the scalp had hair loss?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested etrasimod on different groups of study participants to find out if etrasimod taken for 24 weeks reduced how much of the scalp has hair loss.

Researchers then compared the results of study participants taking etrasimod to the results of those taking a placebo. A placebo does not have any medicine in it, but it looks just like etrasimod.

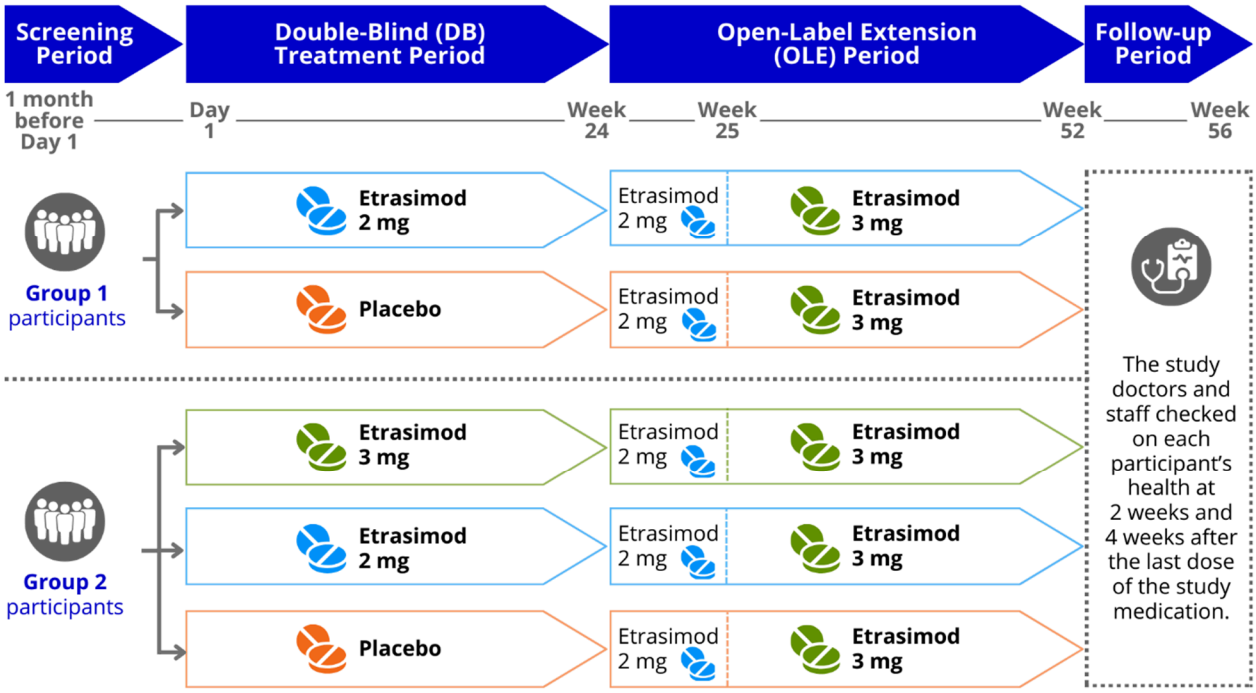
In the original study plan, etrasimod 2 milligrams (also called mg) was to be tested and compared against a placebo.

In the middle of the study, the study plan was changed so that etrasimod 3 mg could be tested along with etrasimod 2 mg and compared against a placebo. Then, it was decided to have 2 groups of participants.

- **Group 1** included participants who had already been enrolled in the study before the study plan was changed.
- **Group 2** included participants who were enrolled in the study after the study plan was changed.

Figure 1 shows what happened to Groups 1 and 2 in the study after the study plan was changed.

Figure 1. What happened in the study?



Throughout the study, the study doctors and staff checked on each participant's health and safety.

The study had 4 periods:

1. **Screening period:** The study doctors and staff checked on each participant to see if they met the requirements to join the study.

2. **Double-blind (DB) treatment period:** "Double-blind" means that study participants and researchers did not know who took etrasimod and who took a placebo.

   Participants in both groups took etrasimod or a placebo 1 time daily for 24 weeks.

Group 1:	Participants were assigned to take **etrasimod 2 mg** or **a placebo** by chance. Each participant had 2 in 3 chances (67%) to get etrasimod 2 mg and 1 in 3 chances (33%) to get a placebo.
Group 2:	Participants were assigned to take **etrasimod 2 mg, etrasimod 3 mg,** or **a placebo** by chance. Each participant had 4 in 7 chances (57%) to get etrasimod 3 mg, 1 in 7 chances (14%) to get etrasimod 2 mg, and 2 in 7 chances (29%) to get a placebo.

3. **Open-label extension (OLE) period:** "Open-label" means that study participants and researchers knew that participants took etrasimod during this period.

   - Participants who completed the DB treatment period entered the OLE period. They took etrasimod 1 time daily for up to an additional 28 weeks.
   - A placebo was not given during the OLE period.

Group 1:	Before the study plan was changed, some participants had already been taking etrasimod 2 mg during the OLE period. After the study plan was changed, these participants were switched from etrasimod 2 mg to etrasimod 3 mg. Participants who entered the OLE period after the change in study plan took etrasimod 2 mg for 1 week before switching to etrasimod 3 mg. The study doctor allowed some participants to continue taking etrasimod 2 mg based on their Severity of ALopecia Tool (SALT) scores.
Group 2:	Participants in this group took etrasimod 2 mg for 1 week before they were switched to etrasimod 3 mg.

Severity of **AL**opecia **T**ool (**SALT**) helps the study doctors check the degree of AA based on how much of the scalp area has hair loss. A higher SALT score means more hair loss.

- A SALT score of **0** means no hair loss.
- A SALT score of **100** means complete hair loss.

4. **Follow-up period:** Participants entered this period after taking their last dose of etrasimod or a placebo. The study doctors and staff continued to check on each participant's health until the study ended.

Where did this study take place?

The Sponsor ran this study at 26 locations in the United States (US) and 3 locations in Canada. One location in the US did not sign up participants.

When did this study take place?

It began on 29 July 2020 and ended on 07 June 2023.

Who participated in this study?

The study included men and women who:

- were from 18 to 70 years of age.
- had moderate-to-severe AA based on their SALT scores.
    - **Group 1** included participants with SALT score from 50 to 100.
    - **Group 2** included participants with SALT score from 25 to below 95.
- had AA that has not gotten better in the last 6 months before joining the study.
- were willing to keep the same style and color of hair during the study.

DB Treatment Period:
Overall, 80 participants joined the DB treatment period. Out of the 80 participants, 79 received at least 1 dose of etrasimod or a placebo. • A total of 21 men and 58 women participated. • Participants were from 18 to 70 years old. • On average, participants had AA for about 12 years. Out of the 79 participants who received at least 1 dose of etrasimod or a placebo, 65 participants completed the DB treatment period.

OLE Period:
All 65 participants who completed the DB treatment period joined the OLE period. • A total of 19 men and 46 women participated. • Participants were from 18 to 67 years old. • On average, participants had AA for about 12 years.

Some participants stopped taking etrasimod or placebo during the study. The most common reason was because of their choice to stop taking part in the study.

- **DB treatment period:** 14 participants stopped taking etrasimod or placebo.
- **OLE period:** 13 participants stopped taking etrasimod.

How long did the study last?

Study participants were in the study for up to 60 weeks. The entire study took about 2 years and 10 months to complete.

When the study ended in June 2023, 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?

Did taking etrasimod for 24 weeks reduce how much of the scalp had hair loss?

To answer this question, researchers checked how much the SALT scores have changed for participants after taking etrasimod or a placebo for 24 weeks compared to “baseline”.

Baseline is the time at the start of the study (Day 1) before participants started taking etrasimod or a placebo.

Researchers measured the SALT score change in percentage, also called “percent change in SALT scores”.

Figure 2. What were the percent changes in SALT scores after 24 weeks of taking etrasimod or placebo?

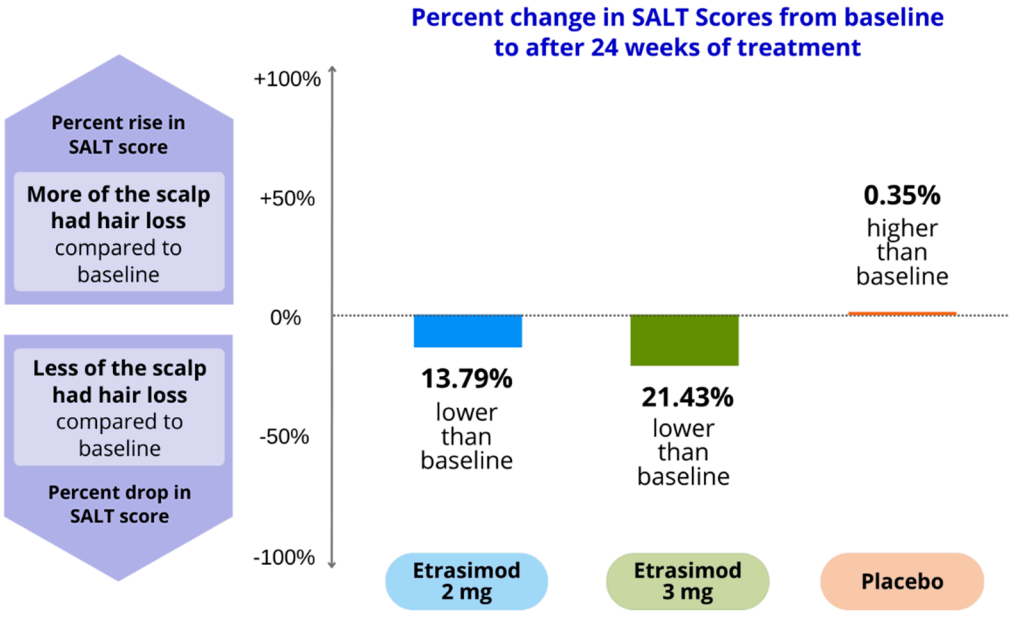


Figure 2 shows the average results after 24 weeks of treatment compared to baseline:

- Participants who took **etrasimod 2 mg: 13.79% less** of the scalp had hair loss.
- Participants who took **etrasimod 3 mg: 21.43% less** of the scalp had hair loss.
- Participants who took a **placebo: 0.35% more** of the scalp had hair loss or had no change.

However, researchers have decided that these results are likely due to chance. This means **etrasimod 2 mg or 3 mg** may not help reduce how much of the scalp had hair loss after 24 weeks of treatment.

More studies are needed to better understand the effect of etrasimod on AA.

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 medication might have on a participant.

In this study, etrasimod 2 mg and 3 mg were well-tolerated (did not cause major discomfort) by participants with moderate-to-severe AA.

No pregnancies were reported during the study.

DB Treatment Period:

In total, 59 out of 79 participants (74.7%) had at least 1 medical problem during the DB treatment period.

- 21 out of 31 participants (67.7%) in the etrasimod 2 mg group.
- 20 out of 25 participants (80.0%) in the etrasimod 3 mg group.
- 18 out of 23 participants (78.3%) in the placebo group.

Overall, 2 participants stopped taking etrasimod or a placebo and left the study because of medical problems they had during this period. Of these participants:

- 1 participant stopped taking etrasimod 2 mg because of tiredness.
- 1 participant stopped taking a placebo because of joint pain.

Table 1 describes the most common medical problems – those reported by 5% or more participants in at least 1 treatment group – during the DB treatment period.

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 DB treatment period. All medical problems reported by 5% or more participants in at least 1 treatment group are listed.
- The **2nd** column tells how many of the 31 participants taking etrasimod 2 mg reported each medical problem. Next to this number is the percentage of the 31 participants taking etrasimod 2 mg who reported the medical problem.
- The **3rd** column tells how many of the 25 participants taking etrasimod 3 mg reported each medical problem. Next to this number is the percentage of the 25 participants taking etrasimod 3 mg who reported the medical problem.
- The **4th** column tells how many of the 23 participants taking a placebo reported each medical problem. Next to this number is the percentage of the 23 participants taking a placebo who reported the medical problem.
- For example, using these instructions, you can see how many participants reported a headache:
  - 4 out of 31 participants (12.9%) taking etrasimod 2 mg.
  - 2 out of 25 participants (8.0%) taking etrasimod 3 mg.
  - 4 out of 23 participants (17.4%) taking a placebo.

Table 1. Commonly reported medical problems by study participants during the DB treatment period

Medical Problem	Etrasimod 2 mg (31 Participants)	Etrasimod 3 mg (25 Participants)	Placebo (23 Participants)
Headache	4 out of 31 participants (12.9%)	2 out of 25 participants (8.0%)	4 out of 23 participants (17.4%)
COVID-19	1 out of 31 participants (3.2%)	2 out of 25 participants (8.0%)	3 out of 23 participants (13.0%)
High amount of gamma-glutamyl transferase (GGT), a liver enzyme in the blood	2 out of 31 participants (6.5%)	2 out of 25 participants (8.0%)	1 out of 23 participants (4.3%)
Muscle aches	3 out of 31 participants (9.7%)	1 out of 25 participants (4.0%)	1 out of 23 participants (4.3%)
Infection of the upper lung airways	1 out of 31 participants (3.2%)	1 out of 25 participants (4.0%)	3 out of 23 participants (13.0%)
High amount of alanine aminotransferase (ALT), a liver enzyme in the blood	2 out of 31 participants (6.5%)	1 out of 25 participants (4.0%)	1 out of 23 participants (4.3%)

Table 1. Commonly reported medical problems by study participants during the DB treatment period

Medical Problem	Etrasimod 2 mg (31 Participants)	Etrasimod 3 mg (25 Participants)	Placebo (23 Participants)
Joint pain	2 out of 31 participants (6.5%)	0 out of 25 participants (0%)	2 out of 23 participants (8.7%)
Queasy feeling or nausea	2 out of 31 participants (6.5%)	1 out of 25 participants (4.0%)	1 out of 23 participants (4.3%)
Urinary tract infection, also called UTI	0 out of 31 participants (0%)	3 out of 25 participants (12.0%)	1 out of 23 participants (4.3%)
Dizziness	0 out of 31 participants (0%)	2 out of 25 participants (8.0%)	1 out of 23 participants (4.3%)
Infection of the hair follicles	0 out of 31 participants (0%)	0 out of 25 participants (0%)	2 out of 23 participants (8.7%)
Joint injury	0 out of 31 participants (0%)	0 out of 25 participants (0%)	2 out of 23 participants (8.7%)
Pain in the arms or legs	0 out of 31 participants (0%)	2 out of 25 participants (8.0%)	0 out of 23 participants (0%)

OLE Period:

- 48 out of 65 participants (73.8%) taking etrasimod 2 mg or 3 mg had at least 1 medical problem during the OLE period.
- 2 participants stopped taking etrasimod and left the study because of medical problems they had during this period. Of these participants, 1 participant had a lung infection from COVID-19 and 1 had a high amount of gamma-glutamyl transferase (GGT), a liver enzyme in the blood.

Table 2 describes the most common medical problems – those reported by 5% or more of the total participants – during the OLE period.

Below are instructions on how to read Table 2.

Instructions for Understanding Table 2.

- The **1st** column of Table 2 lists medical problems that were commonly reported during the OLE period. All medical problems reported by 5% or more of the total participants are listed. Participants taking etrasimod (2 mg or 3 mg) during the OLE period were combined into the total group.
- The **2nd** column tells how many of the 65 participants in the total group reported each medical problem. Next to this number is the percentage of the 65 participants in the total group who reported the medical problem.
- For example, using these instructions, you can see that 7 out of 65 participants (10.8%) reported an infection of the upper lung airways.

Table 2. Commonly reported medical problems by study participants during the OLE period	
Medical Problem	**Total participants taking etrasimod 2 mg or 3 mg (65 Participants)**
Infection of the upper lung airways	7 out of 65 participants (10.8%)
Common cold	6 out of 65 participants (9.2%)
Low amount of lymphocyte, a type of white blood cell that helps to fight infections	5 out of 65 participants (7.7%)
COVID-19	4 out of 65 participants (6.2%)
High amount of gamma-glutamyl transferase (GGT), a liver enzyme in the blood	4 out of 65 participants (6.2%)

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.

No participant died during the study.

DB Treatment Period:

No participant in the etrasimod (2 mg or 3 mg) or placebo groups had serious medical problems during the DB treatment period.

OLE Period:

Overall, 2 out of 65 participants (3.1%) had serious medical problems during the OLE period. Of these participants:

- 1 participant taking etrasimod 2 mg had a lung infection from COVID-19.
- 1 participant taking etrasimod 3 mg had nerve and spinal cord problems.

Researchers do not believe that these serious medical problems were caused by etrasimod.

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 **C5041008 (APD334-205)**

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

www.clinicaltrials.gov	Use the study identifier **NCT04556734**

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!