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: Pfizer Inc.

Medicine Studied: Vepdegestrant (formerly ARV-471 or PF-07850327)

Protocol Number: C4891039

Date of Study: 8 February 2024 to 13 May 2024

Title of this Study: A Study to Learn If the Study Medicine Called Vepdegestrant Changes How the Body Processes the Other Study Medicine Called Midazolam

[An Interventional, Phase 1, Open-Label, Fixed Sequence, 2-Period Study to Estimate the Effect of Single and Multiple Doses of Vepdegestrant (ARV-471, PF-07850327) on the Pharmacokinetics of Single Dose Midazolam in Healthy Adult Females of Non-Childbearing Potential]

Date of this Report: 08 May 2025

090177e1a37ac481\Approved\Approved On: 09-May-2025 12:13 (GMT)

Pfizer

– 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 breast cancer?

Breast cancer is a disease where the cells in the breast grow out of control. There are different kinds of breast cancer depending on which cells grow out of control. In some types of breast cancer, the signal for the cells to grow comes from hormones in the body such as estrogen and progesterone. Estrogen binds to estrogen receptors on the breast cell and signals for the breast cancer cells to grow. These types of breast cancers are called estrogen receptor positive (ER+).

What is vepdegestrant?

Vepdegestrant (vep-DEG-e-STRANT), also known as ARV-471, is being studied as a possible treatment for ER+ breast cancer.

Vepdegestrant is a "PROteolysis TArgeting Chimera" (PROTAC) protein degrader that binds to estrogen receptors. PROTAC protein degraders are designed to bind specific proteins of interest in cells, which causes those proteins to be marked for elimination by a natural protein disposal system in the body.

Researchers think that vepdegestrant works by causing estrogen receptors to be eliminated, which could block the activity of estrogen and could potentially stop ER+ breast cancer tumors from growing or cause the tumors to shrink.

090177e1a37ac481\Approved\Approved On: 09-May-2025 12:13 (GMT)

Vepdegestrant is taken as tablets, by mouth.

What is midazolam?

Midazolam (muh-da-zuh-lam) is an approved medication. It is used to treat anxiety, seizures, and sleep problems. It is taken as a tablet, by mouth.

What was the purpose of this study?

The purpose of this study was to understand how the amount of midazolam changes in the body when it is taken with vepdegestrant. To do this, researchers looked at the amount of midazolam in the blood when it was taken alone or with vepdegestrant.

Researchers wanted to know:

- **How did midazolam act in the body when taken with and without vepdegestrant?**
- **What medical problems did participants have during the study?**

This study will help researchers plan future studies. This study did not test if vepdegestrant helps to treat patients with breast cancer.

What happened during the study?

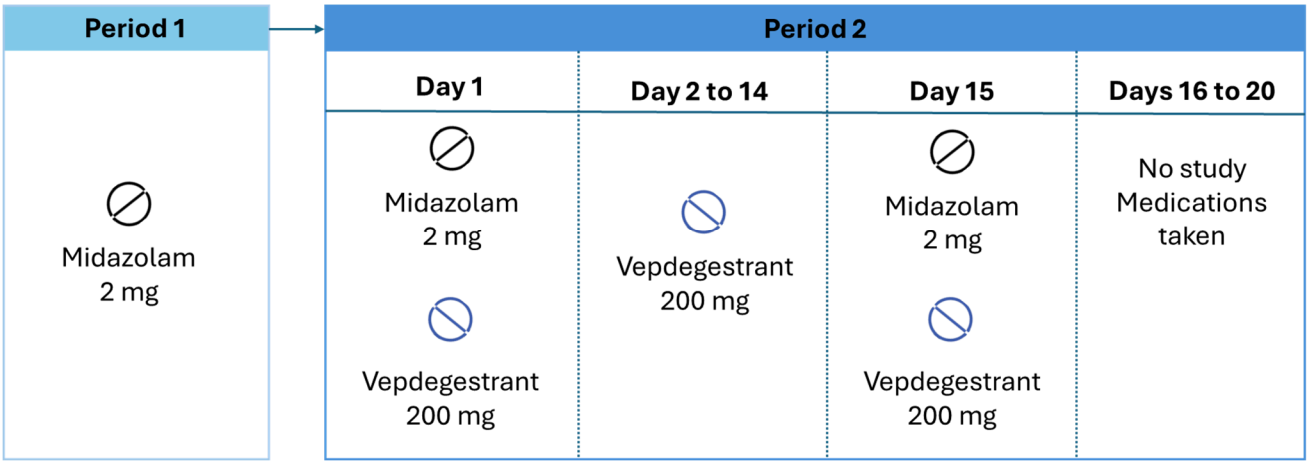
How was the study done?

Researchers tested midazolam on a group of healthy participants to learn how it acted in the body when taken with and without vepdegestrant. The study was done in 2 periods. Participants stayed at the clinic for 22 days. The participants took part in both periods.

The figure below shows what happened during Period 1 and Period 2.

090177e1a37ac481\Approved\Approved On: 09-May-2025 12:13 (GMT)

Figure 1. What happened during Period 1 and Period 2



Participants also had a follow-up phone call about a month after they left the clinic.

Researchers took samples of blood from participants during the study and measured the amount of midazolam. Researchers also checked the participants' health during the study and asked them how they were feeling. Researchers then compared the results when participants took midazolam alone and when they took midazolam with vepdegestrant.

The participants and researchers knew what study drugs the participants were taking. This is called an "open label" study.

Where did this study take place?

The Sponsor ran this study at 1 location in Belgium.

When did this study take place?

It began 8 February 2024 and ended 13 May 2024.

Who participated in this study?

The study included healthy women who were at least 18 years old.

090177e1a37ac481\Approved\Approved On: 09-May-2025 12:13 (GMT)

- A total of 15 women participated
- All participants were between the ages of 51 years and 74 years.

Of the 15 participants who started the study, 14 finished. One (1) participant did not finish the study because of a medical problem.

How long did the study last?

Study participants were in the study for about 3 weeks. The entire study took about 3 months to complete. The study was completed as planned and did not end early.

When the study ended in May 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 did midazolam act in the body when taken with and without vepdegestrant?

Researchers answered this question by looking at 2 types of blood test results.

- What was the highest amount of midazolam in the blood when taken alone and with vepdegestrant?
- What was the total amount of midazolam in the blood from when it was taken until it was removed from the body?

Researchers looked at the levels of midazolam in the blood when participants.

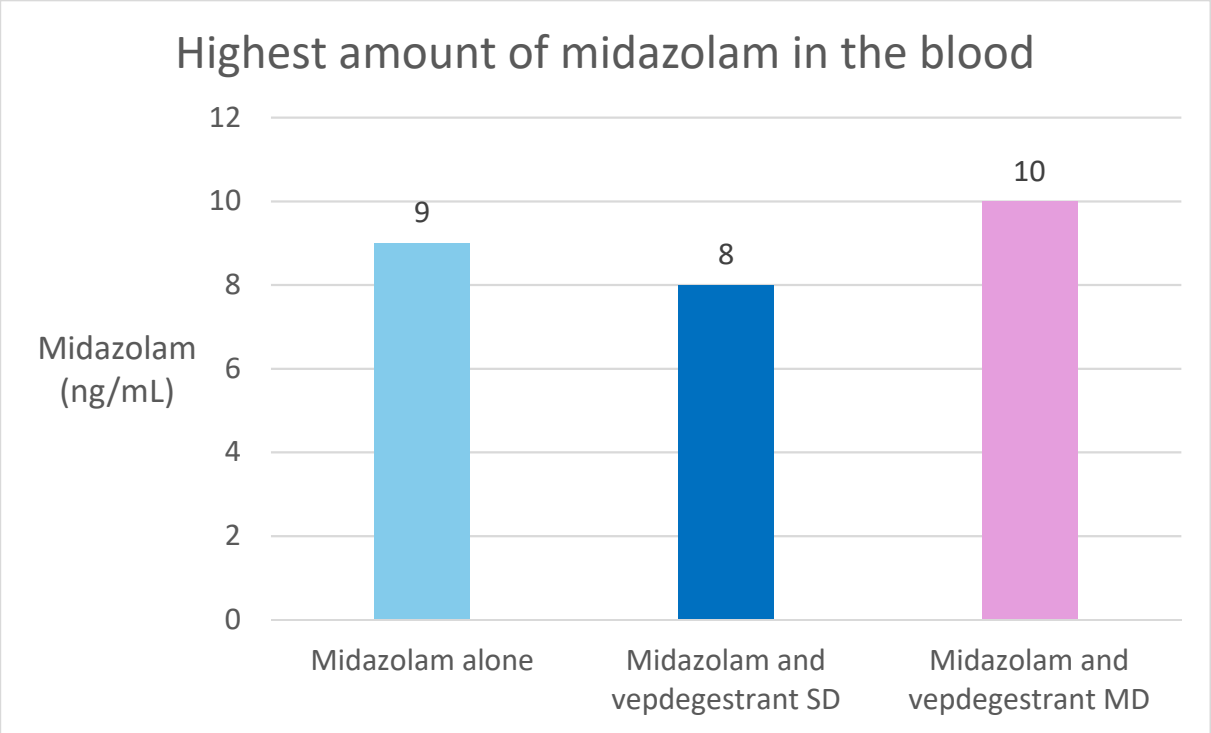
- Took midazolam alone
- Took midazolam with a single dose (SD) of vepdegestrant
- Took midazolam with multiple doses (MD) of vepdegestrant

090177e1a37ac481\Approved\Approved On: 09-May-2025 12:13 (GMT)

What was the highest amount of midazolam in the blood after participants took midazolam alone, with vepdegestrant SD, and with vepdegestrant MD?

The highest amount of midazolam in the blood after participants took it alone, with vepdegestrant SD, and vepdegestrant MD is shown in Figure 2. The amount of midazolam in the blood was measured in nanograms per milliliter, also called ng/mL.

Figure 2. Highest amount of midazolam in the blood



Researchers found that

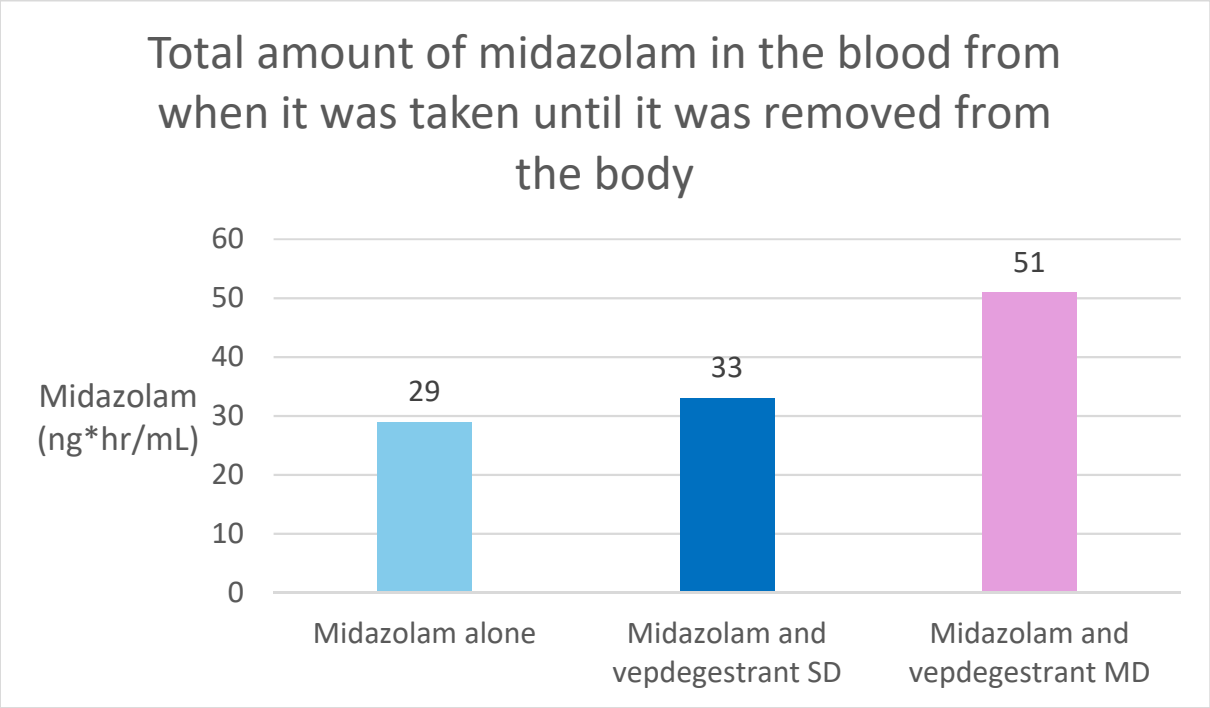
- A single dose of vepdegestrant slightly lowered the highest amount of midazolam in the blood.
- Multiple doses of vepdegestrant increased the highest amount of midazolam in the blood by about 15%.

090177e1a37ac481\Approved\Approved On: 09-May-2025 12:13 (GMT)

What was the total amount of midazolam in the blood from when it was taken until it was removed from the body when it was taken alone, with vepdegestrant SD, and with vepdegestrant MD?

The total amount of midazolam in the blood over time is shown in Figure 3. It shows the amount of midazolam in the blood after participants took it alone, with vepdegestrant SD, and vepdegestrant MD is shown in. The amount of medicine in the blood was measured in nanogram hours per milliliter, also called ng*hr/mL.

Figure 3. Total amount of midazolam in the blood over time



Researchers found that

- A single dose of vepdegestrant has little effect on the total amount of midazolam over time.
- Multiple doses of vepdegestrant increased the total amount of midazolam over time by about 74%.

090177e1a37ac481\Approved\Approved On: 09-May-2025 12:13 (GMT)

Based on these results, the researchers have decided that the results are not likely due to chance.

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 unknown 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.

Thirteen (13) out of 15 participants (87%) in this study had at least 1 medical problem. A total of 1 participant (7%) left the study because of medical problems. The most common medical problems – those reported by more than 10% of participants in any group – are described below.

090177e1a37ac481\Approved\Approved On: 09-May-2025 12:13 (GMT)

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.
- The grey and white rows in Table 1 show individual medical problems that were commonly reported by more than 10% of participants in any group.
- The **1st** column of Table 1 tells how many of the 15 participants who took midazolam alone reported each medical problem. Below the number is the percentage of 15 participants who took midazolam and reported the medical problem.
- The **2nd** column of Table 1 tells how many of the 14 participants who took vepdegestrant SD and midazolam reported each medical problem. Below the number is the percentage of 14 participants who took vepdegestrant SD and midazolam and reported the medical problem.
- The **3rd** column of Table 1 tells how many of the 14 participants who took vepdegestrant alone reported each medical problem. Below the number is the percentage of 14 participants who took vepdegestrant alone and reported the medical problem.
- The **4th** column of Table 1 tells how many of the 14 participants who took vepdegestrant MD and midazolam reported each medical problem. Below the number is the percentage of 14 participants who took vepdegestrant MD and midazolam and reported the medical problem.

090177e1a37ac481\Approved\Approved On: 09-May-2025 12:13 (GMT)

Table 1. Commonly reported medical problems by study participants			
Midazolam Alone (15 Participants)	**Vepdegestrant SD and Midazolam (14 Participants)**	**Vepdegestrant Alone (14 Participants)**	**Vepdegestrant MD and Midazolam (14 Participants)**
Abdominal Pain			
0	1 out of 14 participants (7%)	2 out of 14 participants (14%)	0
Tiredness			
1 out of 15 participants (7%)	2 out of 14 participants (14%)	0	0
Abdominal Discomfort			
0	2 out of 14 participants (14%)	0	0
Headache			
0	0	2 out of 14 participants (14%)	0

090177e1a37ac481\Approved\Approved On: 09-May-2025 12:13 (GMT)

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.

None of the participants had serious medical problems.

090177e1a37ac481\Approved\Approved On: 09-May-2025 12:13 (GMT)

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 **C4891039**

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

www.clinicaltrials.gov	Use the study identifier **NCT06256510**
https://euclinicaltrials.eu	Use the study identifier **2023-508518-40-00**

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!

090177e1a37ac481\Approved\Approved On: 09-May-2025 12:13 (GMT)

Pfizer