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:	Pfizer Inc.
Medicine(s) Studied:	PF-07850327/ARV-471/Vepdegestrant
Protocol Number:	C4891009
Dates of Study:	23 February 2023 to 22 May 2023
Title of this Study:	A Study to Understand the Effect of Itraconazole on the Levels of a Study Medicine Called ARV-471 in Healthy Adults [An Interventional, Phase 1, Open-Label, Fixed Sequence, 2-Period Study to Estimate the Effect of Multiple Doses of Itraconazole on the Pharmacokinetics of Single Dose ARV-471 in the Fed Condition in Healthy Adult Males, and Females of Nonchildbearing Potential]
Date(s) of this Report:	12 January 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 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-de-guess-trent), also known as ARV-471, is a new drug that is being studied as a possible treatment for ER+ breast cancer. Vepdegestrant is not currently an approved drug.

Vepdegestrant is a **PRO**teolysis **TA**rgeting **C**himera (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.

Vepdegestrant is taken as tablets, by mouth.

What is itraconazole?

Itraconazole (eye-tra-con-ah-zole) (Sporanox®) is an approved medicine. It is used to treat fungal infections ("antifungal"). It is used to treat yeast infections of the mouth and throat. It can also be used to stop a person from getting a fungal infection if they have a poor immune system due to other illnesses, like cancer. It is normally taken as a liquid, by mouth, on an empty stomach, eg., 1 hour before food.

What was the purpose of this study?

The purpose of this study was to understand how the amount of vepdegestrant changes in the body when it is taken with itraconazole. To do this, researchers looked at the amount of vepdegestrant in the blood when it was taken alone or with itraconazole. Researchers also looked at the amount of ARV-473 in the blood. ARV-473 is a version of vepdegestrant that has a slight physical difference in its structure (this is known as an "epimer").

The participants in the study were healthy adults.

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

Researchers wanted to know:

- **How did the amount of vepdegestrant in the blood change when participants took vepdegestrant alone or vepdegestrant with itraconazole?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

First, a study doctor checked each participant to make sure they were able to join the study. This is known as a screening period.

Participants stayed at the study center for 19 days and 18 nights. There were 2 study periods. Period 1 lasted 6 days and Period 2 lasted 12 days. Participants arrived at the study center on Day -1 of Period 1, the day before the 1st treatment. Participants left the study center on Day 12 of Period 2, which was the 19th day at the study center.

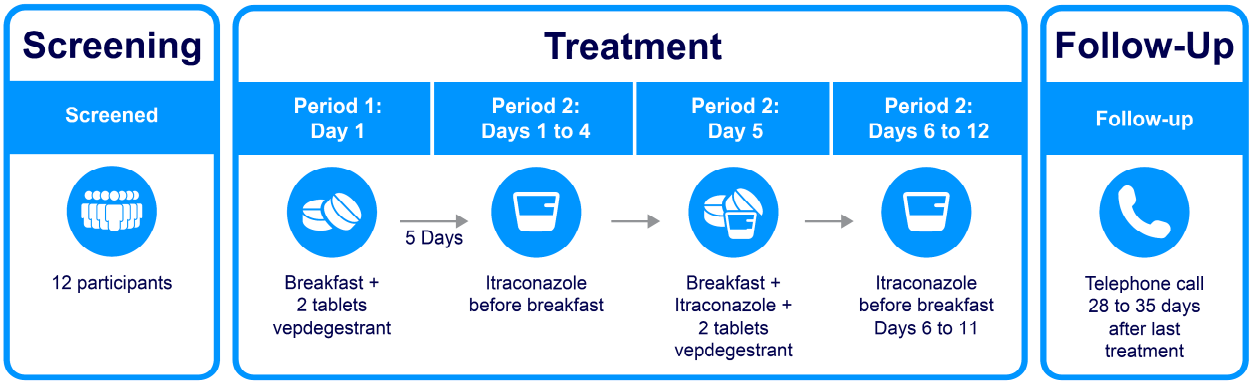
- On Day 1 of Period 1, participants ate breakfast and then took two 100 mg tablets of vepdegestrant.
- No treatments were given for the next 5 days.
- On Days 1 to 4 of Period 2, participants drank 4 teaspoons of the itraconazole liquid on an empty stomach at least 1 hour before breakfast.
- On Day 5 of Period 2, participants ate breakfast and then drank 4 teaspoons of the itraconazole liquid and took two 100 mg tablets of vepdegestrant.
- On Days 6 to 11 of Period 2, participants drank 4 teaspoons of the itraconazole liquid on an empty stomach at least 1 hour before breakfast.

Each breakfast was a high fat, high calorie meal of around 800 to 1000 calories. Participants were asked to eat all their breakfast within 20 minutes.

Researchers took samples of blood and urine from participants during the study. Researchers measured the amount of vepdegestrant and ARV-473 in the blood. Researchers also checked the participants' health during the study and asked them how they were feeling.

Figure 1 shows the design of the study.

Figure 1. Study Plan



Participants spent 19 days and 18 nights in the treatment center from the day before their 1st dose on Day 1 until after all checks had been completed on Day 12 of Period 2.

Researchers then compared the results of participants when they took vepdegestrant alone to the results when participants took vepdegestrant with itraconazole.

Where did this study take place?

The Sponsor ran this study at 1 location in Belgium.

When did this study take place?

It began 23 February 2023 and ended 22 May 2023.

Who participated in this study?

The study included healthy participants.

- A total of 11 men participated
- A total of 1 woman participated
- All participants were between the ages of 24 and 60 years

All 12 participants finished the study.

How long did the study last?

Study participants were in the study for about 12 weeks, from screening to follow-up calls. The entire study took 12 weeks to complete.

When the study ended in May 2023, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

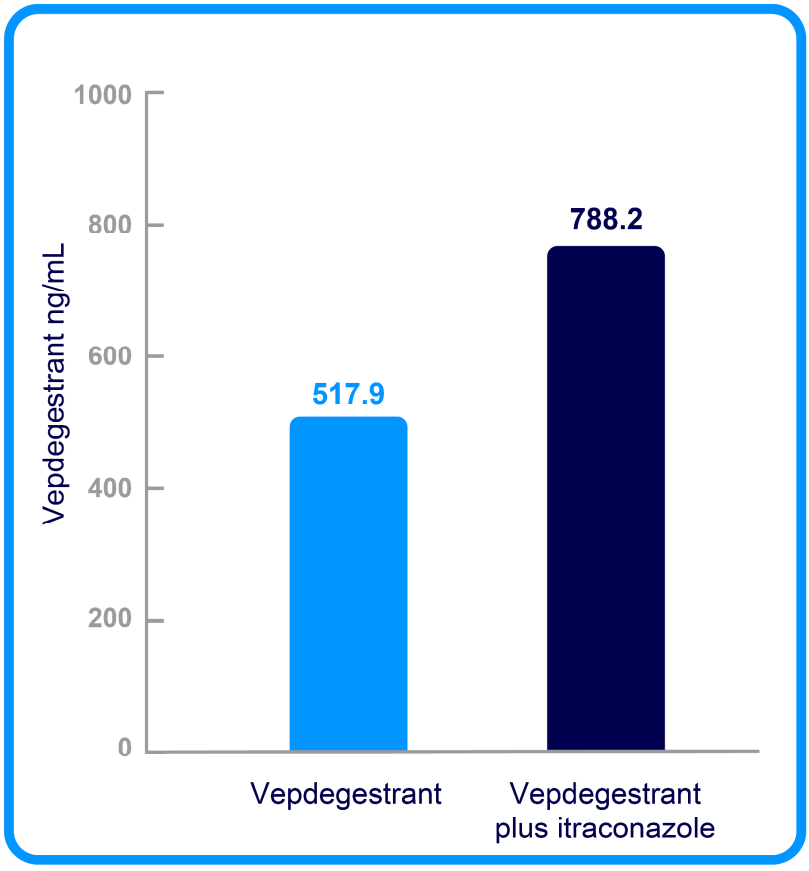
What were the results of the study?

How did the amount of vepdegestrant in the blood change when participants took vepdegestrant alone or vepdegestrant with itraconazole?

What was the amount of vepdegestrant in the blood after participants took vepdegestrant alone or vepdegestrant with itraconazole?

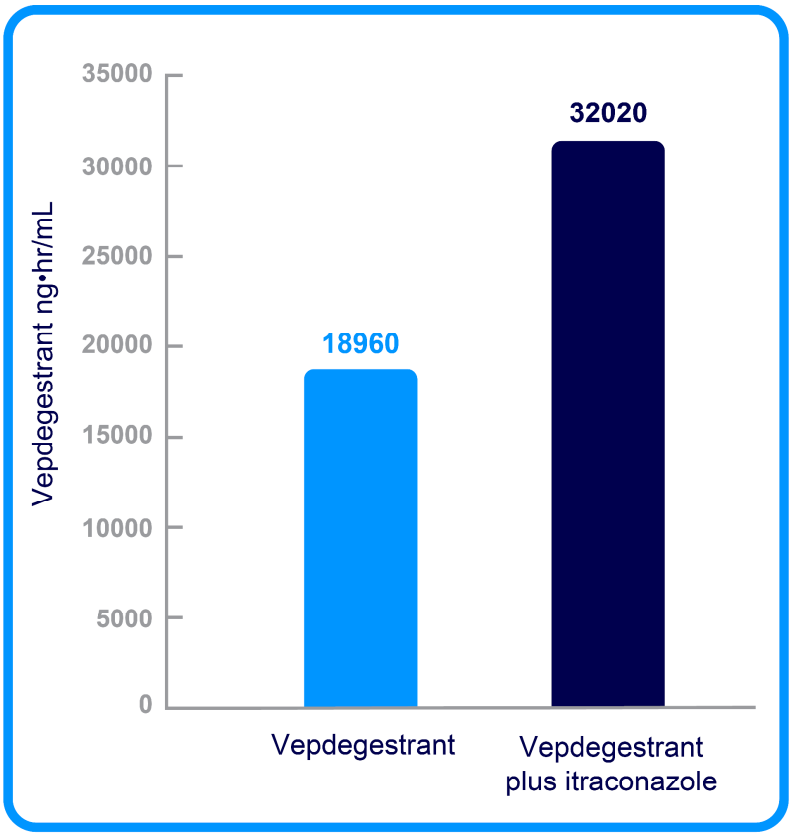
- The highest amount of vepdegestrant in the blood after participants took vepdegestrant alone or vepdegestrant with itraconazole is shown in Figure 2. The amount of drug in the blood is measured in nanograms per milliliter, also called ng/mL. The highest amount was 517.9 ng/mL for vepdegestrant alone and 788.2 ng/mL for vepdegestrant with itraconazole. From these results, researchers calculated that there was a 52% increase in the highest amount of vepdegestrant in the blood when vepdegestrant was taken with itraconazole compared to when vepdegestrant was taken alone.

Figure 2. Highest amount of vepdegestrant in the blood



- The estimated total amount of vepdegestrant in the blood over time is shown in Figure 3. This estimate is of the total amount of vepdegestrant in the blood from when it was taken until vepdegestrant was removed from the body, and is measured in nanogram hours per milliliter (ng•hr/mL). The estimated total amount was 18960 ng•hr/mL when vepdegestrant was taken alone and 32020 ng•hr/mL when vepdegestrant was taken with itraconazole. From these results, researchers calculated there was a 69% increase in the estimated total amount of vepdegestrant in the blood over time when vepdegestrant was taken with itraconazole compared to when vepdegestrant was taken alone.

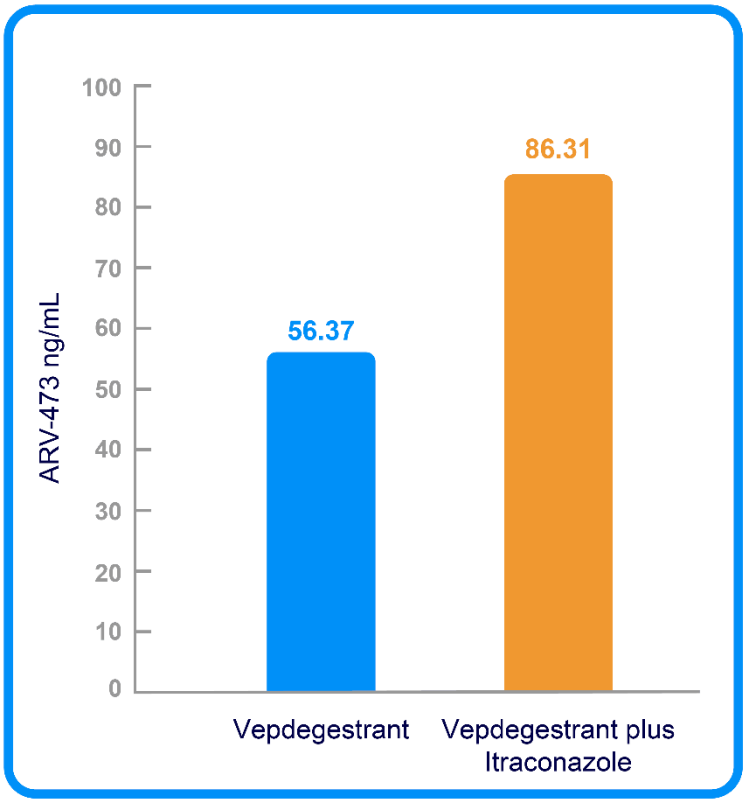
Figure 3. Estimated total amount of vepdegestrant in the blood over time



What was the amount of ARV-473 in the blood after participants took vepdegestrant alone or vepdegestrant with itraconazole?

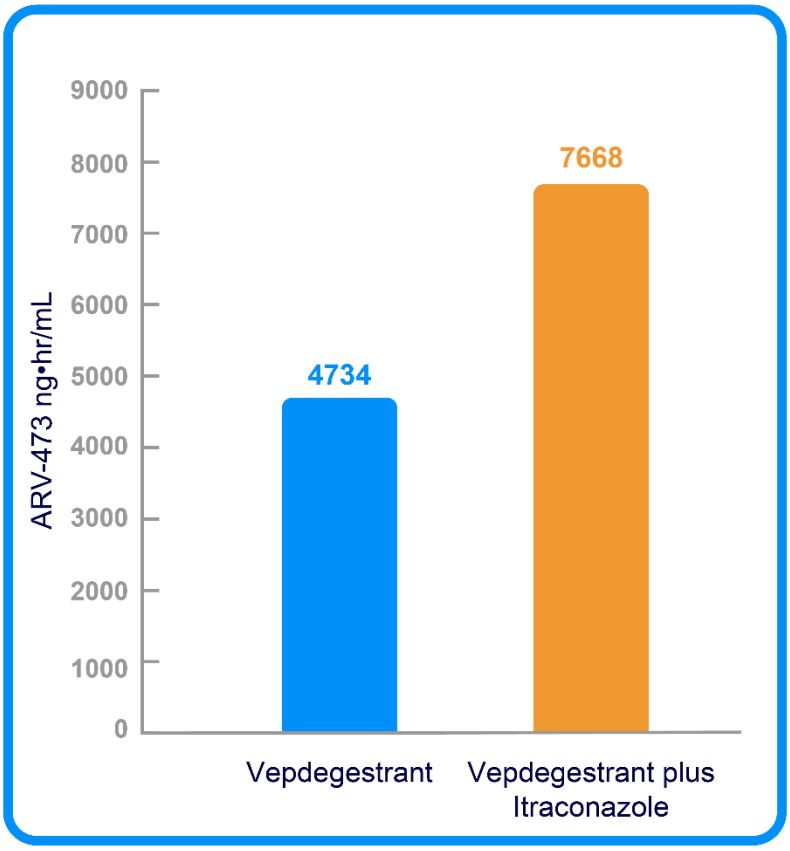
- The highest amount of ARV-473 in the blood after participants took vepdegestrant alone or vepdegestrant with itraconazole is shown in Figure 4. The amount of ARV-473 in the blood is measured in nanograms per milliliter, also called ng/mL. The highest amount was 56.37 ng/mL for vepdegestrant alone and 86.31 ng/mL for vepdegestrant with itraconazole. From these results, researchers calculated that there was a 53% increase in the highest amount of ARV-473 in the blood when vepdegestrant was taken with itraconazole compared to when vepdegestrant was taken alone.

Figure 4. Highest amount of ARV-473 in the blood



- The total amount of ARV-473 in the blood over 120 hours is shown in Figure 5. This is the total amount of ARV-473 in the blood from when it was taken until 120 hours later, and is measured in nanogram hours per milliliter (ng•hr/mL). The total amount over 120 hours was 4734 ng•hr/mL when vepdegestrant was taken alone and 7668 ng•hr/mL when vepdegestrant was taken with itraconazole. From these results, researchers calculated there was a 62% increase in the estimated total amount of ARV-473 in the blood over 120 hours when vepdegestrant was taken with itraconazole compared to when vepdegestrant was taken alone.

Figure 5. Total amount of ARV-473 in the blood over 120 hours



Based on these results, the researchers have decided that the results are not likely the result of chance. Vepdegestrant may act differently in the body when it is taken with itraconazole compared to when vepdegestrant is taken alone.

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.

- A total of 5 out of 12 (41.7%) participants in this study had at least 1 medical problem.

No participants left the study because of medical problems. All medical problems reported in the study are described below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists all medical problems that were reported during the study.
- The **2nd** column tells how many of the 12 participants reported each medical problem when they took vepdegestrant alone. Next to this number is the percentage of the 12 participants who reported the medical problem when they took vepdegestrant alone.
- The **3rd** column tells how many of the 12 participants reported each medical problem when they took itraconazole alone. Next to this number is the percentage of the 12 participants who reported the medical problem when they took itraconazole alone.
- The **4th** column tells how many of the 12 participants reported each medical problem when they took vepdegestrant with itraconazole. Next to this number is the percentage of the 12 participants who reported the medical problem when they took vepdegestrant with itraconazole.
- Using these instructions, you can see that 1 out of the 12 (8.3%) participants reported abdominal pain when they took vepdegestrant alone, 1 out of 12 (8.3%) participants reported abdominal pain when they took itraconazole alone, and 0 participants reported abdominal pain when they took vepdegestrant with itraconazole.

Table 1. Commonly reported medical problems by study participants			
Medical Problem	Vepdegestrant Alone (12 Participants)	Itraconazole Alone (12 Participants)	Vepdegestrant With Itraconazole (12 Participants)
Abdominal pain	1 out of 12 participants (8.3%)	1 out of 12 participants (8.3%)	0
Loose stools	1 out of 12 participants (8.3%)	1 out of 12 participants (8.3%)	1 out of 12 participants (8.3%)
Sore gums	0	1 out of 12 participants (8.3%)	0
Feeling tired	0	0	1 out of 12 participants (8.3%)
Back pain	1 out of 12 participants (8.3%)	0	0
Sleepiness	0	0	1 out of 12 participants (8.3%)

Table 1. Commonly reported medical problems by study participants			
Medical Problem	**Vepdegestrant Alone (12 Participants)**	**Itraconazole Alone (12 Participants)**	**Vepdegestrant With Itraconazole (12 Participants)**
Blocked nose	0	1 out of 12 participants (8.3%)	0

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 12 participants had serious medical problems, and 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 C4891009

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

www.clinicaltrials.gov	Use the study identifier **NCT05538312**
www.clinicaltrialsregister.eu	Use the study identifier 2022-003282-38

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!