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:	C4891008
Dates of Study:	27 January 2023 to 19 April 2023
Title of this Study:	A Study to Understand the Effect of a Study Medicine Called ARV-471 on Dabigatran Etexilate in Healthy Adults [An Interventional, Phase 1, Open-Label, Fixed-Sequence, 2-Period Study to Evaluate the Effect of a Single Oral Dose of ARV-471 (PF-07850327) on the Pharmacokinetics of Dabigatran in Healthy Participants]
Date(s) of this Report:	06 December 2023

– 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 dabigatran?

Dabigatran (dab-ee-gat-ran) (Pradaxa®), also called dabigatran etexilate, is an approved medicine. Dabigatran is used to reduce the risk of stroke and blood clots. It is a blood thinning medicine called an anticoagulant that lowers the chance of clots forming in the body. Dabigatran is taken as capsules, by mouth.

What was the purpose of this study?

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

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 dabigatran in the blood change when participants took dabigatran alone or vepdegestrant with dabigatran?**
- **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 were to stay at the study center for 8 days and 7 nights. There were 2 treatments in this study and 2 treatment periods. Period 1 was 4 days long and Period 2 was 3 days long. Participants arrived at the study center on Day -1, which was the day before the 1st treatment. The 1st treatment was given on Day 1 of Period 1, which was the 2nd day at the study center. The 2nd treatment was given on Day 1 of Period 2, which was the 6th day at the study center. Participants left the study center on Day 3 of Period 2, which was the 8th day at the study center.

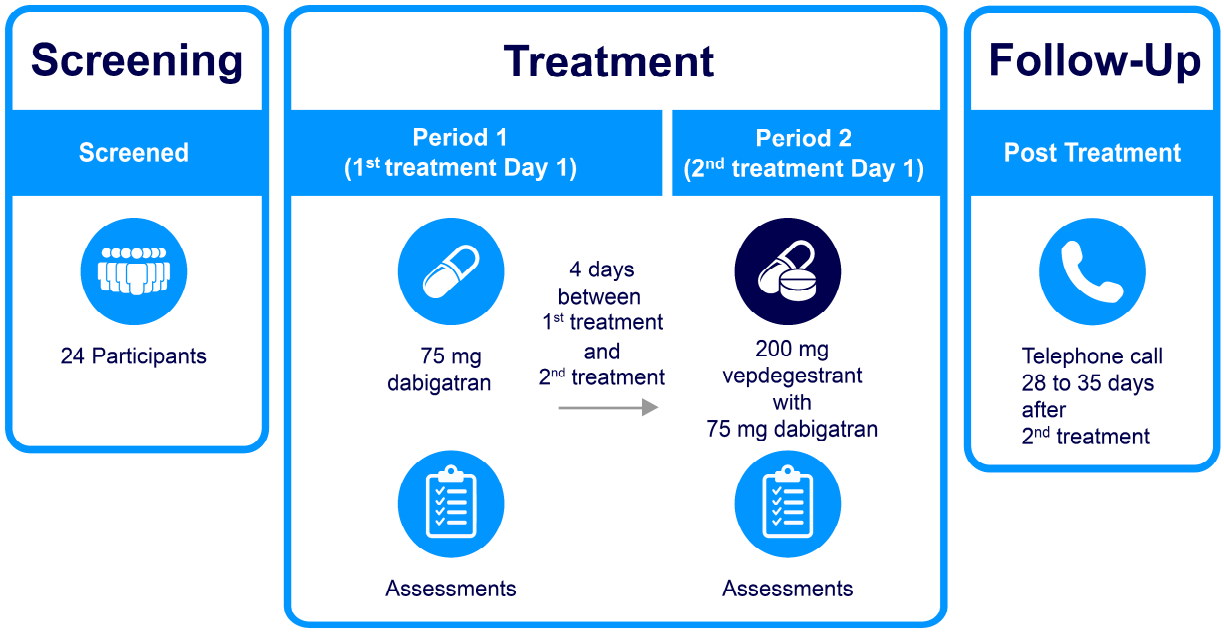
- For the 1st treatment, participants took one 75 mg capsule of dabigatran around 2 hours after starting breakfast.
- The 2nd treatment was given at least 4 days after the 1st treatment. Participants took two 100 mg tablets of vepdegestrant 30 minutes after starting breakfast. Then they took one 75 mg capsule of dabigatran around 2 hours after starting breakfast (1.5 hours after taking vepdegestrant).

Breakfast was a standard type with around 700 calories and around 35% fat. Participants were asked to eat it all within 20 minutes.

Researchers took samples of blood and urine from participants during the study. Researchers measured the amount of dabigatran 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 stayed at the study center from the day before Day 1, Period 1, until the end of the 3rd day of Period 2.

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

Where did this study take place?

The Sponsor ran this study at 1 location in Belgium.

When did this study take place?

It began 27 January 2023 and ended 19 April 2023.

Who participated in this study?

The study included healthy adult participants.

- A total of 20 men participated
- A total of 4 women participated
- All participants were between the ages of 25 and 70

All 24 participants finished the study.

How long did the study last?

Study participants were in the study for about 10 weeks, from screening to follow-up calls. The entire study took around 3 months to complete.

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

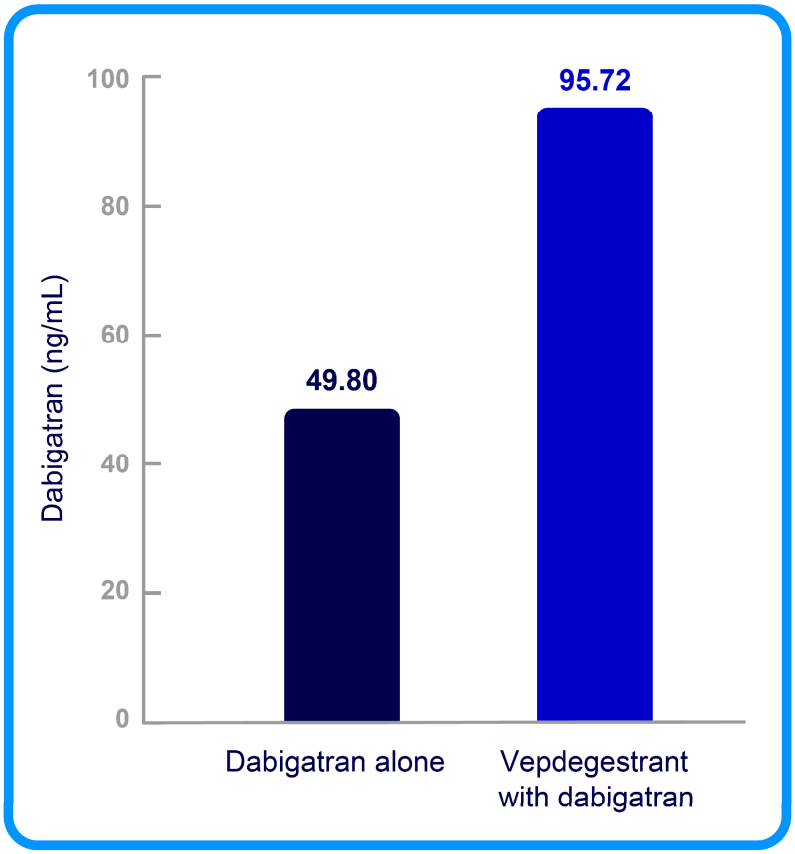
What were the results of the study?

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

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

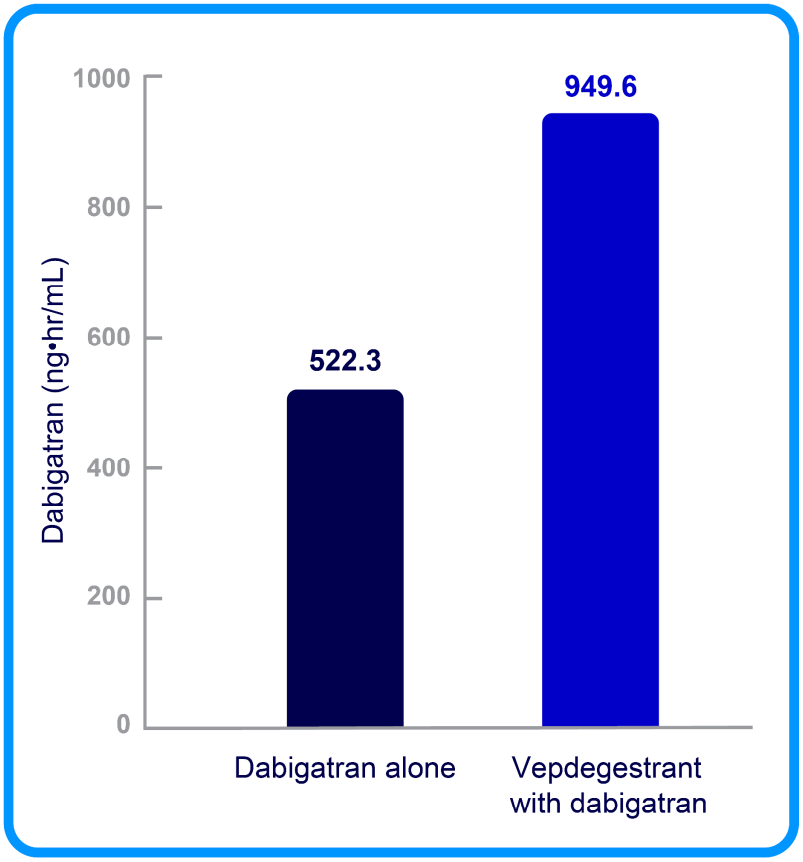
- The highest amount of dabigatran in the blood after participants took dabigatran alone or vepdegestrant with dabigatran is shown in Figure 2. The amount of drug in the blood was measured in nanograms per milliliter, also called ng/mL, and was 49.80 ng/mL for dabigatran alone and 95.72 ng/mL for vepdegestrant with dabigatran. From these results, researchers calculated there was a 92% increase in the highest amount of dabigatran in the blood when vepdegestrant was taken with dabigatran compared to when dabigatran was taken alone.

Figure 2. Highest amount of dabigatran in the blood



- The estimated total amount of dabigatran in the blood over time is shown in Figure 3. This estimate is of the total amount of dabigatran in the blood from when it was taken until dabigatran was removed from the body and is measured in ng•hr/mL. The estimated total amount of dabigatran in the blood over time was 522.3 ng•hr/mL for dabigatran alone and 949.6 ng•hr/mL for vepdegestrant with dabigatran. From these results, researchers calculated there was a 98% increase when vepdegestrant was taken with dabigatran compared to when dabigatran was taken alone.

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



Based on these results, the researchers have decided that the results are not likely the result of chance. Dabigatran may act differently in the body when vepdegestrant is taken with dabigatran compared to when dabigatran 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 13 out of the 24 participants (54.17%) in this study had at least 1 medical problem.

None of the 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 commonly reported during the study.
- The **2nd** column tells how many of the 24 participants reported each medical problem when they took dabigatran alone. Next to this number is the percentage of the 24 participants who reported the medical problem when they took dabigatran alone.
- The **3rd** column tells how many of the 24 participants reported each medical problem when they took vepdegestrant with dabigatran. Next to this number is the percentage of the 24 participants who reported the medical problem when they took vepdegestrant with dabigatran.
- Using these instructions, you can see that 1 out of the 24 (4.2%) participants reported loose stools when they took dabigatran alone and 0 participants reported loose stools when they took vepdegestrant with dabigatran.

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Dabigatran (24 Participants)**	**Dabigatran with vepdegestrant (24 Participants)**
Loose stools	1 out of 24 participants (4.2%)	0 out of 24 participants (0%)
Lip dry	1 out of 24 participants (4.2%)	0 out of 24 participants (0%)
Nausea (feeling like being about to vomit)	1 out of 24 participants (4.2%)	0 out of 24 participants (0%)
Influenza	0 out of 24 participants (0%)	1 out of 24 participants (4.2%)
Bruising	0 out of 24 participants (0%)	2 out of 24 participants (8.3%)
Wound	0 out of 24 participants (0%)	1 out of 24 participants (4.2%)
Muscle pain	1 out of 24 participants (4.2%)	0 out of 24 participants (0%)
Headache	0 out of 24 participants (0%)	1 out of 24 participants (4.2%)
Dry throat	1 out of 24 participants (4.2%)	0 out of 24 participants (0%)
Throat pain	0 out of 24 participants (0%)	1 out of 24 participants (4.2%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Dabigatran (24 Participants)**	**Dabigatran with vepdegestrant (24 Participants)**
Runny nose	0 out of 24 participants (0%)	1 out of 24 participants (4.2%)
Dry skin	1 out of 24 participants (4.2%)	0 out of 24 participants (0%)
Collection of blood under the skin	2 out of 24 participants (8.3%)	0 out of 24 participants (0%)
Hot flush	1 out of 24 participants (4.2%)	0 out of 24 participants (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 24 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 C4891008

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

www.clinicaltrials.gov	Use the study identifier **NCT05673889**
www.clinicaltrialsregister.eu	Use the study identifier 2022-003397-23

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!