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:	Nirmatrelvir (PF-07321332)
Protocol Number:	C4671014
Dates of Study:	15 July 2021 to 9 October 2021
Title of this Study:	Drug-Drug Interaction Study Assessing the Effect of Carbamazepine on nirmatrelvir (PF-07321332) Boosted With Ritonavir [A Phase 1, Open-Label, Fixed Sequence, 2-Period Crossover Study to Estimate the Effect of Carbamazepine on the Pharmacokinetics of PF-07321332 Boosted With Ritonavir in Healthy Participants]
Date(s) of this Report:	29 March 2022

– 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 COVID-19?

A new respiratory disease appeared in Wuhan, China in December 2019 and has since rapidly spread to many other countries around the world. The cause of this disease was found to be a new Coronavirus and the disease it causes was named COVID-19 (Coronavirus disease 2019). Since then, many companies around the world have quickly started to look for ways to treat COVID-19.

What are nirmatrelvir, ritonavir, and carbamazepine?

At the time this study was done, nirmatrelvir was a new investigational drug that was being studied for the treatment of COVID-19. An investigational drug is one that has not been approved for use outside of research studies. Nirmatrelvir has now been approved for use in some countries. Nirmatrelvir is a tablet that is taken by mouth.

Participants in this study also received ritonavir. Ritonavir is an antiviral medicine. In this study, ritonavir was used as a "booster" to help increase the level of nirmatrelvir in the blood. Ritonavir has no activity on the virus that causes COVID-19. Ritonavir is taken by mouth.

Additionally, participants in this study received carbamazepine. Carbamazepine is a seizure medicine. In this study, carbamazepine was used to see if it would have an effect on the levels of nirmatrelvir and ritonavir in the blood. Carbamazepine is taken by mouth.

What was the purpose of this study?

The purpose of this study was to learn how carbamazepine would affect the way that nirmatrelvir given with ritonavir moved through the body and how long it stayed in the body.

After nirmatrelvir and ritonavir are swallowed and absorbed, nirmatrelvir and ritonavir enter the bloodstream and the body organs (for example, stomach, liver, and

kidneys). Afterwards, nirmatrelvir is removed from the body through urine and ritonavir is removed from the body through feces.

This study did not test if nirmatrelvir helps to treat COVID-19.

Researchers wanted to know:

- **How did a single dose of nirmatrelvir given with ritonavir move and act in the body, compared to a single dose of nirmatrelvir given with ritonavir following multiple doses of carbamazepine?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested nirmatrelvir, ritonavir, and carbamazepine on a group of healthy participants to learn how carbamazepine affected the way that nirmatrelvir moved and acted in the body.

This study included 2 periods. During Period 1, participants received a single dose of nirmatrelvir 300 mg together with a single dose of ritonavir 100 mg.

During Period 2, participants received:

- Days 1 to 3: carbamazepine 100 mg twice per day
- Days 4 to 7: carbamazepine 200 mg twice per day
- Days 8 to 15: carbamazepine 300 mg twice per day

- Day 14: Nirmatrelvir 300 mg together with a single dose of ritonavir 100 mg (given at the same time as carbamazepine)

This was an open-label study, which means that the participants and the researchers knew which medicines the participants received.

Researchers took samples of blood from participants during the study and measured the amount of nirmatrelvir that was in their bodies. Researchers then compared the blood samples from Period 1 and Period 2. Researchers also checked the participants' health during the study and asked them how they were feeling.

Where did this study take place?

The Sponsor ran this study at 1 location in the United States.

When did this study take place?

It began 15 July 2021 and ended 9 October 2021.

Who participated in this study?

Healthy participants between the ages of 18 and 60 years who were not pregnant could join this study. Study participants did not have COVID-19.

- A total of 11 men participated
- One woman participated
- All participants were between the ages of 22 and 56

Of the 12 participants who started the study, 10 (83%) finished it. Two participants (17%) left the study early during Period 2 (1 participant left for personal reasons and 1 participant left because of a medical problem).

How long did the study last?

Study participants were in the study for about 54 days. The entire study took about 3 months to complete and was completed as planned.

When the study ended in October 2021, 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?

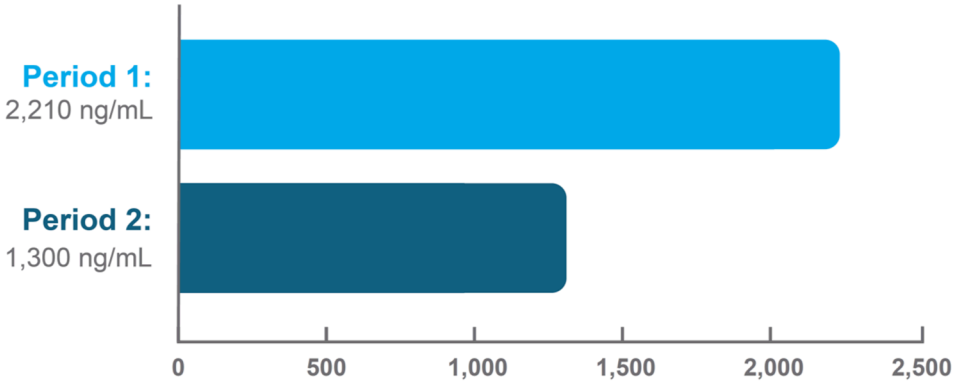
How did a single dose of nirmatrelvir given with ritonavir move and act in the body, compared to a single dose of nirmatrelvir given with ritonavir following multiple doses of carbamazepine?

To answer this question, the researchers compared the participants' blood samples from Period 1 and Period 2.

What was the highest amount of nirmatrelvir measured in the blood after participants took nirmatrelvir given with ritonavir, or nirmatrelvir given with ritonavir following multiple doses of carbamazepine?

- The highest amount of nirmatrelvir measured in the blood after participants took nirmatrelvir given with ritonavir (Period 1) or nirmatrelvir given with ritonavir following multiple doses of carbamazepine (Period 2) is shown in Figure 1. The amount of drug in the blood was measured in nanograms per milliliter, also called ng/mL. In this study, carbamazepine lowered the amount of nirmatrelvir measured in the blood.

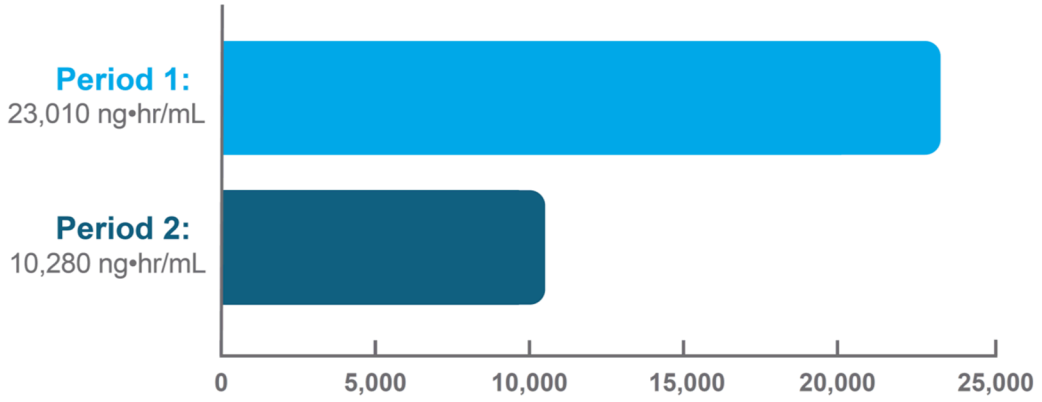
Figure 1: Highest Amount of Nirmatrelvir in Blood



What was the overall amount of nirmatrelvir in the blood after participants took nirmatrelvir given with ritonavir, or nirmatrelvir given with ritonavir following multiple doses of carbamazepine?

The overall amount of nirmatrelvir in the blood after participants took nirmatrelvir given with ritonavir (Period 1) or nirmatrelvir given with ritonavir following multiple doses of carbamazepine (Period 2) is shown in Figure 2. The amount of drug in the blood was measured in nanogram hours per milliliter (ng•hr/mL). In this study, carbamazepine lowered the overall amount of nirmatrelvir in the blood.

Figure 2: Overall Amount of Nirmatrelvir in Blood



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.

During Period 1, 4 out 12 (33%) participants had at least 1 medical problem. During Period 2, 9 out 12 (75%) participants had at least 1 medical problem. One (8%) participant left the study because of medical problems. No participants in this study had medical problems that were severe. The most common medical problems – those reported by 2 or more participants during either period –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 2 or more participants during either period are listed.
- The **2nd** column tells how many of the 12 participants taking the study medication reported each medical problem during Period 1. Next to this number is the percentage of the 12 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 12 participants taking the study medication reported each medical problem during Period 2. Next to this number is the percentage of the 12 participants taking the study medication who reported the medical problem.
- Using these instructions, you can see that 0 out of the 12 participants in Period 1 had increased liver enzymes. A total of 5 out of the 12 (42%) participants in Period 2 had increased liver enzymes.

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Period 1 (Nirmatrelvir + Ritonavir) (12 Participants)**	**Period 2 (Carbamazepine + Nirmatrelvir + Ritonavir) (12 Participants)**
Liver enzymes increased	0 out of 12 participants (0%)	5 out of 12 participants (42%)
Dermatitis contact (Skin irritation caused by touching something)	0 out of 12 participants (0%)	2 out of 12 participants (17%)

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 participants in this study 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.clinicaltrials.gov Use the study identifier **NCT04962230**

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!