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 study participants. 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:	C4671015
Dates of Study:	20 July 2021 to 30 September 2021
Title of this Study:	Study to Estimate the Effect of Itraconazole on the Level of Nirmatrelvir (PF-07321332) in the Blood of Healthy Participants Treated with Nirmatrelvir/Ritonavir [COVID-19: A Phase 1, Open-Label, Fixed Sequence, 2-Period Crossover Study to Estimate the Effect of Itraconazole on the Pharmacokinetics of PF-07321332/Ritonavir in Healthy Participants]
Date(s) of this Report:	01 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?

In December 2019, Coronavirus disease 2019 (COVID-19) was identified as a new, potentially deadly, respiratory infection caused by the novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). The World Health Organization (WHO) declared COVID-19 a Public Health Emergency of International Concern (PHEIC) on 20 January 2020 and further described the disease outbreak as a pandemic on 11 March 2020.

SARS-CoV-2 needs a main protease enzyme, also known as 3CL protease, to replicate or reproduce. Enzymes speed up chemical reactions in the body, but do not get used up in the process; therefore, can be used repeatedly. If the activity of this enzyme is inhibited, or stopped, the SARS-CoV-2 virus stops replicating. Medications known as main protease enzymes or 3CL inhibitors can be used as treatments for SARS-CoV-2 infections.

What is Nirmatrelvir?

Nirmatrelvir (also known as PF-07321332) is an effective inhibitor of the SARS-CoV-2 main protease enzyme and has shown that it has the potential to be used as a treatment for SARS-CoV-2 infections. Co-administration with a low dose of ritonavir helps slow the metabolism, or breakdown, of nirmatrelvir for it to remain active in the body for longer periods of time. Higher levels make nirmatrelvir a more effective treatment against COVID-19. Ritonavir is not used to treat the SARS-CoV-2 virus and it is not effective against the virus. In this study, nirmatrelvir was given with ritonavir.

Itraconazole is a medicine used to treat fungal infections and it may work in a similar way to ritonavir and increase the amount of nirmatrelvir in the blood.

What was the purpose of this study?

The purpose of this study was to compare the levels of nirmatrelvir seen in the blood after participants had taken nirmatrelvir and ritonavir together compared with when participants had taken nirmatrelvir, ritonavir, and itraconazole all at the same time.

Researchers wanted to know:

- **How did the amount of nirmatrelvir in the blood change when this was taken with ritonavir or with ritonavir and itraconazole?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested nirmatrelvir and ritonavir in healthy adult participants to learn how the amount of nirmatrelvir in the blood was changed when participants took nirmatrelvir and ritonavir together compared with when nirmatrelvir, ritonavir, and itraconazole were all taken at the same time.

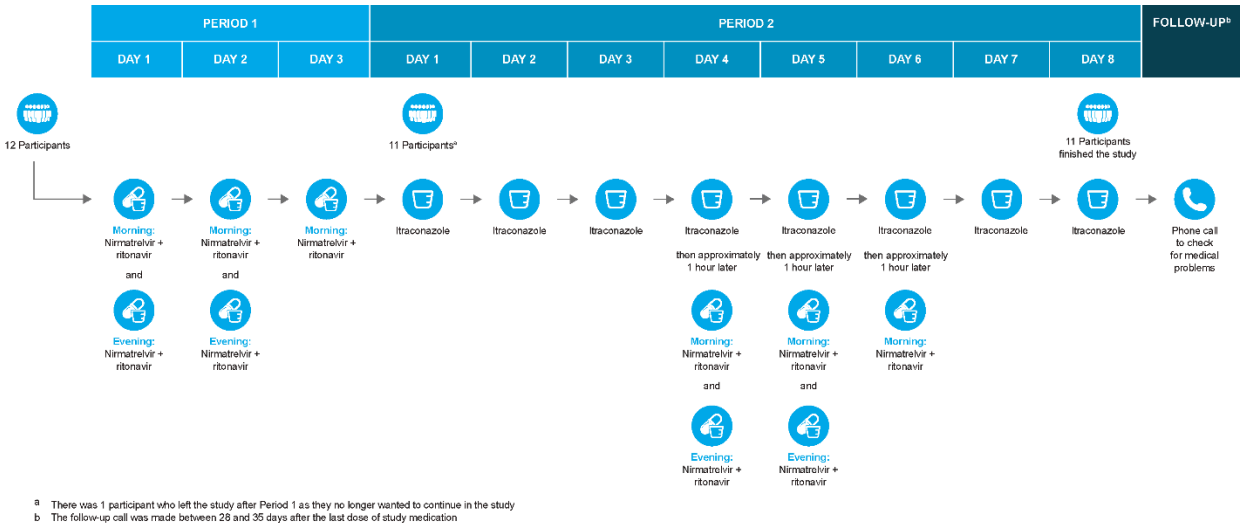
Participants were to stay at the study center for study periods 1 to 2 and were to take the study treatments as follows:

- Period 1: Nirmatrelvir and ritonavir taken twice daily (once in the morning and once 12 hours later in the evening before eating) on Day 1 and Day 2 and then the morning dose of nirmatrelvir and ritonavir was given on Day 3

- Period 2: Nirmatrelvir and ritonavir taken twice daily (once in the morning and once 12 hours later in the evening before eating) on Day 4 and Day 5 and then the morning dose of nirmatrelvir and ritonavir was given on Day 6 as well as itraconazole once daily in the morning on Day 1 through Day 8

Researchers took samples of blood from participants during the study. Researchers also checked the participants' health during the study and asked them how they were feeling.

Participants received a telephone call between 28 and 35 days after their last dose of study medication to check on their health.



[a] There was 1 participant who left the study after Period 1 as they no longer wanted to continue in the study
[b] The follow-up call was made between 28 and 35 days after the last dose of study medication

Researchers compared the levels of nirmatrelvir in the blood of participants who had taken nirmatrelvir and ritonavir together or when nirmatrelvir, ritonavir, and itraconazole were all given at the same time.

The participants and researchers knew who took each type of medicine. This is known as a "open-label" study.

Where did this study take place?

The Sponsor ran this study at a 1 location in Belgium.

When did this study take place?

It began 20 July 2021 and ended 30 September 2021.

Who participated in this study?

The study included adult participants who were healthy.

- A total of 11 men participated
- A total of 1 woman participated
- All participants were between the ages of 28 and 60 years

Of the 12 participants who started the study, all 12 received treatment with nirmatrelvir and ritonavir in Period 1. One participant left the study after Period 1, and 11 participants received treatment with nirmatrelvir, ritonavir, and itraconazole in Period 2. All 11 participants finished the study.

How long did the study last?

Study participants were in the study for about 10 weeks. The entire study took almost 2½ months to complete.

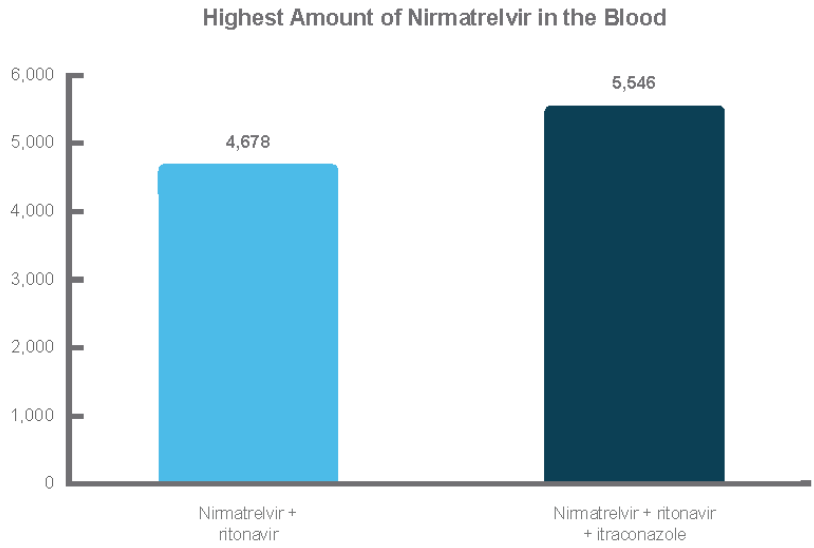
When the study ended in September 2021, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

How did the amount of nirmatrelvir in the blood change when this was taken with ritonavir or with ritonavir and itraconazole?

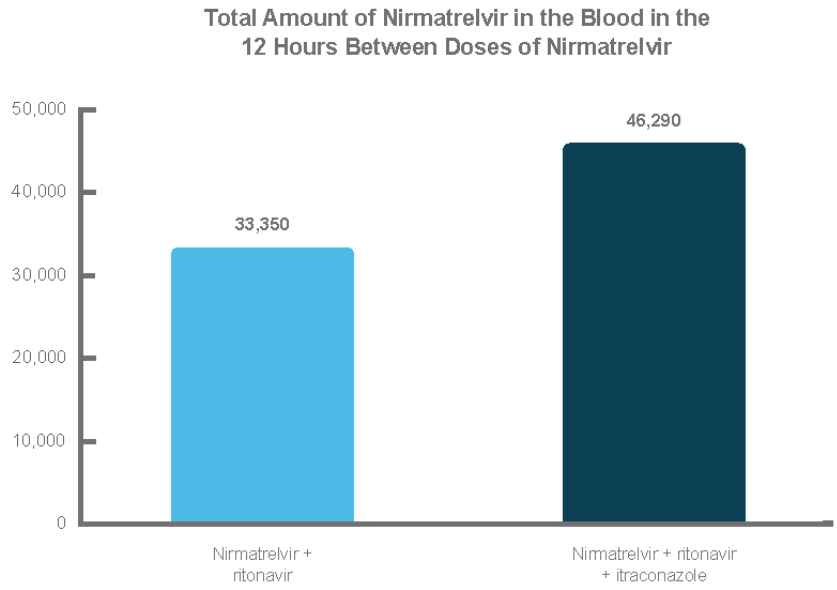
What was the highest amount of nirmatrelvir in the blood after participants took nirmatrelvir and ritonavir or nirmatrelvir, ritonavir, and itraconazole?

- The highest amount of nirmatrelvir in the blood was 4678 nanogram per milliliter, also called ng/mL, when participants took nirmatrelvir and ritonavir together. The ng/mL is a unit used to measure the amount of drug in the blood. When nirmatrelvir and ritonavir were taken along with itraconazole, this amount was increased to 5546 ng/mL (see figure below).



What was the total amount of nirmatrelvir in the blood during the 12 hours between doses after participants took nirmatrelvir and ritonavir or nirmatrelvir, ritonavir, and itraconazole?

- Participants took nirmatrelvir and ritonavir together every 12 hours. The total amount of nirmatrelvir in the blood during the 12 hours between doses was 33,350 ng•hr/mL (nanogram hours per milliliter). The ng•hr/mL is a unit used to measure the total amount of drug over time in the blood. When nirmatrelvir and ritonavir were taken along with itraconazole, this was increased to 46,290 ng•hr/mL (see figure below).



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 medication might have on a participant.

In Period 1 when participants took nirmatrelvir and ritonavir, 7 out of 12 (58%) participants had at least 1 medical problem. In Period 2, when participants took nirmatrelvir and ritonavir with itraconazole, 10 out of 11 (91%) participants had at least 1 medical problem. The most common types of medical problems – those reported by more than 3 participants – are described in Table 1. Examples of these type of medical problem are shown below:

- Gastrointestinal disorders, such as nausea, constipation, heart burn, diarrhea, tummy pain, stomach upset
- General disorders and administration site conditions, such as general pain, feeling tired, itching all over
- Nervous system disorders, such as headache, dizziness, sleepiness

None of the participants stopped taking the study medication because of medical problems.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists the type of medical problems that were commonly reported during the study. All medical problems reported by more than 3 participants are listed.
- The **2nd** column tells how many of the 12 participants in Period 1 reported each type of medical problem. Below this number is the percentage of the 12 participants in the study who reported that type of medical problem. Using these instructions, you can see that 5 out of the 12 (42%) participants in the study had gastrointestinal disorders.
- The **3rd** column tells how many of the 11 participants in Period 2 reported each type of medical problem. Below this number is the percentage of the 11 participants in the study who reported that type of medical problem. Using these instructions, you can see that 7 out of the 11 (64%) participants in the study had gastrointestinal disorders.

Table 1. Commonly reported medical problems by study participants

Type of Medical Problem	Period 1: Nirmatrelvir and Ritonavir (12 Participants)	Period 2: Nirmatrelvir, Ritonavir, and Itraconazole (11 Participants)
Gastrointestinal disorders	5 out of 12 participants (42%)	7 out of 11 participants (64%)
General disorders and administration site conditions	2 out of 12 participants (17%)	7 out of 11 participants (64%)
Nervous system disorders	6 out of 12 participants (50%)	6 out of 11 participants (55%)

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. Serious medical problems could also increase the length of a hospital stay.

No participants had serious medical problems during the study.

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 NCT04962022 (EudraCT Number: 2021-003308-42)
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number C4671015

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!