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:	Paxlovid (PF-07321332 (Nirmatrelvir)/Ritonavir)
Protocol Number:	C4671028
Dates of Study:	07 September 2022 to 11 July 2023
Title of this Study:	A Study of Nirmatrelvir/Ritonavir in Adult Participants With COVID-19 and Severe Kidney Disease [A Phase 1, Open-Label, Non-Randomized Study to Investigate the Safety and PK Following Multiple Oral Doses of PF-07321332 (Nirmatrelvir)/Ritonavir in Adult Participants With COVID-19 and Severe Renal Impairment Either on Hemodialysis or Not on Hemodialysis]
Date(s) of this Report:	09 April 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 COVID-19?

In December 2019, Coronavirus disease 2019 (COVID-19) was identified as a new, potentially deadly, respiratory infection caused by the 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.

The SARS-CoV-2 virus needs a special protein known as "3-chymotrypsin-like protease" enzyme (or "3CL") to make more copies of itself. If the activity of this enzyme is stopped, the SARS-CoV-2 virus stops making copies of itself. Medications known as "3CL inhibitors" block the activity of this enzyme and can be used as treatments for SARS-CoV-2 infections.

What are Nirmatrelvir and Ritonavir?

Nirmatrelvir (PF-07321332) is a new medicine developed for the treatment of SARS-CoV-2 infection. It works by blocking the activity of the 3CL enzyme which the virus needs to make copies of itself. To treat COVID-19, nirmatrelvir is given orally with another drug called ritonavir.

Ritonavir helps nirmatrelvir stay active in the body for longer periods of time. It does this by slowing down the breakdown of nirmatrelvir inside the body when used in people with COVID-19. Ritonavir (on its own) is not effective against the virus.

When nirmatrelvir and ritonavir are prescribed together, the treatment is given the brand name of Paxlovid.

What was the purpose of this study?

The purpose of this study was to see if nirmatrelvir/ritonavir were safe when given to participants who had COVID-19 and severe kidney disease. Severe kidney disease is when the kidneys are not working properly to remove waste products from the blood. Some of the participants in this study needed hemodialysis. Hemodialysis is a procedure that filters a person's blood outside of their body to remove the body's waste products. Doctors use hemodialysis when a person's kidneys are not able to remove waste products. Once the hemodialysis machine has cleaned the person's blood, their blood is put back into their body.

Researchers wanted to know:

- **How safe was nirmatrelvir/ritonavir in participants with severe kidney disease?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested a lower dose of nirmatrelvir/ritonavir taken fewer times on a group of participants with recently diagnosed COVID-19 and severe kidney disease. They did this to find out if the lower and less frequent dose was safe for participants with severe kidney disease who were not on hemodialysis and participants with severe kidney disease who were receiving hemodialysis. The participants with COVID-19 and severe kidney

disease were divided into 2 groups and treated with nirmatrelvir/ritonavir as follows and as shown in Figure 1.

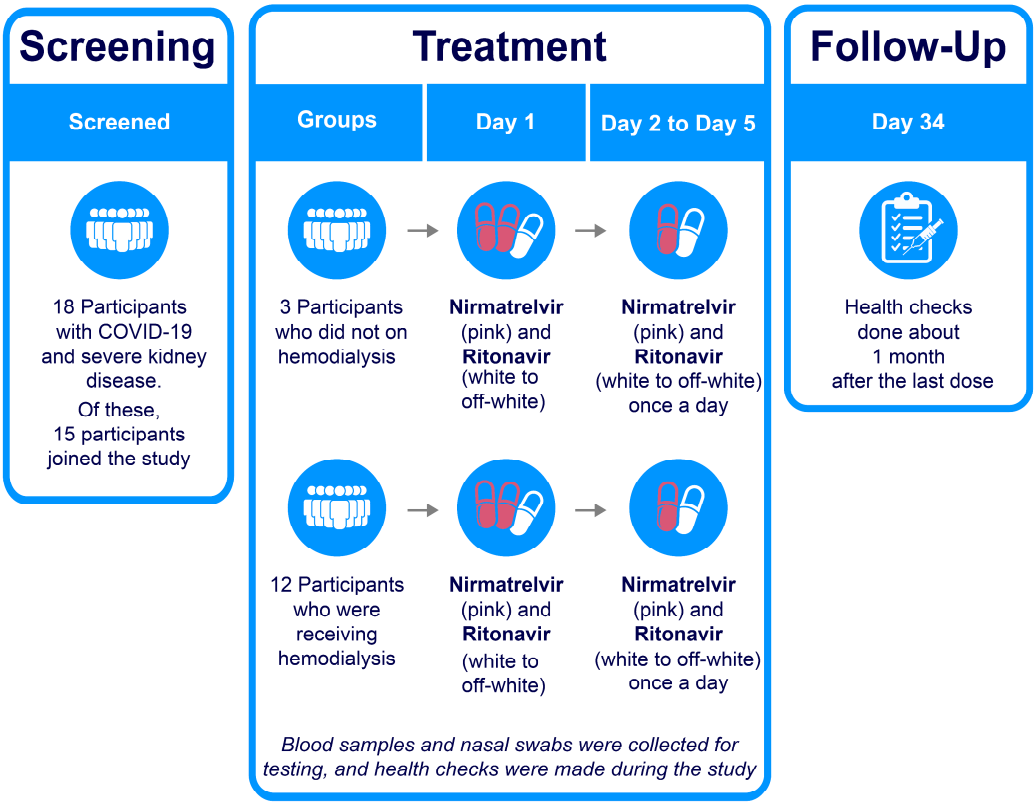
- 3 participants who were not on hemodialysis
- 12 participants who were receiving hemodialysis

On Day 1, each participant took 2 tablets of nirmatrelvir (pink) and 1 capsule of ritonavir (white to off-white). On Day 2 to Day 5, each participant took 1 tablet of nirmatrelvir (pink) and 1 capsule of ritonavir (white to off-white). All participants in this study took nirmatrelvir and ritonavir.

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

Researchers then reviewed the safety of nirmatrelvir/ritonavir in participants.

Figure 1. What Happened During the Study?



Where did this study take place?

The Sponsor ran this study at 7 locations in the United States.

When did this study take place?

It began 07 September 2022 and ended 11 July 2023.

Who participated in this study?

The study included participants who had recently developed symptoms of COVID-19 and who had severe kidney disease.

- A total of 7 men participated
- A total of 8 women participated

- All participants were between the ages of 29 and 84 years

Of the 18 participants who started the study, 3 were not treated as the doctors did not think the study was right for them. The remaining 15 participants were treated with nirmatrelvir/ritonavir, and all finished the study. There was 1 participant who did not finish treatment with nirmatrelvir/ritonavir. This was because the participant had medical problems and was hospitalized.

How long did the study last?

Study participants were in the study for up to 38 days. The entire study took just over 10 months to complete. The study ended early. This was because there were not as many people catching COVID-19. The researchers also thought they had collected enough information on how hemodialysis and severe kidney disease affected the use of nirmatrelvir/ritonavir.

When the study ended in July 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 safe was nirmatrelvir/ritonavir in participants with severe kidney disease?

To learn more about the safety of nirmatrelvir/ritonavir in participants with severe kidney disease, the study doctors did tests and examinations, including lab tests, physical examinations, and vital sign measurements (blood pressure, oral temperature, heart rate, breathing rate, oxygen level in the blood, and heart rate). There were no meaningful changes found on these tests.

The researchers also looked at the medical problems that participants experienced during the study. This information is provided in the next section.

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.

Three (3) out of 15 participants (20.0%) in this study had at least 1 medical problem. There was 1 participant who stopped taking nirmatrelvir/ritonavir because of medical problems. These medical problems were vomiting, COVID-19, and kidney damage caused by long term high blood pressure. 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 medical problems that were reported during the study.
- The **2nd** column tells how many of the 3 participants taking nirmatrelvir/ritonavir who were not on hemodialysis reported each medical problem. Next to this number is the percentage of the 3 participants who reported the medical problem.
- The **3rd** column tells how many of the 12 participants taking nirmatrelvir/ritonavir who were receiving hemodialysis reported each medical problem. Next to this number is the percentage of the 12 participants who reported the medical problem.
- Using these instructions, you can see that 1 out of the 3 participants taking nirmatrelvir/ritonavir who were not on hemodialysis reported loose stools (diarrhea). There were no participants taking nirmatrelvir/ritonavir and who were receiving hemodialysis who reported loose stools (diarrhea).

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Nirmatrelvir/Ritonavir and Who Were Not on Hemodialysis (3 Participants)**	**Nirmatrelvir/Ritonavir and Who Were Receiving Hemodialysis (12 Participants)**
Loose stools (diarrhea)	1 out of 3 participants (33.3%)	0
Vomiting	0	1 out of 12 participants (8.3%)
Chills	0	1 out of 12 participants (8.3%)
COVID-19	0	1 out of 12 participants (8.3%)
Blood marker showing increased stress on the heart	0	1 out of 12 participants (8.3%)
Headache	0	2 out of 12 participants (16.7%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Nirmatrelvir/Ritonavir and Who Were Not on Hemodialysis (3 Participants)**	**Nirmatrelvir/Ritonavir and Who Were Receiving Hemodialysis (12 Participants)**
Kidney damage caused by long term high blood pressure	0	1 out of 12 participants (8.3%)

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.

One (1) out of 15 the participants (6.7%) had serious medical problems. This participant was taking nirmatrelvir/ritonavir and was receiving hemodialysis. The serious medical problems were vomiting, COVID-19, and kidney damage caused by long term high blood pressure. The participant was hospitalized and stopped taking nirmatrelvir/ritonavir. None of these serious medical problems were thought related to nirmatrelvir/ritonavir.

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 **C4671028**

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

www.clinicaltrials.gov	Use the study identifier **NCT05487040**
www.clinicaltrialsregister.eu	Use the study identifier **2023-503870-19-00**

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!