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: C4671010

Dates of Study: 31 August 2021 to 07 December 2021

Title of this Study: Study to Compare the Effects of Moderate Liver Impairment on the Pharmacokinetics (PK) of PF-07321332 Enhanced With Ritonavir in Participants With Moderate Abnormal Liver Function Compared to Healthy Participants With Normal Liver Function

[A Phase 1, Non-Randomized, Open-Label Study to Assess the Pharmacokinetics, Safety and Tolerability of PF-07321332 Boosted With Ritonavir in Adult Participants With Moderate Hepatic Impairment and Healthy Participants With Normal Hepatic Function]

Date(s) of this Report: 21 April 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 fatal, 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 on 20 January 2020 and further characterized 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. An enzyme is a protein molecule in cells which works as a biological promoter to facilitate biological reactions. Enzymes speed up chemical reactions in the body, but do not get used up in the process. Therefore, enzymes can be used over and over again. If the activity of this main enzyme is inhibited or stopped, the SARS-CoV-2 virus stops replicating. Medications known as 3CL inhibitors can be used as treatments for SARS-CoV-2 infections.

What is Nirmatrelvir?

Nirmatrelvir (also known as PF-07321332) is an effective and selective inhibitor of the SARS-CoV-2 main enzyme. Nirmatrelvir has shown that it has the potential to be used as a treatment for SARS-CoV-2 infections. When taken together with a low dose of ritonavir, the level of nirmatrelvir in the body is increased by slowing down the breakdown of nirmatrelvir. This helps the nirmatrelvir to remain active in the body for longer periods of time to help combat the virus. Ritonavir is not used to treat the SARS-CoV-2 virus by itself as it is unlikely to be effective against the virus. In this study, nirmatrelvir was enhanced with ritonavir.

What was the purpose of this study?

The purpose of this study was to compare the level of nirmatrelvir seen in the blood of participants with moderate abnormal liver function with the level of nirmatrelvir seen in the blood of healthy participants with normal liver function after both groups had taken nirmatrelvir enhanced with ritonavir.

Researchers wanted to know:

- **How did the amount of nirmatrelvir in the blood compare between participants with moderate abnormal liver function and healthy participants with normal liver function after taking nirmatrelvir enhanced with ritonavir?**
- **What medical problems did participants have during the study?**

What happened during the study?

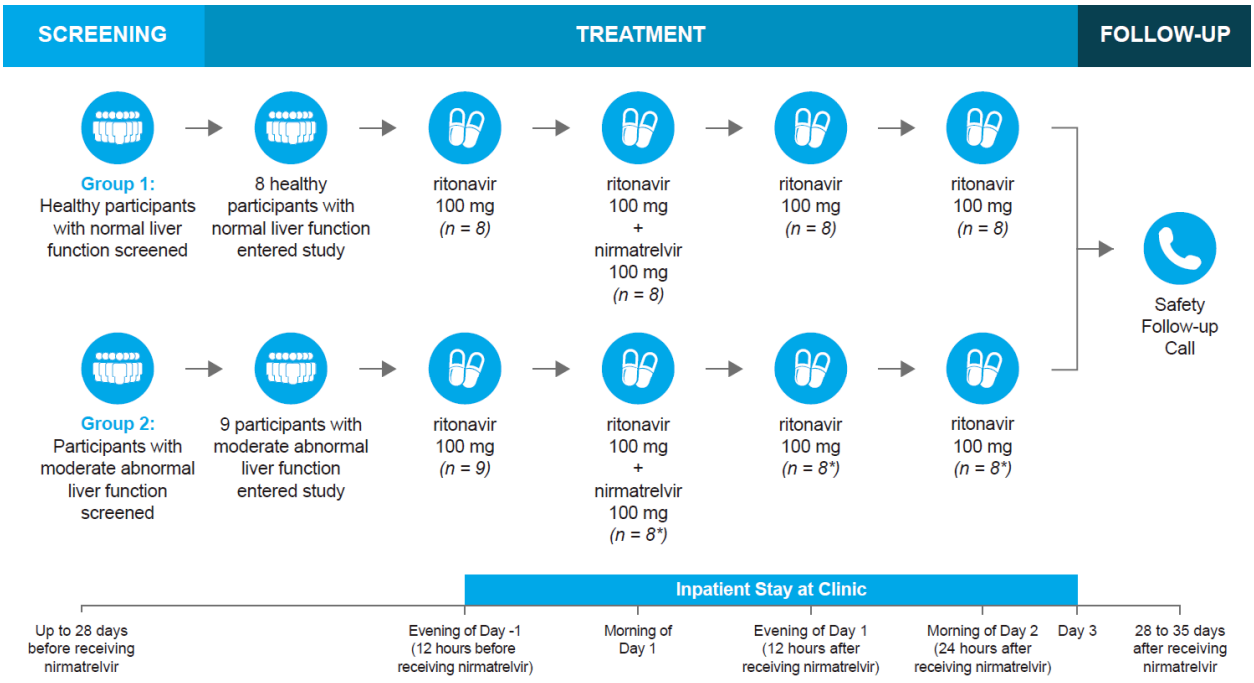
How was the study done?

Researchers tested giving nirmatrelvir enhanced with ritonavir to adult participants with moderate abnormal liver function and to healthy adult participants with normal liver function to learn how differences in liver function affected the levels of nirmatrelvir in the blood.

All participants stayed at the study center for 3 nights. On the first night, participants were given ritonavir. The next morning (12 hours after receiving ritonavir), participants were given nirmatrelvir together with ritonavir after a "fast" (period of no eating) of at least 6 hours. Participants received 2 additional doses of ritonavir, 12 and 24 hours after taking nirmatrelvir together with ritonavir.

Researchers took samples of blood from participants during the study and measured the amount of nirmatrelvir. 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 receiving nirmatrelvir to check on their health.



* 1 participant in the moderate abnormal liver function group (Group 2) entered the study but did not receive nirmatrelvir. This participant is not included in the study results presented in this summary

Researchers compared the levels of nirmatrelvir in the blood of participants with moderate abnormal liver function and in the blood of healthy participants with normal liver function.

The participants and researchers knew who was in each group. This is known as a "open-label" study.

Where did this study take place?

The Sponsor ran this study at 2 locations in the United States.

When did this study take place?

It began 31 August 2021 and ended 07 December 2021.

Who participated in this study?

The study included adult participants with moderate abnormal liver function and healthy adult participants with normal liver function.

- A total of 14 men participated (7 participants with moderate abnormal liver function, 7 healthy participants with normal liver function)
- A total of 2 women participated (1 participant with moderate abnormal liver function, 1 healthy participant with normal liver function)
- All participants were between the ages of 42 and 67 years

Of the 16 participants who received nirmatrelvir, 16 finished the treatment and follow-up phases of the study. No participants left before the study was over by their choice or a doctor decided it was best for a participant to stop being in the study.

How long did the study last?

Study participants were in the study for up to 9 weeks. The entire study took almost 14 weeks to complete.

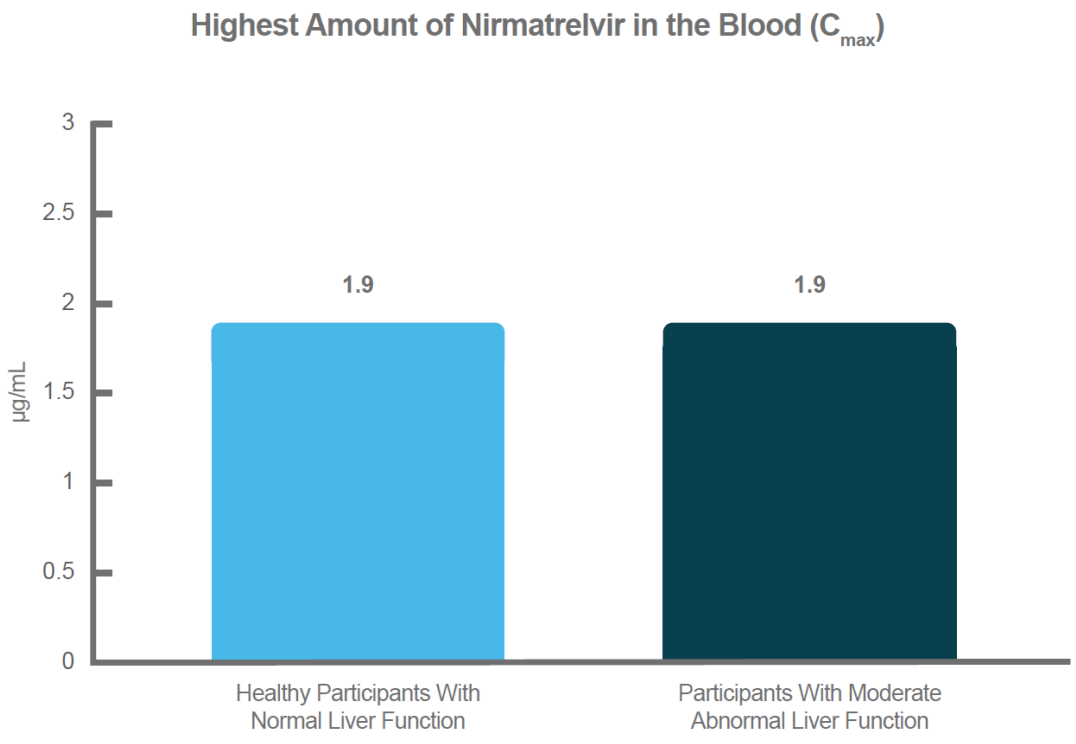
When the study ended in December 2021, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

How did the amount of nirmatrelvir in the blood compare between participants with moderate abnormal liver function and healthy participants with normal liver function after taking nirmatrelvir enhanced with ritonavir?

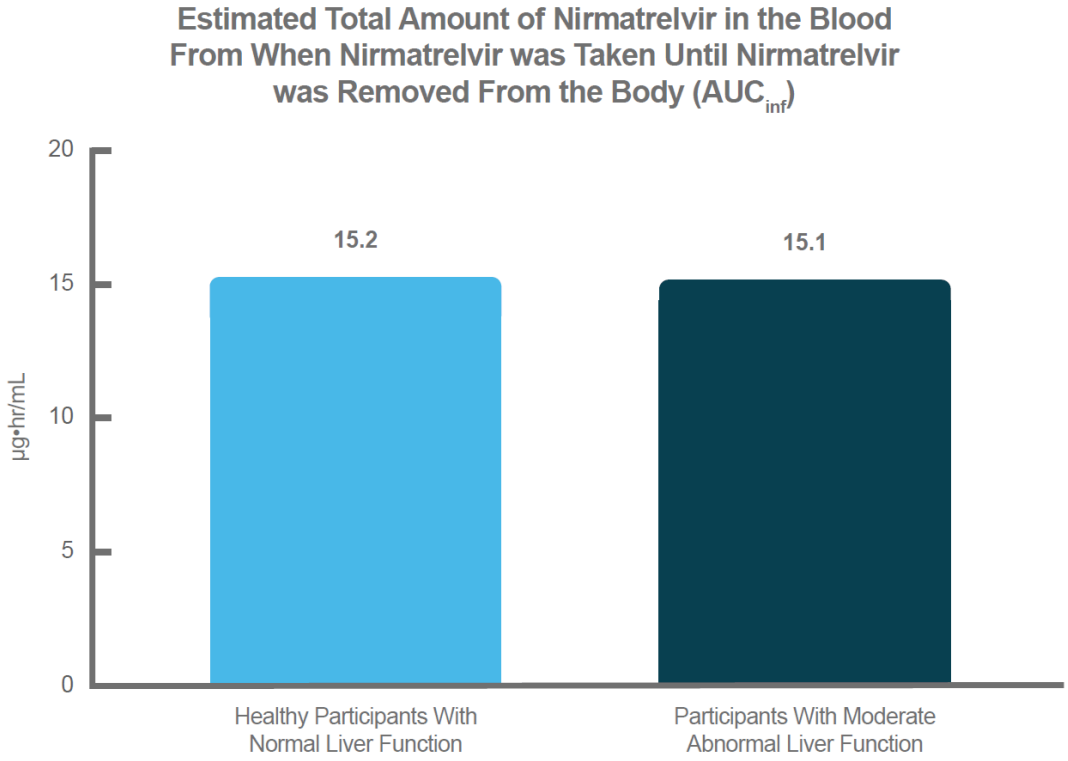
What was the highest amount of nirmatrelvir in the blood after participants were given nirmatrelvir enhanced with ritonavir?

- The highest amount of nirmatrelvir in the blood after participants took nirmatrelvir enhanced with ritonavir (known as C_{max}) was 1.9 µg/mL for both healthy participants with normal liver function and participants with moderate abnormal liver function (see figure below). The amount of drug in the blood was measured in micrograms per milliliter, also called µg/mL.



What was the estimated total amount of nirmatrelvir in the blood of participants from when nirmatrelvir was taken until nirmatrelvir was removed from the body?

- The estimated total amount of nirmatrelvir in the blood from when nirmatrelvir was taken until nirmatrelvir was removed from the body (known as AUC_{inf}) is measured in microgram hours per milliliter, also called µg•hr/mL. The µg•hr/mL is a unit used to measure total amount of drug over time in the blood. The AUC_{inf} was 15.2 µg•hr/mL for healthy participants with normal liver function and 15.1 µg•hr/mL for participants with moderate abnormal liver function (see figure below).



Researchers considered the differences in the results as minor. 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 this study, 3 out of 8 (38%) healthy participants with normal liver function and 4 out of 8 (50%) participants with moderate abnormal liver function had at least 1 medical problem. No participants left the study because of medical problems. Medical problems reported by 1 or more participant 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. All medical problems reported by 1 or more participant are listed.
- The **2nd** column tells how many of the 8 healthy participants with normal liver function taking the study medication reported each medical problem. Next to this number is the percentage of the 8 healthy participants with normal liver function taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 8 participants with moderate abnormal liver function taking the study medication reported each medical problem. Next to this number is the percentage of the 8 participants with moderate abnormal liver function taking the study medication who reported the medical problem.
- Using these instructions, you can see that 0 out of the 8 (0%) healthy participants with normal liver function taking the study medication reported "bad taste in mouth". A total of 2 out of the 8 (25%) participants with moderate abnormal liver function taking the study medication reported "bad taste in mouth".

Table 1. Medical problems reported by study participants		
Medical Problem	Nirmatrelvir and ritonavir Healthy Participants With Normal Liver Function (8 Participants)	Nirmatrelvir and ritonavir Participants With Moderate Abnormal Liver Function (8 Participants)
Bad taste in mouth	0 out of 8 participants (0%)	2 out of 8 participants (25%)
Abnormally colored urine	0 out of 8 participants (0%)	1 out of 8 participants (13%)
Back pain	0 out of 8 participants (0%)	1 out of 8 participants (13%)
Bruising	1 out of 8 participants (13%)	0 out of 8 participants (0%)
Dizziness	1 out of 8 participants (13%)	0 out of 8 participants (0%)
Feeling sleepy	0 out of 8 participants (0%)	1 out of 8 participants (13%)
Infection of the kidneys, bladder, or urethra	0 out of 8 participants (0%)	1 out of 8 participants (13%)
Itching where the injection was given	1 out of 8 participants (13%)	0 out of 8 participants (0%)
Nausea	0 out of 8 participants (0%)	1 out of 8 participants (13%)
Red, inflamed skin resulting from contact with an allergen	0 out of 8 participants (0%)	1 out of 8 participants (13%)

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 had serious medical problems.

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 **NCT05005312**

www.pfizer.com/research/research_clinical_trials/trial_results
Use the protocol number C4671010

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!