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: C4671019

Dates of Study: 12 November 2021 to 12 January 2022

Title of this Study: Food Effect Study to Evaluate the Effect of a High Fat Meal on the Level of Nirmatrelvir (PF-07321332) in the Blood of Healthy Adult Participants

[A Phase 1, Open-label, Randomized, Single Dose, 2-Sequence, 2-Period Crossover Study to Evaluate the Effect of High-Fat Meal on the Relative Bioavailability of PF-07321332 Boosted With Ritonavir in Healthy Adult Participants]

Date(s) of this Report: 28 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 deadly, respiratory infection caused by 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. 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 (PF-07321332) is a new oral medicine developed by the researchers for the treatment of SARS-CoV-2 infection. It works by inhibiting the main protease enzyme which the virus needs to replicate. For the treatment of COVID-19, nirmatrelvir is given with a low dose of another drug called ritonavir. Ritonavir helps to 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 (on its own) is not effective against the virus.

Nirmatrelvir is administered together with ritonavir and is approved to be used for 5 days for patients with mild to moderate COVID-19 at high risk for progression to severe COVID-19.

In this study, nirmatrelvir was taken together with ritonavir. In this report, this is written as nirmatrelvir/ritonavir. This treatment is also described elsewhere as nirmatrelvir boosted with ritonavir and this can be written as ritonavir-boosted nirmatrelvir.

What was the purpose of this study?

The purpose of this study was to see what effect eating a high fat meal had on the levels of nirmatrelvir in the blood after participants had taken nirmatrelvir/ritonavir. The researchers looked at this in healthy volunteers rather than in people who have COVID-19. The information collected in this study can be used to help determine future dosing instructions for nirmatrelvir/ritonavir in people with COVID-19.

Researchers wanted to know:

- **How did the amount of nirmatrelvir in the blood change when nirmatrelvir/ritonavir were taken on an empty stomach or after a high fat meal?**
- **What medical problems did participants have during the study?**

This study did not test if nirmatrelvir/ritonavir helps people who have COVID-19.

What happened during the study?

How was the study done?

Researchers tested nirmatrelvir/ritonavir in healthy adult participants to learn how the amount of nirmatrelvir in the blood changed when participants had eaten a high fat meal.

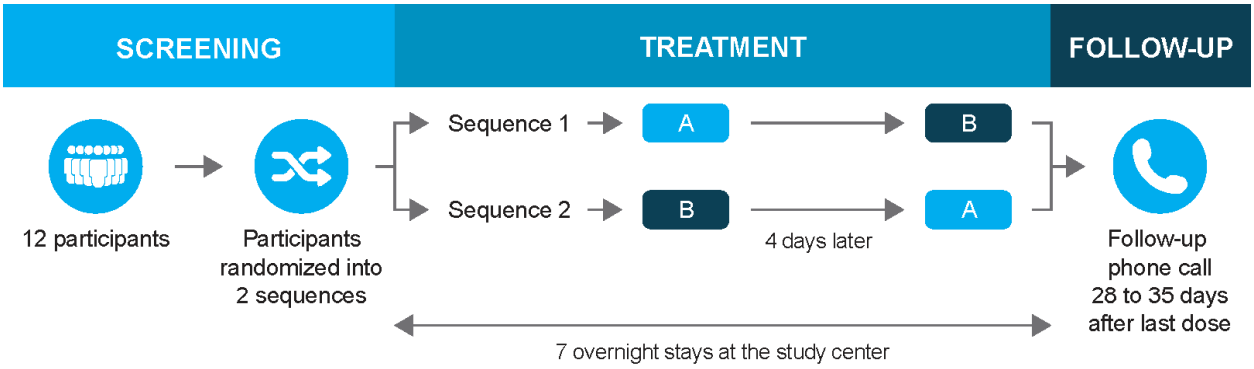
Participants were to stay at the study center for 8 days and 7 nights. During this time, they were given Treatment A followed 4 days later by Treatment B or Treatment B followed 4 days later by Treatment A as follows:

- Treatment A: A night-time dose of ritonavir (100 mg) before sleep followed 12 hours later by nirmatrelvir (300 mg)/ritonavir (100 mg) taken on an empty stomach and then a final dose of ritonavir (100 mg) around 12 hours later

- Treatment B: A night-time dose of ritonavir (100 mg) before sleep followed 12 hours later by nirmatrelvir (300 mg)/ritonavir (100 mg) taken immediately after a high fat breakfast and then a final dose of ritonavir (100 mg) around 12 hours later

Researchers took samples of blood and urine from participants during the study. Researchers also checked the participants' health during the study and asked them how they were feeling. Participants also received a telephone call between 28 and 35 days after their last dose of ritonavir to check on their health.

A diagram showing what happened in this study is provided below.



Treatment A: Ritonavir on a night before sleep then 12 hours later nirmatrelvir/ritonavir taken on an empty stomach next morning, and then ritonavir 12 hours later

Treatment B: Ritonavir on a night before sleep then 12 hours later nirmatrelvir/ritonavir taken after a high fat meal next morning, and then ritonavir 12 hours later

In this study, nirmatelvir was taken with ritonavir, and this is written as nirmatrelvir/ritonavir

Researchers compared the levels of nirmatrelvir in the blood of participants who had taken nirmatrelvir/ritonavir on an empty stomach or after a high fat meal.

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 single location in the United States (US).

When did this study take place?

It began 12 November 2021 and ended 12 January 2022.

Who participated in this study?

The study included adult participants who were healthy.

- A total of 6 men participated
- A total of 6 woman participated
- All participants were between the ages of 25 and 73 years

Of the 12 participants who started the study, all 12 received treatment with nirmatrelvir/ritonavir and all 12 participants finished the study.

How long did the study last?

Study participants were in the study for about 35 days. This does not include the time between screening and dosing, which could be up to 28 days. The entire study took around 2 months to complete.

When the study ended in January 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

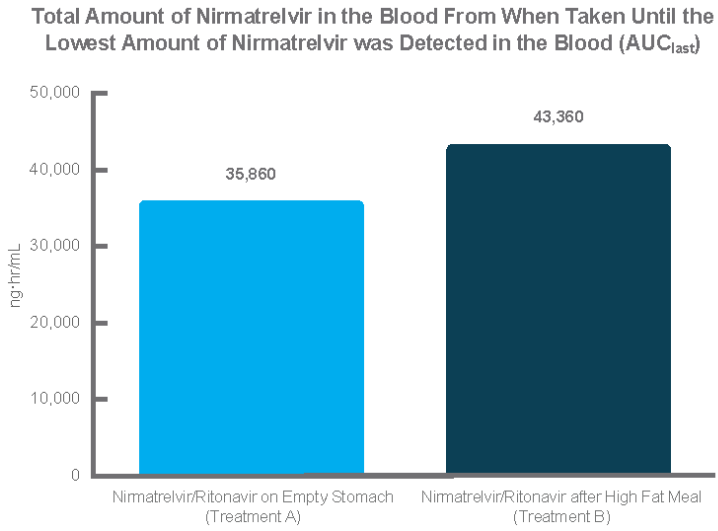
What were the results of the study?

How did the amount of nirmatrelvir in the blood change when nirmatrelvir/ritonavir were taken on an empty stomach or after a high fat meal?

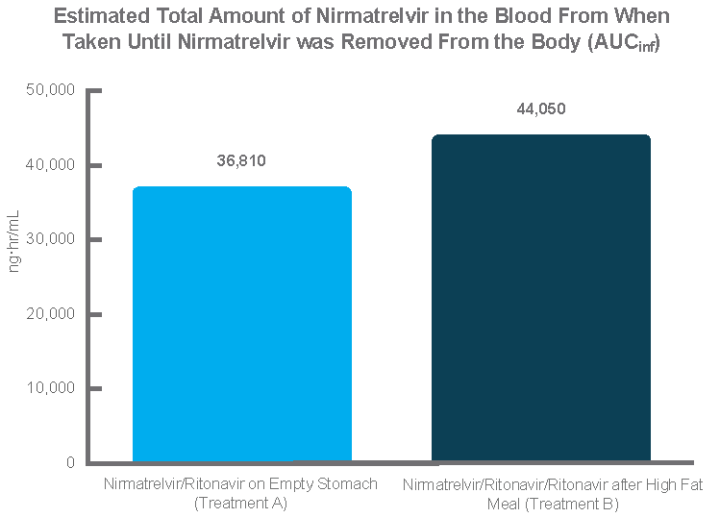
To answer this question, the researchers compared the participants' blood test results after they had taken Treatment A and after they had taken Treatment B.

What was the amount of nirmatrelvir in the blood when nirmatrelvir/ritonavir were taken on an empty stomach and after a high fat meal?

- The total amount of nirmatrelvir in the blood from when nirmatrelvir/ritonavir were taken on an empty stomach to the time when the lowest amount was detected in the blood is measured in nanogram hours per milliliter, also called ng•hr/mL. This is known as the area under the curve to time last (AUC_{last}) and this was 35,860 ng•hr/mL. The ng•hr/mL is a unit used to measure the total amount of drug over time in the blood. When nirmatrelvir/ritonavir were taken after a high fat meal, this was increased a small amount to 43,360 ng•hr/mL (see figure below).

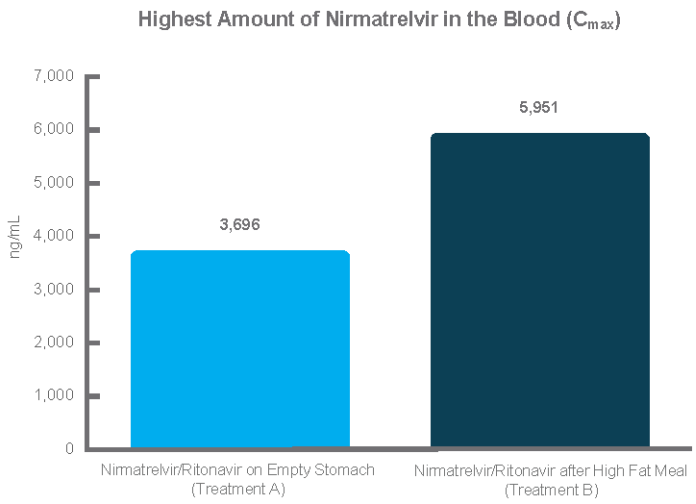


- The estimated total amount of nirmatrelvir in the blood from when nirmatrelvir/ritonavir were taken on an empty stomach until nirmatrelvir was removed from the body is measured in ng•hr/mL. This is known as the area under the curve to time infinity (AUC_{inf}) and this was 36,810 ng•hr/mL. When nirmatrelvir/ritonavir were taken after a high fat meal, this was increased a small amount to 44,050 ng•hr/mL (see following figure).



What was the highest amount of nirmatrelvir in the blood when nirmatrelvir/ritonavir were taken on an empty stomach and after a high fat meal?

- The highest amount of nirmatrelvir in the blood is known as the maximum concentration (C_{max}). After participants took nirmatrelvir/ritonavir on an empty stomach, this was 3,696 nanogram per milliliter, also called ng/mL. The ng/mL is a unit used to measure the amount of drug in the blood. When nirmatrelvir/ritonavir were taken after a high fat meal, this was increased a large amount to 5,951 ng/mL (see following figure).



Based on these results, the researchers think that nirmatrelvir levels are lower in the body when nirmatrelvir/ritonavir is taken on an empty stomach compared to after a high fat meal.

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.

Eleven (11) out of the 12 (92%) participants in this study had at least 1 medical problem. None of participants left the study because of medical problems. Medical problems seen in this 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 the medical problems reported during the study. All medical problems are listed.
- The **2nd** column tells how many of the 12 participants had medical problems after Treatment A, which was nirmatrelvir/ritonavir taken on an empty stomach. Next to this number is the percentage of the 12 participants in the study who reported the medical problem.
- The **3rd** column tells how many of the 12 participants had medical problems after Treatment B, which was nirmatrelvir/ritonavir taken after a high fat meal. Next to this number is the percentage of the 12 participants in the study who reported the medical problem.
- Using these instructions, you can see that 1 out of the 12 (8%) participants in the study had stomach discomfort after Treatment A and none of the 12 (0%) participants had stomach discomfort after Treatment B.

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Treatment A Nirmatrelvir/ Ritonavir on Empty Stomach (12 Participants)**	**Treatment B Nirmatrelvir/ Ritonavir After High Fat Meal (12 Participants)**
Stomach discomfort	1 out of 12 participants (8%)	0 out of 12 participants (0%)
COVID-19	0 out of 12 participants (0%)	1 out of 12 participants (8%)
Infection of the nose and throat (cold)	1 out of 12 participants (8%)	0 out of 12 participants (0%)
Pain from a medical procedure	1 out of 12 participants (8%)	0 out of 12 participants (0%)
Bad or unusual taste in the mouth	3 out of 12 participants (25%)	5 out of 12 participants (42%)
Bruising (often purple) of the skin	1 out of 12 participants (8%)	0 out of 12 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.

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 **NCT05129475**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number C4671019

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!