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)/Ritonavir

Protocol Number: C4671024

Dates of Study: 10 March 2022 to 19 May 2022

Title of this Study: Relative Bioavailability Study of 3 Different Delivery Vehicles of PF-07321332/Ritonavir Oral Powder Compared to the Commercial Tablet Formulation in Healthy Participants

[A Phase 1, Open-label, Randomized, Single-Dose, Crossover Study to Estimate the Relative Bioavailability of PF-07321332/Ritonavir Oral Powder in 3 Different Delivery Vehicles Relative to the Commercial PF-07321332/Ritonavir Tablets in Healthy Adult Participants Under Fasted Conditions]

Date(s) of this Report: 04 January 2023

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– 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.

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 Ritonovir?

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 with a low dose of another drug called ritonavir orally. 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, which helps make nirmatrelvir a more effective treatment against COVID-19. Ritonavir (on its own) is not effective against the virus.

What was the purpose of this study?

The purpose of this study was to measure the levels of nirmatrelvir and ritonavir in blood after participants had taken the medication using 3 different delivery vehicles (water, applesauce, and vanilla pudding) compared to the commercial tablet formulation. Delivery vehicles means what the medicine was mixed with before swallowing.

Researchers wanted to know:

- **How did nirmatrelvir administered using 3 different delivery vehicles (water, applesauce, and vanilla pudding) act in the body compared to the commercial tablet formulation?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

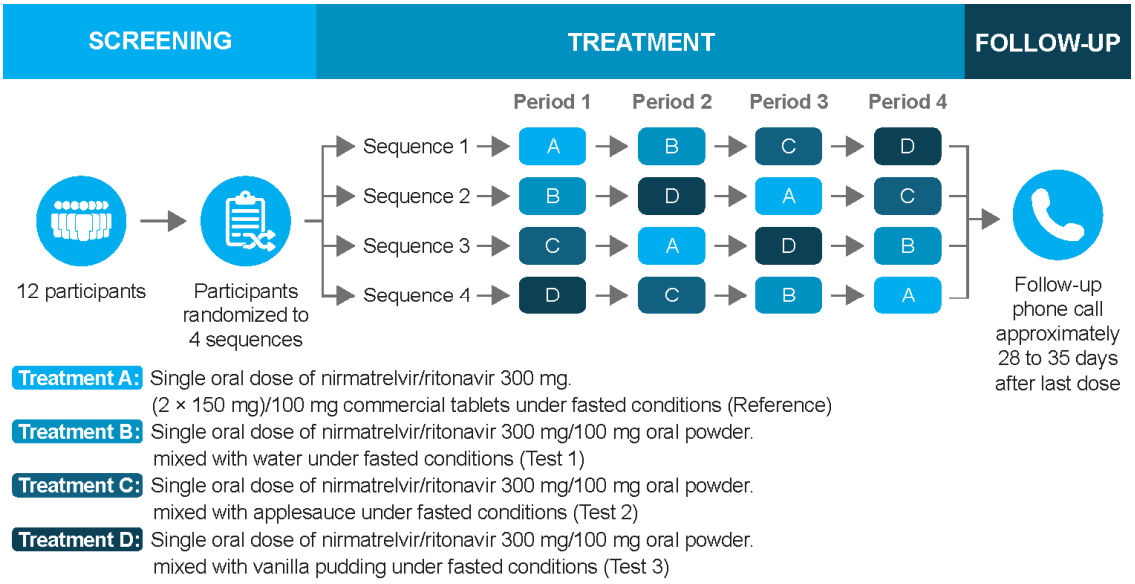
Researchers tested 3 different delivery vehicles to administer nirmatrelvir in healthy adult participants to learn how the different delivery vehicles affected the amount of nirmatrelvir in the blood compared to the commercial tablets of nirmatrelvir under fasted conditions. Water, applesauce, and vanilla pudding were used as delivery vehicles. The study consisted of 4 treatments:

- Treatment A: Single oral (by mouth) dose of nirmatrelvir /ritonavir 300 mg (2 × 150 mg)/100 mg commercial tablets under fasted conditions (Reference)
- Treatment B: Single oral dose of nirmatrelvir/ritonavir 300 mg/100 mg oral powder mixed with water under fasted conditions (Test 1)
- Treatment C: Single oral dose of nirmatrelvir/ritonavir 300 mg/100 mg oral powder mixed with applesauce under fasted conditions (Test 2)
- Treatment D: Single oral dose of nirmatrelvir/ritonavir 300 mg/100 mg oral powder mixed with vanilla pudding under fasted conditions (Test 3)

All participants were given Treatments A, B, C, or D. However, the order in which they received the treatments was different. There were 4 different sequences, with

3 participants each. A summary of how the study was done is shown in the below figure 1.

Figure 1: How was the study done?



Researchers took many samples of blood from participants in each study period 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 also received a telephone call between 28 and 35 days after their last dose of study treatment to check on their health.

Researchers then compared the results of participants taking nirmatrelvir powder administered in 3 different vehicles to the results of participants taking commercial tablets of nirmatrelvir.

The participants and researchers knew who took the different treatments at each period of the study. This is known as a "open-label" study. Participants were assigned to each treatment sequence by chance alone. This is known as a "randomized" study, and it helps make the treatments balanced and more even to compare.

Where did this study take place?

The Sponsor ran this study at one site in the United States of America.

When did this study take place?

It began 10 March 2022 and ended 19 May 2022.

Who participated in this study?

The study included 12 healthy participants who met the inclusion/exclusion criteria for things such as age and weight.

A total of 8 men participated in the Study.

A total of 4 women participated in the study.

All participants were between the ages of 25 and 60

Of the 12 participants who started the study, 11 finished the study. One participant did not finish the study due to a family emergency.

How long did the study last?

The entire study from the screening visit to the last follow-up phone call took approximately 11 weeks to complete.

When the study ended in May 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?

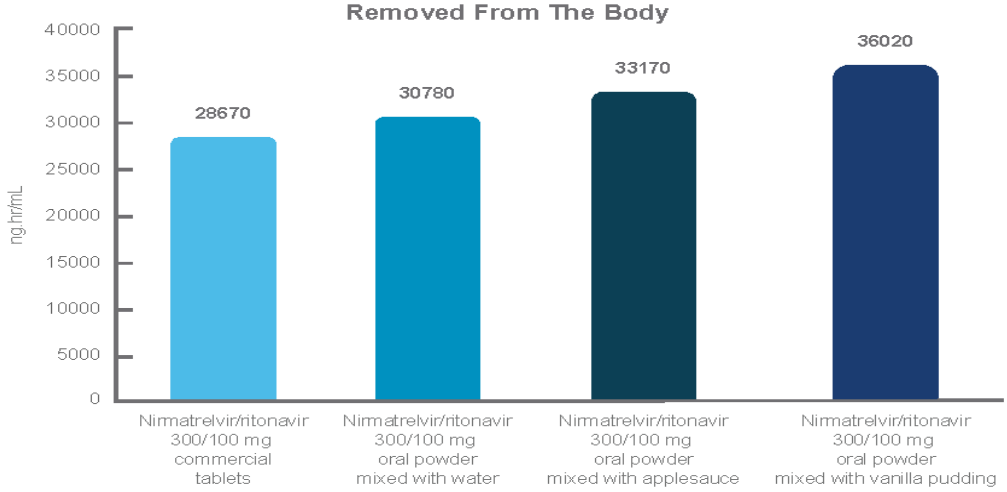
How did nirmatrelvir administered using 3 different vehicles such as water, applesauce, and vanilla pudding, act in the body compared to the commercial tablet formulation?

To answer this question, the researchers compared the participants' blood test results after each treatment period.

What was the total amount of nirmatrelvir in the blood after participants took nirmatrelvir using different vehicles of administration?

- Figure 2 below shows the average estimated total amount of nirmatrelvir in the blood from when nirmatrelvir was taken until it was removed by the body. The total amount of drug in the blood over time was measured in nanogram hours per milliliter, also called ng.hr/mL. Researchers considered the difference in the results between the different vehicles of administration and the commercial tablets as minor.

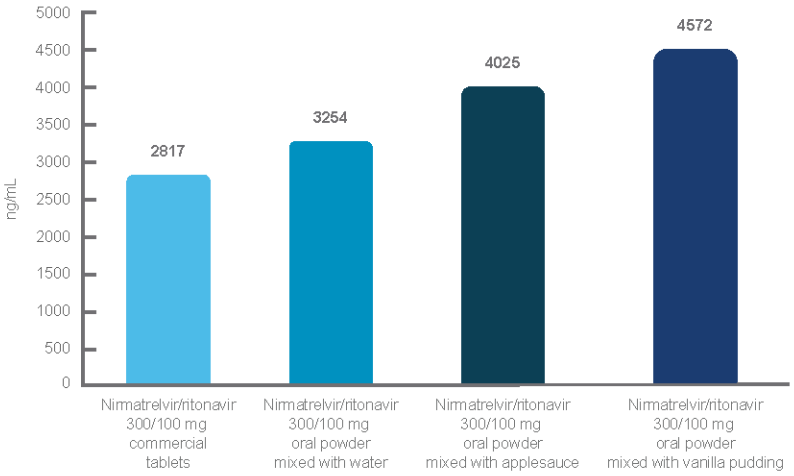
Figure 2: Average Estimated Total Amount of Nirmatrelvir in the Blood From When It Was Taken and Until It was Removed From The Body



What was the highest amount of nirmatrelvir in the blood after participants took different formulations of nirmatrelvir?

The average highest amount of nirmatrelvir measured in the blood is shown in the figure 3 below. The amount of drug in the blood is measured as ng/mL.

Figure 3 **Average Highest Amount of Nirmatrelvir in the Blood**



Based on these results, the researchers think that nirmatrelvir powder levels are higher in the blood when nirmatrelvir is taken with applesauce or vanilla pudding with ritonavir compared to other tablet formulations of nirmatrelvir/ritonavir.

Researchers found that generally, nirmatrelvir/ritonavir 300/100 mg oral powder mixed with applesauce or mixed with vanilla pudding were more favorable in taste than when mixed with water.

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.

All participants in this study had at least 1 medical problem No participants left the study because of medical problems. All of the medical problems reported by the participants 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 the participants are listed.
- The **2nd** column tells how many of the 11 participants taking the nirmatrelvir/ritonavir commercial tablets reported each medical problem. Next to this number is the percentage of the 11 participants who reported the medical problem.
- The **3rd** column tells how many of the 11 participants taking nirmatrelvir/ritonavir oral powder mixed with water reported each medical problem. Next to this number is the percentage of the 11 participants who reported the medical problem.

- The **4th** column tells how many of the 12 participants taking nirmatrelvir/ritonavir oral powder mixed with applesauce reported each medical problem. Next to this number is the percentage of the 12 participants who reported the medical problem.
- The **5th** column tells how many of the 11 participants taking nirmatrelvir/ritonavir oral powder mixed with vanilla pudding reported each medical problem. Next to this number is the percentage of the 11 participants who reported the medical problem.
- Using these instructions, you can see that 1 out of the 11 participants (9%) taking **Nirmatrelvir/ritonavir oral powder in vanilla pudding** reported upper stomach pain. A total of 0 out of the 11 participants (0%) taking **Nirmatrelvir/ritonavir commercial tablets** reported upper stomach pain.

Table 1. Medical problems reported by study participants

Medical Problem	Treatment A 11 Participants	Treatment B 11 Participants	Treatment C 12 Participants	Treatment D 11 Participants
Upper Stomach Pain	0 out of 11 participants (0%)	0 out of 11 participants (0%)	0 out of 12 participants (0%)	1 out of 11 participants (9%)
Diarrhoea	1 out of 11 participants (9%)	0 out of 11 participants (0%)	0 out of 12 participants (0%)	0 out of 11 participants (0%)
Dry Mouth	0 out of 11 participants (0%)	0 out of 11 participants (0%)	0 out of 12 participants (0%)	1 out of 11 participants (9%)
Stomach Bloating	1 out of 11 participants (9%)	0 out of 11 participants (0%)	0 out of 12 participants (0%)	0 out of 11 participants (0%)
Nausea	0 out of 11 participants (0%)	0 out of 11 participants (0%)	1 out of 12 participants (8%)	1 out of 11 participants (9%)
Injection Puncture Site Bruise	1 out of 11 participants (9%)	0 out of 11 participants (0%)	0 out of 12 participants (0%)	0 out of 11 participants (0%)
Injection Puncture Site Pain	0 out of 11 participants (0%)	0 out of 11 participants (0%)	0 out of 12 participants (0%)	1 out of 11 participants (9%)
Complication at the Site of Cut	1 out of 11 participants (9%)	0 out of 11 participants (0%)	0 out of 12 participants (0%)	0 out of 11 participants (0%)
Joint Pain	1 out of 11 participants (9%)	0 out of 11 participants (0%)	0 out of 12 participants (0%)	0 out of 11 participants (0%)

Bad Taste in the Mouth	1 out of 11 participants (9%)	2 out of 11 participants (18.2%)	1 out of 12 participants (8.3%)	1 out of 11 participants (9%)
Headache	2 out of 11 participants (18%)	0 out of 11 participants (0%)	0 out of 12 participants (0%)	1 out of 11 participants (9%)
Tingling in the Arms and Legs	0 out of 11 participants (0%)	0 out of 11 participants (0%)	0 out of 12 participants (0%)	1 out of 11 participants (9%)
Tension Headache	0 out of 11 participants (0%)	0 out of 11 participants (0%)	0 out of 12 participants (0%)	1 out of 11 participants (9%)
Burning sensation in the Vagina	1 out of 11 participants (9%)	0 out of 11 participants (0%)	0 out of 12 participants (0%)	0 out of 11 participants (0%)
Dry Skin	0 out of 11 participants (0%)	0 out of 11 participants (0%)	0 out of 12 participants (0%)	1 out of 11 participants (9%)

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 the study had serious medical problems.

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:

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

www.clinicaltrials.gov
Use the study identifier **NCT05263921**

www.pfizer.com/research/research_clinical_trials/trial_results
Use the protocol number C4671024

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!