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)/Ritonavir
Protocol Number:	C4671023
Dates of Study:	31 August 2022 to 07 November 2022
Title of this Study:	Study of Relative Bioavailability of Nirmatrelvir and Ritonavir as 4 Different Fixed Dose Combination Tablet Formulations Relative to the Commercial Tablet Formulation [A Phase 1, Open-Label, Randomized, Single Dose, Crossover Study to Estimate the Relative Bioavailability of Nirmatrelvir and Ritonavir Following Oral Administration of 4 Different Fixed Dose Combination Tablet Formulations Relative to the Commercial Tablet Formulation in Healthy Adult Participants Under Fasted Condition]
Date(s) of this Report:	23 October 2023

– 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 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 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/ritonavir in blood after participants had taken 4 different formulations of the medication under fasting conditions compared to taking the commercial tablet formulation under fasting conditions.

Researchers wanted to know:

- **How did different types of formulations/preparations of nirmatrelvir and ritonavir act in the body compared to the commercial formulation?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested 4 different formulations of nirmatrelvir/ritonavir on a group of healthy participants to learn how the different formulations acted in the body compared to the commercial tablet formulation.

Treatment A: Single oral dose of nirmatrelvir/ritonavir 300 (2 × 150)/100 mg commercial tablets under fasted conditions (Reference)

Treatment B: Single oral dose of nirmatrelvir/ritonavir 300/100 mg (2 × [150/50 mg]) tablets (low disintegrant (dissolves slowly)) under fasted conditions (Test 1)

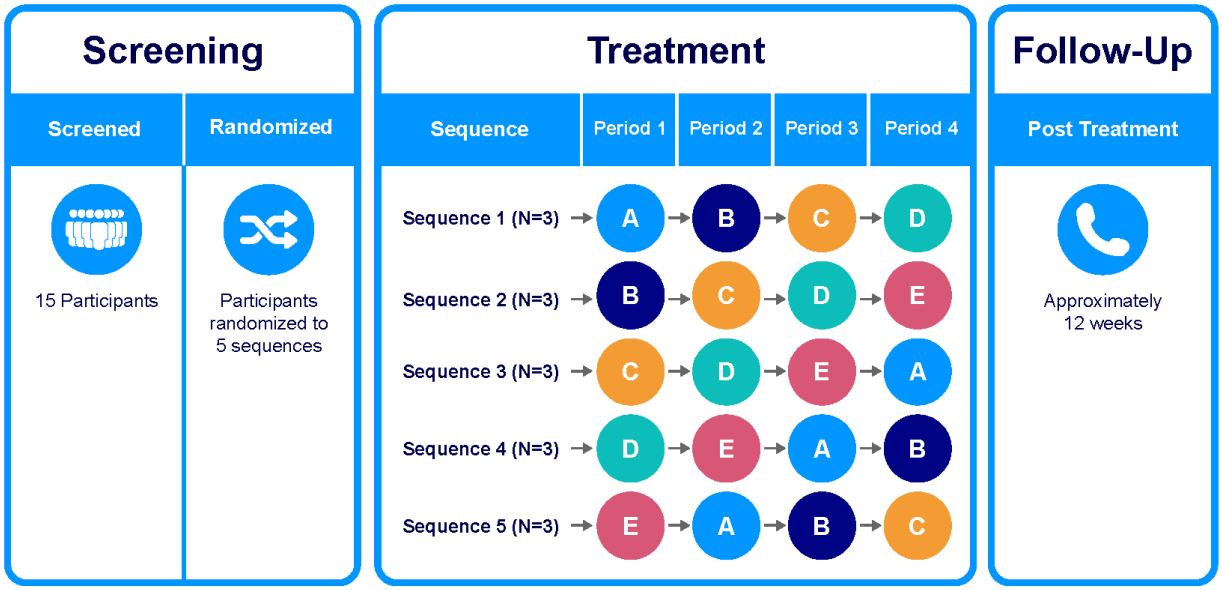
Treatment C: Single oral dose of nirmatrelvir/ritonavir 300/100 mg (2 × [150/50 mg]) (high disintegrant (dissolves rapidly)) tablets under fasted conditions (Test 2)

Treatment D: Single oral dose of nirmatrelvir/ritonavir 300/100 mg (2 × [150/50 mg] (high drug loading (strong single dose)) tablets under fasted conditions (Test 3)

Treatment E: Single oral dose of nirmatrelvir/ritonavir 300/100 mg (3 × [100/33.3 mg]) under fasted conditions (Test 4)

All participants were given 4 out of the 5 Treatments, A, B, C, D or E. However, the order in which they received the treatments was different. There were 5 different sequences, with 3 participants each. A summary of how the study was done is shown in the below figure 1.

Figure 1: How the study was done



Treatment A: *Single oral dose of nirmatrelvir/ritonavir 300 (2 × 150)/100 mg commercial tablets under fasted conditions (Reference)*
Treatment B: *Single oral dose of nirmatrelvir/ritonavir 300/100 mg (2 × [150/50 mg]) tablets (low disintegrant) under fasted conditions (Test 1)*
Treatment C: *Single oral dose of nirmatrelvir/ritonavir 300/100 mg (2 × [150/50 mg]) (high disintegrant) tablets under fasted conditions (Test 2)*
Treatment D: *Single oral dose of nirmatrelvir/ritonavir 300/100 mg (2 × [150/50 mg] (high drug loading) tablets under fasted conditions (Test 3)*
Treatment E: *Single oral dose of nirmatrelvir/ritonavir 300/100 mg (3 × [100/33.3 mg]) under fasted conditions (Test 4)*

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

Researchers then compared the results of participants taking nirmatrelvir and ritonavir in different formulations and compared the results with participants taking the commercial tablets.

Where did this study take place?

The Sponsor ran this study at 1 location in the United States.

When did this study take place?

It began 31 August 2022 and ended 07 November 2022.

Who participated in this study?

The study included healthy participants who were ⩾18 years of age and did not test positive for SARS-CoV-2 infection.

- A total of 13 men participated
- A total of 2 women participated
- All participants were between the ages of 28 and 73.

Of the 15 participants who started the study, 12 participants finished the study. One participant in Sequence 5 and one participant in Sequence 4 temporarily discontinued from study intervention due to an adverse event then were discontinued from the study per Sponsor to avoid delay in study timelines. One participant in Sequence 3 temporarily discontinued from study intervention due to a family emergency and subsequently left the study per sponsor's decision.

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 40 days. The entire study took 2.5 months to complete.

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

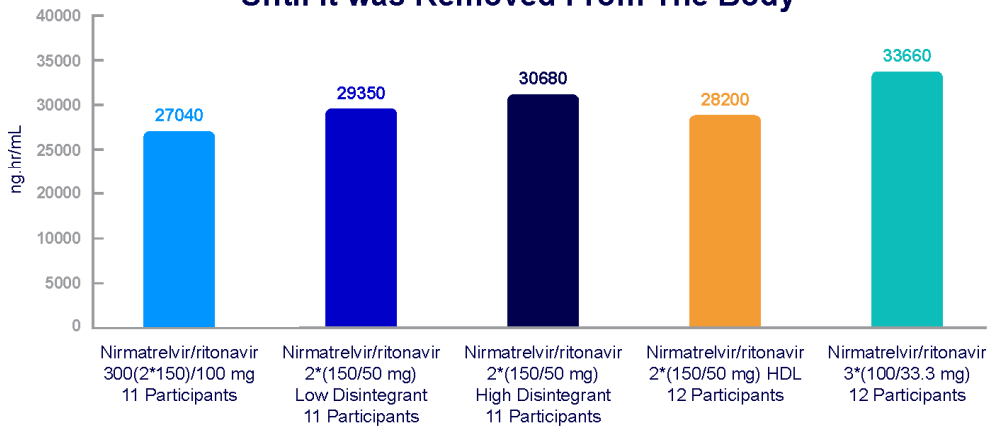
What were the results of the study?

How did different formulations of nirmatrelvir and ritonavir and the standard tablet formulation of nirmatrelvir and ritonavir act in the body?

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

- 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.

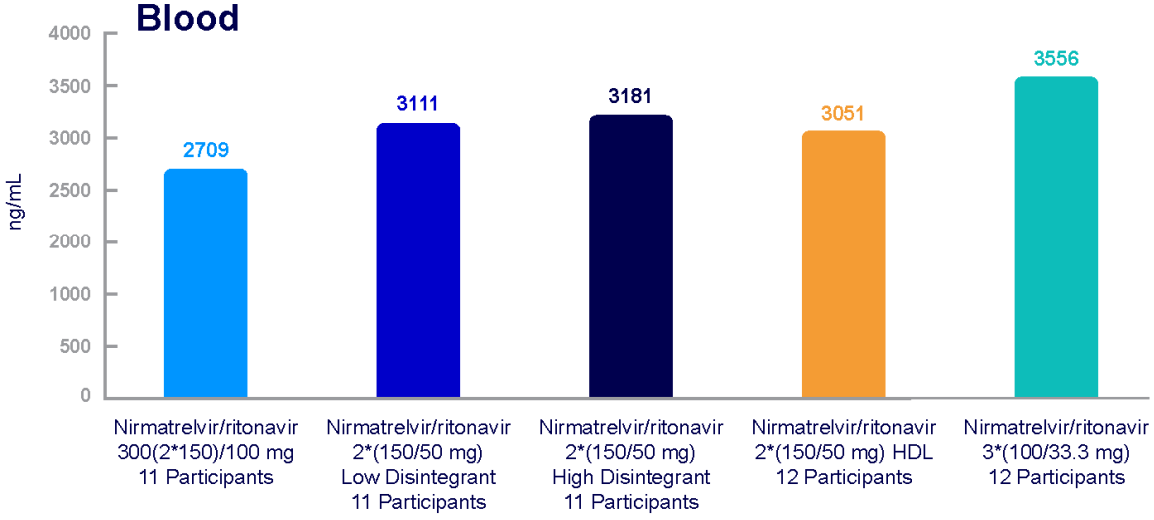
Figure 2. Average Estimated Total Amount of Nirmatrelvir in the Blood From When It Was Taken and Until It was Removed From The Body



What was the highest amount of nirmatrelvir in the blood after the 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 have decided that the results are not likely the result of chance. The different formulations of nirmatrelvir may not act differently in the body than the commercial tablet formulation of nirmatrelvir. These differences could not have been due to chance.

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.

Six out of 15 participants in this study had at least 1 medical problem. A total of 2 participants left the study temporarily because of medical problems. The medical problems experienced by the participants during the study were:

One participant in the Treatment C group and 1 participant in the Treatment D group had constipation.

One participant in the Treatment C group and 2 participants Treatment E group had upper respiratory tract infection.

One participant in the Treatment A group had a wound.

One participant in the Treatment A group and 1 participant in the Treatment E group had dry skin. Some participants may have had more than one adverse event.

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 participant 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.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number C4671023

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

www.clinicaltrials.gov	Use the study identifier **NCT05525910**

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!