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)

Protocol Number: C4671008

Dates of Study: 03 March 2022 to 16 May 2022

Title of this Study: A Phase 1 Relative Bioavailability Study of 4 Different Formulations of PF-07321332 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 Following Oral Administration of 4 Different Formulations Relative to the Commercial Tablet Formulation in Healthy Adult Participants Under Fasted Conditions]

Date(s) of this Report: 28 October 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.

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 3CL is stopped, the SARS-CoV-2 virus stops making copies of itself. Medications known as "3CL inhibitors" block the activity of 3CL and can be used as treatments for SARS-CoV-2 infections.

What is Nirmatrelvir?

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. 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 and compare the levels of nirmatrelvir and ritonavir in blood after participants had taken different formulations (commercial, slowly dissolving, and large particle size formulations) of nirmatrelvir with ritonavir,

and a suspension (liquid) formulation of nirmatrelvir with and without ritonavir. Nirmatrelvir and ritonavir are taken by mouth.

Researchers wanted to know:

- **How did the 4 different formulations of nirmatrelvir 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 4 different formulations of nirmatrelvir in healthy adult participants to learn how the different formulations affected the amount of nirmatrelvir in the blood compared to the commercial tablets of nirmatrelvir under fasted conditions. The study consisted of 5 treatments:

- **Treatment A:** 300 mg of nirmatrelvir (two 150 mg tablets, commercial formulation) with 100 mg of ritonavir (single 100 mg tablet)
- **Treatment B:** 300 mg of nirmatrelvir (two 150 mg tablets, slower dissolution [slowly dissolves] formulation) with 100 mg of ritonavir (single 100 mg tablet)
- **Treatment C:** 300 mg of nirmatrelvir (two 150 tablets, large particle size formulation) with 100 mg of ritonavir (single 100 mg tablet)
- **Treatment D:** 300 mg of nirmatrelvir (liquid suspension formulation) with 100 mg of ritonavir (single 100 mg tablet)
- **Treatment E:** 300 mg of nirmatrelvir (liquid suspension formulation)

Study Treatments A, B, C, and D

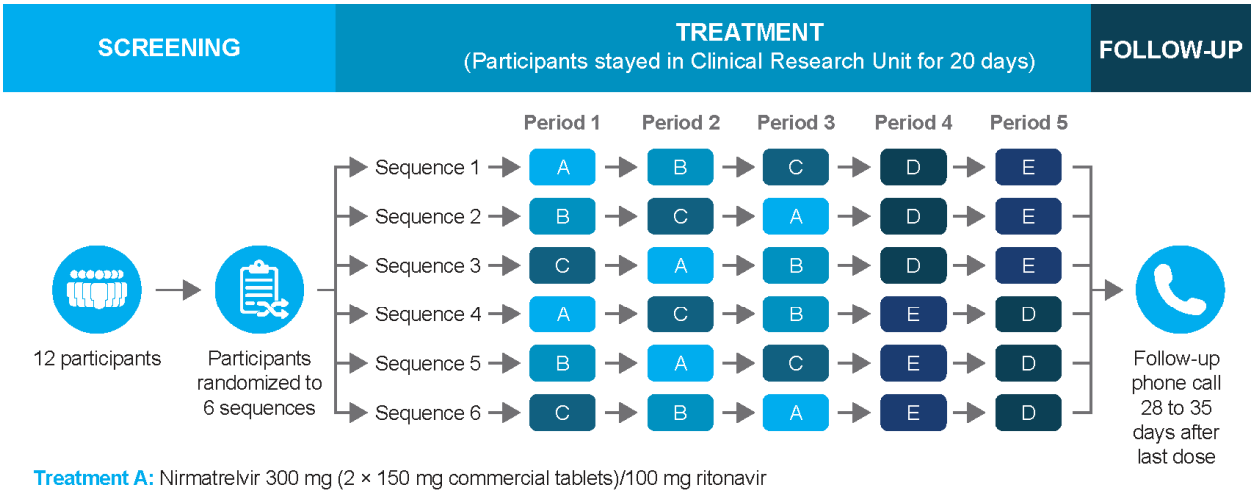
- On Day -1, participants were first given a single 100 mg dose of ritonavir 12 hours before dosing with the nirmatrelvir and ritonavir. This dose was given in the evening. Participants fasted overnight (had nothing to eat or drink except water) for at least 10 hours.
- On Day 1, 12 hours after taking ritonavir, participants were given a single dose of nirmatrelvir (300 mg as two 150 mg tablets, or 300 mg as a liquid suspension) followed by a 100 mg dose of ritonavir. These doses were given in the morning.
- On Day 1, 12 hours after taking nirmatrelvir and ritonavir, participants were given a single 100 mg dose of ritonavir. This dose was given in the evening.

Study Treatment E

- On Day 1 of this study period, participants received a single dose of 300 mg of nirmatrelvir as a suspension after an overnight fast of at least 10 hours.

Each study treatment period lasted for 4 days. There were no treatments given on Days 2, 3, and 4.

All 12 participants were given Treatments A, B, C, D, or E over the course of 20 days. However, the order in which they received the treatments was different. There were 6 different sequences, with 2 participants in each. A summary of how the study was done is shown in the below figure.



Treatment A: Nirmatrelvir 300 mg (2 × 150 mg commercial tablets)/100 mg ritonavir
Treatment B: Nirmatrelvir 300 mg (2 × 150 mg slower dissolution tablets)/100 mg ritonavir
Treatment C: Nirmatrelvir 300 mg (2 × 150 mg large particle size tablets)/100 mg ritonavir
Treatment D: Nirmatrelvir 300 mg (liquid suspension)/100 mg ritonavir
Treatment E: Nirmatrelvir 300 mg (liquid suspension)

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 also received a telephone call between 28 and 35 days after their last dose to check on their health.

Researchers then compared the results of participants taking different formulations of nirmatrelvir to the results of participants taking commercial tablets of nirmatrelvir.

The participants and researchers knew who took the different treatments at each stage 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 similar and more even to compare.

Where did this study take place?

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

When did this study take place?

It began on 03 March 2022 and ended on 16 May 2022.

Who participated in this study?

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

- A total of 10 men participated
- A total of 2 women participated
- All participants were between the ages of 35 and 62

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 47 days. This does not include the time between screening and dosing, which could be up to 28 days. The entire study took 12 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.

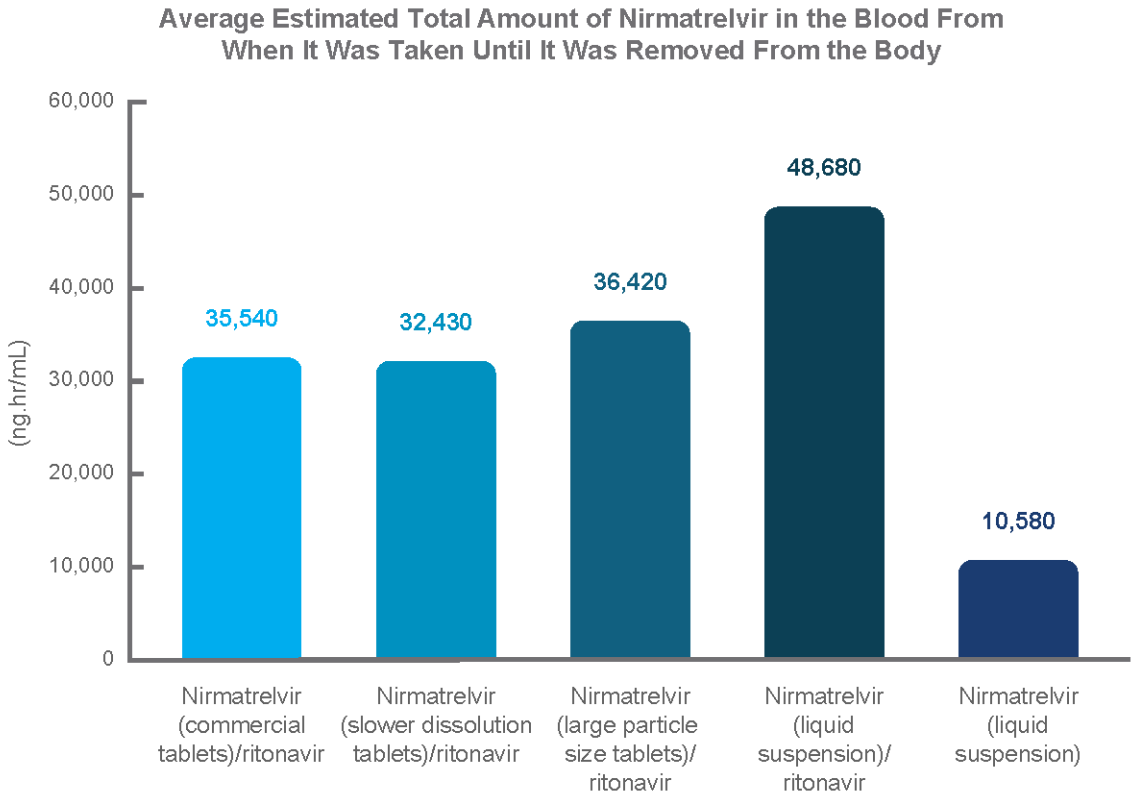
What were the results of the study?

How did the 4 different formulations of nirmatrelvir 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.

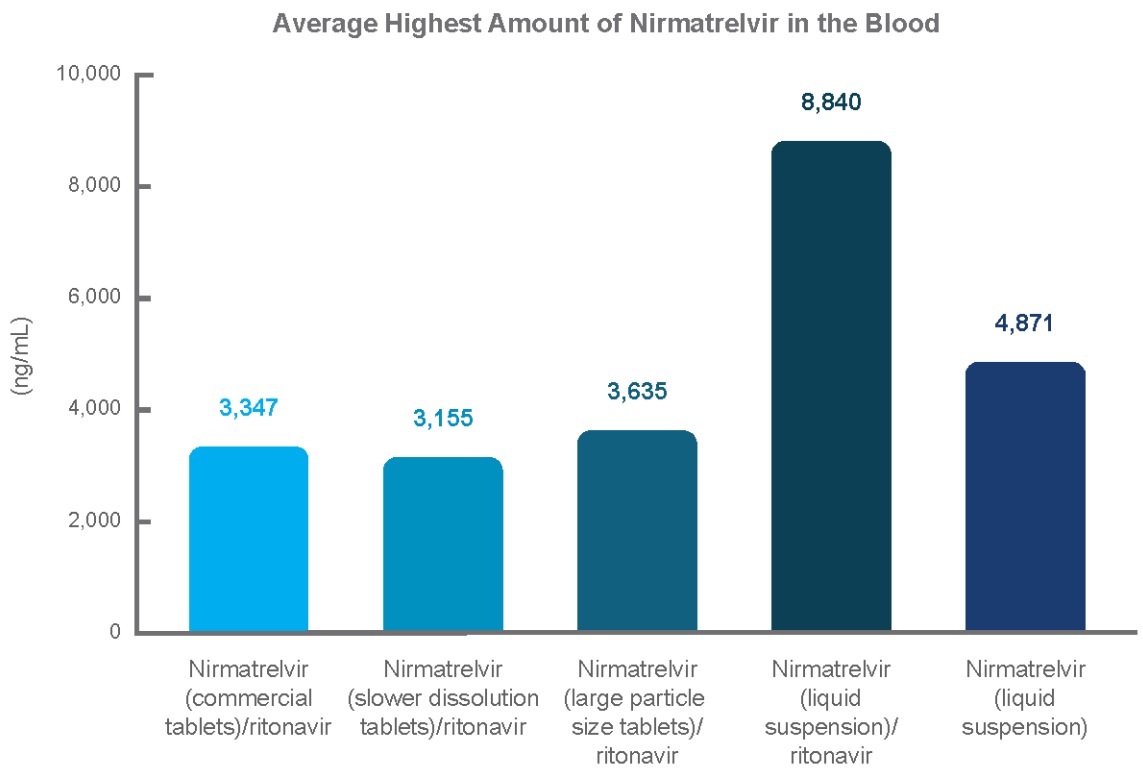
What was the total amount of nirmatrelvir in the blood after participants took different formulations of nirmatrelvir?

The graph below shows the estimated total amount of nirmatrelvir in the blood from when nirmatrelvir was taken until it was removed from 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 liquid suspension and the commercial tablets as minor.



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 below. The amount of drug in the blood is measured as ng/mL.



Based on these results, the researchers think that nirmatrelvir levels are higher in the blood when nirmatrelvir is taken as a liquid formulation with ritonavir compared to liquid formulation without ritonavir and other tablet formulations of nirmatrelvir/ritonavir.

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.

Nine (9) out of 12 (75%) participants in this study had at least 1 medical problem. No participants left the study because of medical problems. All medical problems are described below.

Below are instructions on how to read Table 1

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists all the medical problems that were reported during the study.
- The **2nd - 6th** columns tell how many of the 12 participants taking nirmatrelvir commercial formulation, slower dissolving tablet formulation, large particle size formulation, liquid suspension with ritonavir, or liquid suspension without ritonavir reported each medical problem. Next to this number is the percentage of the 12 participants taking this study medication who reported the medical problem.
- Using these instructions, you can see that 1 out of the 12 (8%) participants taking the commercial formulation of nirmatrelvir with ritonavir reported stomach pain.

Table 1. Medical problems reported by study participants

Medical Problem	Nirmatrelvir (12 participants)				
	Commercial formulation/ ritonavir	Slower dissolving tablet/ ritonavir	Large particle size tablet/ ritonavir	Liquid suspension/ ritonavir	Liquid suspension
Stomach Pain	1 out of 12 participants (8%)	0 out of 12 participants (0%)	0 out of 12 participants (0%)	0 out of 12 participants (0%)	0 out of 12 participants (0%)
Indigestion	0 out of 12 participants (0%)	0 out of 12 participants (0%)	0 out of 12 participants (0%)	0 out of 12 participants (0%)	1 out of 12 participants (8%)
Nausea	0 out of 12 participants (0%)	0 out of 12 participants (0%)	1 out of 12 participants (8%)	0 out of 12 participants (0%)	0 out of 12 participants (0%)
Bad or unusual taste in mouth	4 out of 12 participants (33%)	1 out of 12 participants (8%)	1 out of 12 participants (8%)	0 out of 12 participants (0%)	0 out of 12 participants (0%)
Trouble falling or staying asleep	0 out of 12 participants (0%)	0 out of 12 participants (0%)	1 out of 12 participants (8%)	0 out of 12 participants (0%)	0 out of 12 participants (0%)
Bruising	1 out of 12 participants (8%)	0 out of 12 participants (0%)	0 out of 12 participants (0%)	0 out of 12 participants (0%)	0 out of 12 participants (0%)

Inflammation of a vein	0 out of 12 participants (0%)	0 out of 12 participants (0%)	1 out of 12 participants (8%)	0 out of 12 participants (0%)	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.

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

www.clinicaltrials.gov
Use the study identifier **NCT05263895**

www.pfizer.com/research/research_clinical_trials/trial_results
Use the protocol number **C4671008**

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!