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.

Medicines Studied: Paxlovid™ (nirmatrelvir [also known as PF-07321332] and ritonavir)

Protocol Number: C4671002

Dates of Study: 25 August 2021 to 25 July 2022

Title of this Study: A Study to Learn If Nirmatrelvir (PF-07321332)/ Ritonavir Were Effective and Safe Compared With Placebo in Nonhospitalized Adults With COVID-19 Who Have Low or Standard Risk of Worsening to a Severe Illness

[An Interventional Efficacy and Safety, Phase 2/3, Double-Blind, 2-Arm Study to Investigate Orally Administered PF-07321332/Ritonavir Compared With Placebo in Nonhospitalized Symptomatic Adult Participants With COVID-19 Who are at Low Risk of Progressing to Severe Illness]

Date of this Report: 02 June 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?

The coronavirus disease (COVID-19) led to a global pandemic starting in 2019. COVID-19 is caused by a virus that is easily spread.

People who test positive for COVID-19 can show symptoms such as fever, dry cough, and shortness of breath. Others can also test positive for COVID-19 without having symptoms.

Although most cases of COVID-19 are mild, some people are at a higher risk of getting sicker. COVID-19 can quickly become severe and result in hospitalization or even death.

What are nirmatrelvir and ritonavir?

The study medication Paxlovid™ consists of 2 medicines called nirmatrelvir (tablets) and ritonavir (a capsule). These 2 medicines are given together by mouth.

- Nirmatrelvir (nir-muh-trel-veer) is a study medicine. It can stop a specific type of enzyme in the virus that causes COVID-19 from working. Enzymes are proteins that speed things up in our cells. If this enzyme stops working, the COVID-19 virus cannot multiply and spread through the body.
- Ritonavir (rih-tahn-uh-veer) is a medicine that can help increase the levels of other medicines in the body.

What was the purpose of this study?

The study aimed to find out if nirmatrelvir/ritonavir was more effective than a placebo in treating nonhospitalized adults with COVID-19 who have low or standard risk of worsening to a severe illness. A placebo does not have any medicine in it, but it looks just like the study medication.

Researchers wanted to know:

1. **Did nirmatrelvir/ritonavir help participants with COVID-19 get better faster compared to a placebo?**
2. **Did the participants taking nirmatrelvir/ritonavir have a lower chance of being hospitalized with COVID-19 or dying from any cause compared to those taking a placebo?**

What happened during the study?

How was the study done?

Researchers tested nirmatrelvir/ritonavir on a group of study participants. This was to find out if nirmatrelvir/ritonavir could help participants with COVID-19 who have low or standard risk of worsening to a severe illness. Researchers wanted to know:

- If nirmatrelvir/ritonavir could help participants with COVID-19 get better faster.
- If nirmatrelvir/ritonavir could lower the chance of being hospitalized with COVID-19 or dying from any cause.

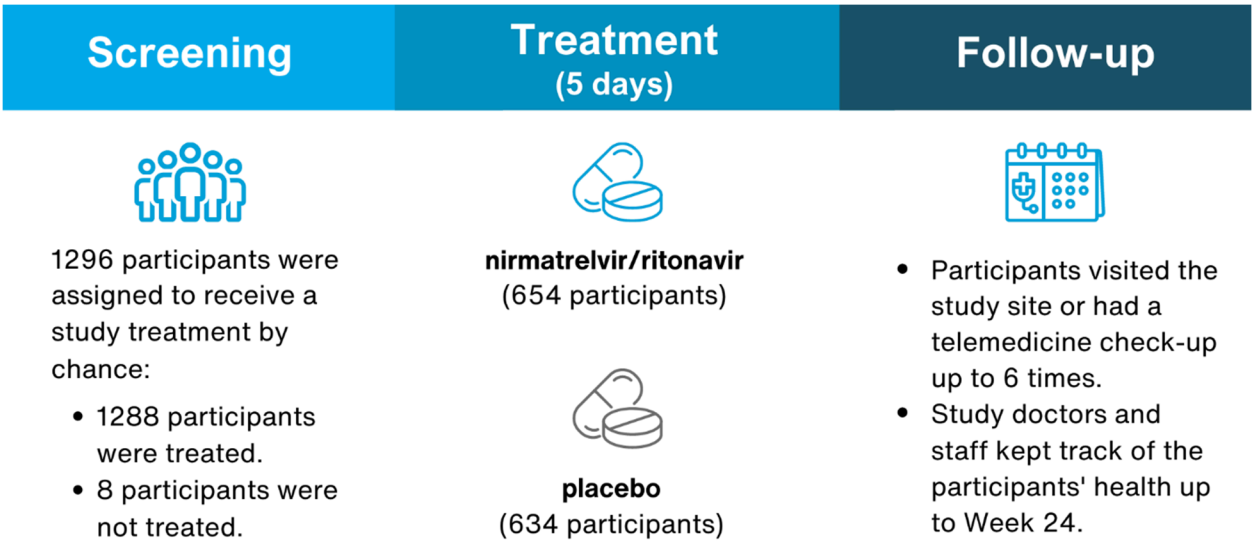
Researchers compared the results of study participants taking nirmatrelvir/ritonavir to those taking a placebo. Placebo does not have any medicine in it, but it looks just like the study medication.

The study participants and researchers did not know which treatment the participants got. This is known as a "blinded" study. The study participants were assigned to a treatment group by chance alone. This is known as a "randomized" study, and it helps make the treatment groups similar and more even to compare.

Participants started treatment within 5 days of their COVID-19 symptoms starting.

The figure below shows what happened during the study.

Figure 1. Overall study design



The study was closed earlier than planned. This was because early results of this study showed a low rate of hospitalization or death among participants with COVID-19 (who have low or standard risk of worsening to a severe illness). It was not because of safety concerns with

nirmatrelvir/ritonavir. Therefore, the Sponsor will focus on studying nirmatrelvir/ritonavir in more vulnerable people, such as:

- Those who are more likely to get sick or be sick for a longer time.
- Those who have a weakened immune system.

Where did this study take place?

The Sponsor ran this study at 352 locations in 20 countries around the world.

When did this study take place?

It began 25 August 2021 and ended 25 July 2022.

Who participated in this study?

The study included adults at least 18 years old. At the start of the study, they: tested positive for COVID-19 and had COVID-19 symptoms, were not hospitalized, and had low or standard risk of worsening to severe COVID-19.

- A total of 592 men and 696 women participated.
- All participants were between the ages of 18 and 87 years.

Of the 1296 participants who started the study, 1288 got at least 1 dose of nirmatrelvir/ritonavir or placebo and 8 did not get a study treatment.

- 1026 participants completed the study.
- 270 participants left before the study was over. The most common reasons for leaving the study were:
    - The Sponsor stopped the study earlier than planned, or
    - Participants left the study by their choice

How long did the study last?

Participants were in the study for up to 24 weeks. The entire study took 11 months to complete.

The Sponsor stopped signing up participants in June 2022 and ended the study earlier than planned. This was because early results showed a low rate of hospitalization or death among participants with COVID-19 (who have low or standard risk of worsening to a severe illness). It was not because of safety concerns with nirmatrelvir/ritonavir.

When the study ended in July 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?

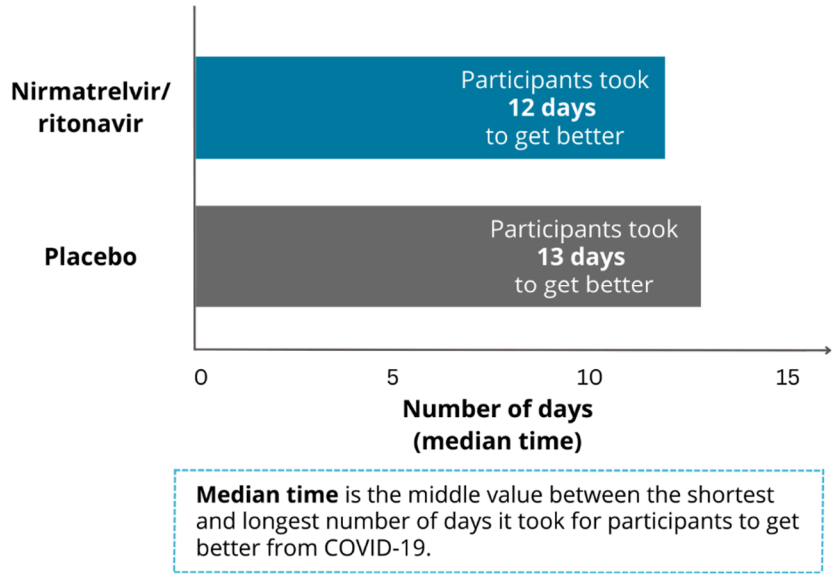
The researchers looked at the results of 1288 participants who got at least 1 dose of nirmatrelvir/ritonavir or placebo. The researchers reviewed the participants' records from Day 1 through Week 24 of the study.

1 Did nirmatrelvir/ritonavir help participants with COVID-19 get better faster compared to a placebo?

Researchers checked how long it took for participants to get better from COVID-19 after taking nirmatrelvir/ritonavir or a placebo within 5 days of the start of their symptoms.

The figure below shows the results.

Figure 2. How long did it take for participants to get better from COVID-19?



Median time is the middle value between the shortest and longest number of days it took for participants to get better from COVID-19.

In this study, the participants who took nirmatrelvir/ritonavir got better from COVID-19 faster by 1 day compared to those who took a placebo.

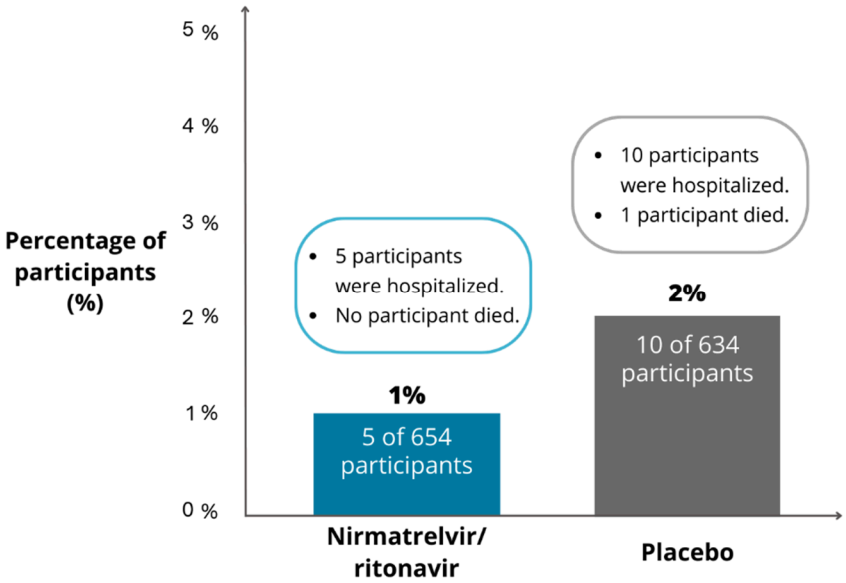
Based on these results, the researchers have decided that the difference between the treatment groups was small and likely due to chance. Nirmatrelvir/ritonavir may not lessen the time it takes to get better from COVID-19 for patients with low or standard risk of worsening to a severe illness.

2 Did the participants taking nirmatrelvir/ritonavir have a lower chance of being hospitalized with COVID-19 or dying from any cause compared to those taking a placebo?

Compared to a placebo, participants who took nirmatrelvir/ritonavir were 51% less likely to be hospitalized for COVID-19 or to die from any cause through Day 28.

The figure below shows how many participants were hospitalized with COVID-19 or died from any cause through Day 28.

Figure 3. How many participants were hospitalized with COVID-19 or died from any cause through Day 28?



In this study, fewer participants who took nirmatrelvir/ritonavir (1%) were hospitalized with COVID-19 or died from any cause compared to those who took a placebo (2%).

While the researchers cannot rule out the possibility that the difference between the treatment groups is due to chance, the results suggest a potential for nirmatrelvir/ritonavir to help lower the risk of hospitalization and death in COVID-19 patients with low or standard risk of worsening to severe illness.

Overall, from Day 1 through Week 24:

- No participant who took nirmatrelvir/ritonavir died from any cause.
- By Day 28, 1 participant who took a placebo died from any cause. This is the same participant shown in Figure 3 above. No participant who took a placebo died from Day 28 through Week 24.

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, researchers try to understand what effects a study medication might have on a participant.

The researchers reviewed the medical problems in 1288 participants who got at least 1 dose of nirmatrelvir/ritonavir or placebo.

Overall, 322 out of 1288 participants (25%) had at least 1 medical problem while in this study. These were seen in:

- 169 of 654 participants (26%) who took nirmatrelvir/ritonavir.
- 153 of 634 participants (24%) who took a placebo.

In total, 1 participant left the study because of a medical problem they had during the study. They were part of the placebo group.

Table 1 shows the most common medical problems – those seen in 1% or more of participants in either group.

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. It lists all medical problems reported by more than 1% of participants.
- The **2nd** column tells how many of the 654 participants taking nirmatrelvir/ritonavir reported each medical problem. Next to this number is the percentage of the 654 participants taking nirmatrelvir/ritonavir who reported the medical problem.
- The **3rd** column tells how many of the 634 participants taking a placebo reported each medical problem. Next to this number is the percentage of the 634 participants taking a placebo who reported the medical problem.
- Using these instructions, you can see how many had a change in the sense of taste. This was seen in:
    - 44 out of the 654 participants (7%) taking nirmatrelvir/ritonavir.
    - 3 out of the 634 participants (1%) taking a placebo.

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Nirmatrelvir/ Ritonavir (654 Participants)**	**Placebo (634 Participants)**
Change in the sense of taste	44 out of 654 participants (7%)	3 out of 634 participants (1%)
Headache	6 out of 654 participants (1%)	8 out of 634 participants (1%)
Loose, watery stools	26 out of 654 participants (4%)	19 out of 634 participants (3%)
Pain or discomfort after eating (indigestion)	8 out of 654 participants (1%)	2 out of 634 participants (less than 1%)
Queasy feeling (nausea)	20 out of 654 participants (3%)	17 out of 634 participants (3%)
Throwing up (vomiting)	11 out of 654 participants (2%)	11 out of 634 participants (2%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Nirmatrelvir/ Ritonavir (654 Participants)**	**Placebo (634 Participants)**
A longer time than usual for blood to form a clot (prolonged "activated partial thromboplastin" time)	7 out of 654 participants (1%)	12 out of 634 participants (2%)
High liver enzyme in the blood called "alanine aminotransferase"	14 out of 654 participants (2%)	8 out of 634 participants (1%)
High liver enzyme in the blood called "aspartate aminotransferase"	9 out of 654 participants (1%)	4 out of 634 participants (1%)
High hormone in the blood that activates the thyroid gland	3 out of 654 participants (1%)	7 out of 634 participants (1%)
High marker of blood clot breakdown products ("fibrin D dimer")	8 out of 654 participants (1%)	9 out of 634 participants (1%)
COVID-19 lung infection	4 out of 654 participants (1%)	10 out of 634 participants (2%)

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.

In total, 20 out of 1288 participants (2%) had at least 1 serious medical problem while in this study. These were seen in:

- 8 of 654 participants (1%) who took nirmatrelvir/ritonavir.
- 12 of 634 participants (2%) who took a placebo.

The list below shows the most common serious medical problems – those seen in 2 or more participants in either group:

- **COVID-19 lung infection** was seen in:
  - 3 of 654 participants (less than 1%) who took nirmatrelvir/ritonavir.
  - 8 of 634 participants (1%) who took a placebo.
- **Lung infection from any cause** was seen in:
  - 1 of 654 participants (less than 1%) who took nirmatrelvir/ritonavir.
  - 2 of 634 participants (less than 1%) who took a placebo.

Researchers did not think that any of the serious medical problems were related to nirmatrelvir/ritonavir.

Overall, through Week 24 of the study:

- 1 participant who took a placebo died from COVID-19 lung infection.
- No participant who took nirmatrelvir/ritonavir died.

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 **C4671002**

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

www.clinicaltrials.gov	Use the study identifier **NCT05011513**
www.clinicaltrialsregister.eu	Use the study identifier **2021-002857-28**

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!