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

Protocol Number: C4671005

Dates of Study: 16 July 2021 to 26 April 2022

Title of this Study: Study of Oral Nirmatrelvir (PF-07321332)/Ritonavir Compared With Placebo in Nonhospitalized Adults Who are at Higher Risk of Severe COVID-19 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 Increased Risk of Progressing to Severe Illness]

Date(s) of this Report: 05 December 2022 and 10 April 2023 (updated)

– 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?

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

Some people who have COVID-19 don't show any symptoms, while others have symptoms such as fever, dry cough, and shortness of breath.

Although most cases of COVID-19 are mild, some people are at a higher risk of getting sicker. COVID-19 can quickly become very serious 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 tablets and capsule are swallowed together.

- 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 main purpose of the study was to see if nirmatrelvir/ritonavir was more effective than placebo for preventing severe COVID-19 (requiring hospitalization or leading to death). A placebo does not have any medicine in it, but it looks like nirmatrelvir/ritonavir. Researchers studied nirmatrelvir/ritonavir to see if it could help prevent COVID-19 from becoming severe.

Researchers also wanted to find out if the medicine caused any unwanted medical problems (also known as side effects).

Researchers wanted to know:

Did the participants taking nirmatrelvir/ritonavir have a lower chance of being hospitalized with COVID-19 or passing away due to any cause than those taking placebo?

What happened during the study?

How was the study done?

Researchers tested nirmatrelvir/ritonavir on a group of study participants. Researchers wanted to find out how many participants taking nirmatrelvir/ritonavir were hospitalized due to COVID-19. They also recorded how many participants passed away due to any cause.

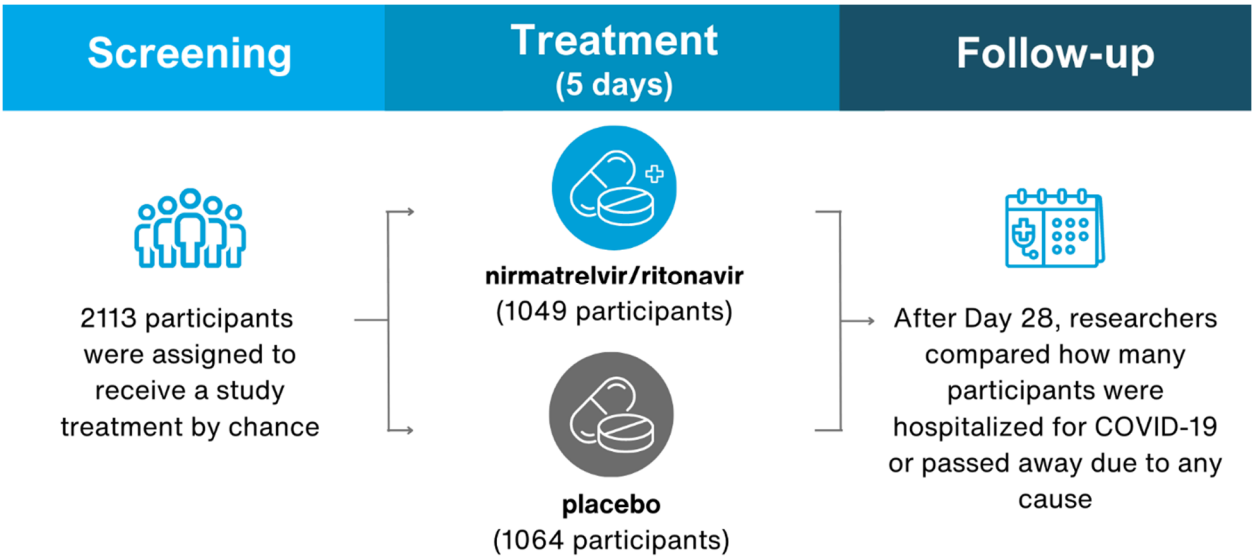
Researchers compared the results of study participants taking nirmatrelvir/ritonavir to the results of study participants taking a placebo. A placebo does not have any medicine in it, but it looks like nirmatrelvir/ritonavir.

The study participants and researchers did not know who took nirmatrelvir/ritonavir and who took the placebo. This is known as a "blinded" study. Study participants were assigned to take nirmatrelvir/ritonavir or placebo by chance alone. This is known as a "randomized" study, and it helps make the treatment groups similar and more even to compare.

The study included participants who were at a higher risk of getting severe COVID-19, such as people who were older or had diabetes.

As shown in the figure, there were a total of 2113 participants who entered the study. Of these participants, 1049 participants were given nirmatrelvir/ritonavir, and 1064 participants were given placebo:

Figure 1. Overall study design



The researchers looked at 2 groups of participants who started treatment within 3 days or 5 days of their COVID-19 symptoms starting:

- Group 1 started treatment within 3 days of their COVID-19 symptoms starting. This group included 671 participants who took nirmatrelvir/ritonavir and 647 participants who took the placebo. They took this medication twice a day for 5 days.
- Group 2 started treatment within 5 days of their COVID-19 symptoms starting. This group included 977 participants who took nirmatrelvir/ritonavir and 989 participants who took the placebo. They also took this medication twice a day for 5 days.

Participants then had follow-up visits up to 24 weeks after starting treatment.

Where did this study take place?

The Sponsor ran this study at 343 locations in 21 countries around the world.

When did this study take place?

It began 16 July 2021 and ended 26 April 2022.

Who participated in this study?

The study included participants who tested positive for COVID-19 and were showing symptoms. They weren't in the hospital yet but were at a higher risk of progressing to more severe illness that could result in hospitalization.

- A total of 1069 men participated.
- A total of 1044 women participated.
- All participants were between the ages of 18 and 88 years.

Of the 2113 participants who started the study:

- 1965 participants completed the study.
- 158 participants left before the study was over. The most common reasons for leaving the study were because they left the study by their choice or they were unreachable.

How long did the study last?

Study participants were treated for 5 days and were followed in the study for up to 24 weeks. The entire study took about 9 months to complete.

The Sponsor reviewed the study results in April 2022 and March 2023. The Sponsor then created reports of the results. This is a summary of those reports.

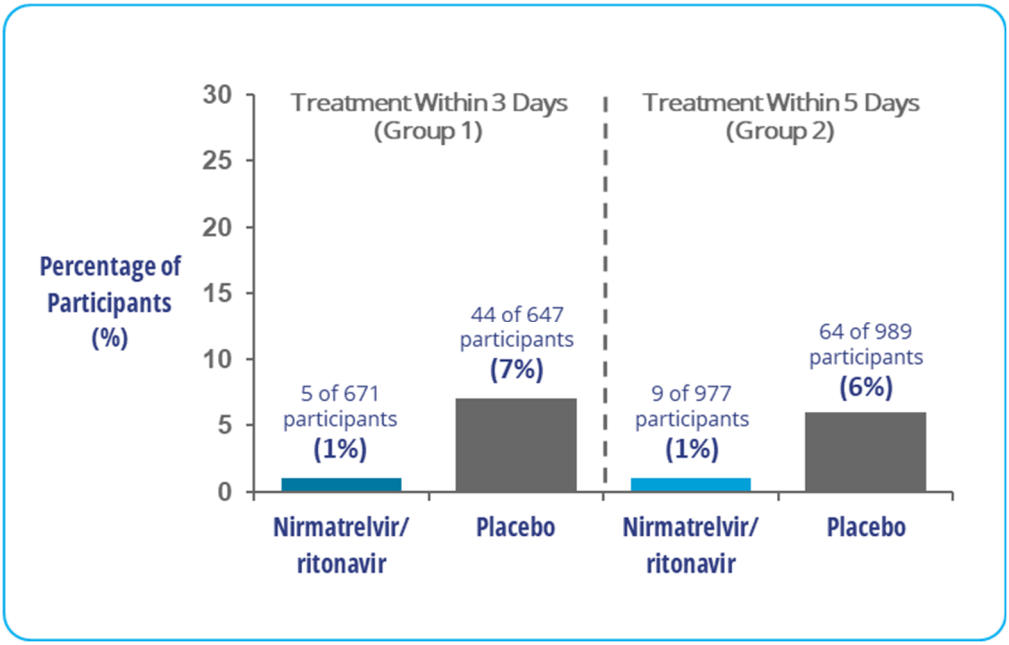
What were the results of the study?

Did the participants taking nirmatrelvir/ritonavir have a lower chance of being hospitalized with COVID-19 or passing away due to any cause than those taking placebo?

Compared to placebo, participants who took nirmatrelvir/ritonavir within 3 days of their symptoms starting were 89% less likely to be hospitalized due to COVID-19 or to pass away for any reason. Participants who took nirmatrelvir/ritonavir within 5 days of getting symptoms were 86% less likely to be hospitalized due to COVID-19 or to pass away for any reason.

The figure below shows how many participants were hospitalized with COVID-19 or passed away due to any cause.

Figure 2. How many participants were hospitalized with COVID-19 or passed away due to any cause?



Twelve (12) participants in the placebo group had passed away by Day 28. Later, by Week 24, a total of 15 participants who took placebo had passed away. No participants who took nirmatrelvir/ritonavir passed away during the study (through the Week 24 visit).

Based on these results, the researchers have decided that the results are not likely the result of chance. Nirmatrelvir/ritonavir may help lower the risk of hospitalization and death in patients who are at a higher risk for severe COVID-19.

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.

The researchers reviewed the medical problems in 2091 participants who got at least 1 dose of nirmatrelvir/ritonavir or placebo. Overall, 484 out of 2091 participants (23%) had at least 1 medical problem by Day 34 of the study. This included 228 participants who took nirmatrelvir/ritonavir and 256 participants who took placebo. Table 1 shows the most common medical problems – those reported by 2% or more of participants in either treatment 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. All medical problems reported by more than 2% of participants are listed.
- The **2nd** column tells how many of the 1038 participants taking nirmatrelvir/ritonavir reported each medical problem. Next to this number is the percentage of the 1038 participants taking nirmatrelvir/ritonavir who reported the medical problem.
- The **3rd** column tells how many of the 1053 participants taking a placebo reported each medical problem. Next to this number is the percentage of the 1053 participants taking a placebo who reported the medical problem.
- Using these instructions, you can see that 48 out of the 1038 participants (5%) taking nirmatrelvir/ritonavir had a change in their sense of taste. One (1) out of the 1053 participants (less than 1%) taking a placebo had a change in their sense of taste.

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Nirmatrelvir/ Ritonavir (1038 Participants)**	**Placebo (1053 Participants)**
Change in the sense of taste	48 out of 1038 participants (5%)	1 out of 1053 participants (less than 1%)
Loose stools	31 out of 1038 participants (3%)	16 out of 1053 participants (2%)
Increase of marker of blood clot breakdown in blood (Fibrin D dimer)	22 out of 1038 participants (2%)	30 out of 1053 participants (3%)
Increase of liver enzyme in blood (alanine aminotransferase)	17 out of 1038 participants (2%)	27 out of 1053 participants (3%)
COVID-19 pneumonia	8 out of 1038 participants (1%)	40 out of 1053 participants (4%)

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.

A total of 89 out of 2091 participants (4%) had at least 1 serious medical problem. These were seen in:

- 18 participants who took nirmatrelvir/ritonavir.
- 71 participants who took placebo.

Most of the serious medical problems were due to COVID-19 pneumonia. One participant who took nirmatrelvir/ritonavir had serious medical problems that the study doctor thought might be related to ritonavir (chest discomfort, difficulty breathing, and heart palpitations). Study doctors did not think that any of these serious medical problems were related to nirmatrelvir.

No participants who took nirmatrelvir/ritonavir passed away during the study.

A total of 15 participants who took placebo passed away during the study. Fourteen (14) of the 15 participants in the placebo group who passed away during the study died from complications of COVID-19.

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 **C4671005**

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

www.clinicaltrials.gov	Use the study identifier **NCT04960202**
www.clinicaltrialsregister.eu	Use the study identifier **2021-002895-38**

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!