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) and ritonavir
Protocol Number:	C4671034
Dates of Study:	03 August 2022 to 13 November 2023
Title of this Study:	A Study to Learn About Nirmatrelvir/Ritonavir in People at Least 12 Years of Age With COVID-19 Who Are Immunocompromised [An Interventional Efficacy and Safety, Phase 2, Randomized, Double-Blind, 3-Arm Study to Investigate Nirmatrelvir/Ritonavir in Nonhospitalized Participants at Least 12 Years of Age With Symptomatic COVID-19 Who Are Immunocompromised]
Date of this Report:	13 May 2024

– Thank You –

If you or your child 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 that started 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.

Most cases of COVID-19 are mild, but immunocompromised people have a higher risk of getting sicker from COVID-19. This is because immunocompromised people have a weak immune system that makes it harder to fight off the virus. Severe COVID-19 can lead to hospitalization or even death.

In people who are **immunocompromised**, their body's defense or immune system against diseases is weak. A person can be born with a weak immune system or have a weak immune system caused by a medical condition such as cancer. There are also treatments, such as chemotherapy, that can weaken the immune system.

Immunocompromised people have a harder time fighting off diseases or infections.

What are nirmatrelvir and ritonavir?

Nirmatrelvir is a study medication taken together with another medicine called ritonavir. This combination is called **nirmatrelvir/ritonavir** or Paxlovid™. Nirmatrelvir/ritonavir is taken by mouth.

- **Nirmatrelvir** (nir-muh-trel-veer) blocks a specific type of enzyme that the COVID-19 virus needs to multiply. Enzymes are proteins that speed things up in the body's cells. If this enzyme stops working, the COVID-19 virus cannot multiply and spread through the body.
- **Ritonavir** (rih-tahn-uh-veer) is usually taken together with another medicine. Ritonavir helps slow down the breakdown of the other medicine it is given with, so that the other medicine can work better in the body.

What was the purpose of this study?

The main purpose of this study was to find out if nirmatrelvir/ritonavir (given for 5 days, 10 days, or 15 days) is safe and can help treat COVID-19 in immunocompromised participants who are non-hospitalized.

Non-hospitalized means that a person does not need to be admitted to a hospital for medical care.

Researchers wanted to know:

- **Was the amount of COVID-19 virus in the body reduced and maintained at low levels after treatment with nirmatrelvir/ritonavir?**
- **What medical problems did participants have during the study?**

Researchers also wanted to learn if nirmatrelvir/ritonavir given as a second course of treatment can help treat COVID-19 rebound. These results are not in this summary because that was not the focus of the study.

COVID-19 rebound is when people have already had COVID-19 or taken medicine for COVID-19, but they get sick again with COVID-19 shortly after.

What happened during the study?

How was the study done?

This study signed up 2 groups of participants.

Main Study Group

- Researchers tested nirmatrelvir/ritonavir on immunocompromised participants who had COVID-19 symptoms at the start of the study and were non-hospitalized.
- Participants in this group had not taken nirmatrelvir/ritonavir recently for COVID-19.

Rebound Group

- Researchers tested nirmatrelvir/ritonavir given as a second treatment on immunocompromised people who had COVID-19 rebound and were non-hospitalized.
- Participants in this group had recently taken nirmatrelvir/ritonavir for 5 days to treat COVID-19, but they got sick again with COVID-19 within 2 weeks after treatment.

During the study:

Participants in the Main Study Group and Rebound Group were assigned to a treatment group by chance (like flipping a coin).

- They had an equal chance of receiving nirmatrelvir/ritonavir for 5, 10, or 15 days out of the 15-day treatment period.
- Those who were assigned to take nirmatrelvir/ritonavir for 5 or 10 days also took a placebo for the remaining days to complete the 15-day treatment period.

  A **placebo** does not contain any medicine, but it looks like nirmatrelvir or ritonavir.

The table below shows how participants in each treatment group took their study medications.

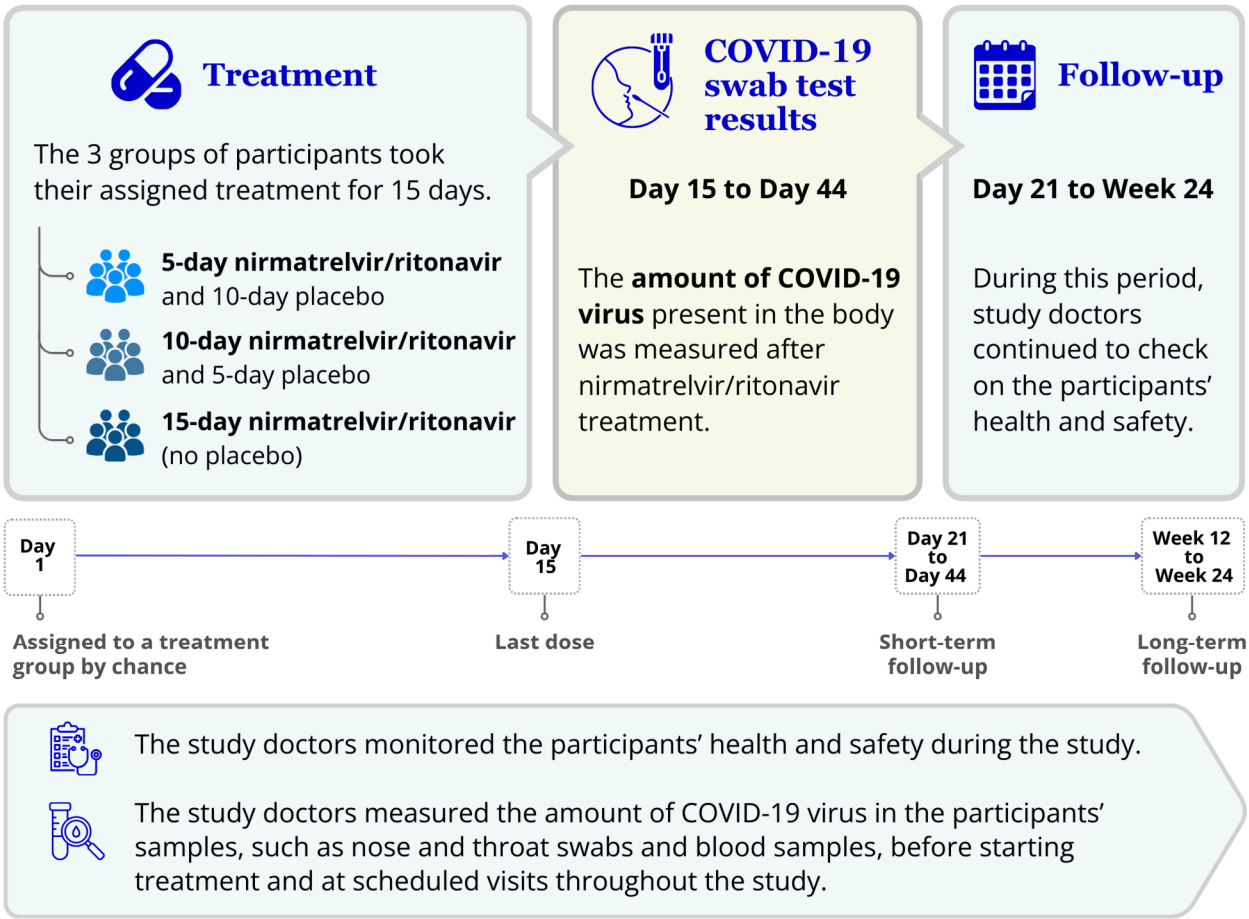
5-day nirmatrelvir/ ritonavir	Participants took nirmatrelvir/ritonavir 2 times daily for 5 days. Then, they took placebo for nirmatrelvir plus placebo for ritonavir 2 times daily for 10 days.
10-day nirmatrelvir/ ritonavir	Participants took nirmatrelvir/ritonavir 2 times daily for 10 days. Then, they took placebo for nirmatrelvir plus placebo for ritonavir 2 times daily for 5 days.
15-day nirmatrelvir/ ritonavir	Participants took nirmatrelvir/ritonavir 2 times daily for 15 days. No placebo was given.

The study participants and researchers did not know if participants were assigned to the 5-day, 10-day, or 15-day nirmatrelvir/ritonavir groups. This is known as a “blinded” study.

Researchers compared the results of study participants taking nirmatrelvir/ritonavir in the 5-day, 10-day, and 15-day treatment groups.

The figure below shows how this study was done in participants from the Main Study Group and Rebound Group.

Figure 1. How was this study done?



Where did this study take place?

The study ran at 73 locations in 9 countries.

- Australia
- Brazil
- Bulgaria
- Canada
- Hungary
- Mexico
- Slovakia
- Spain
- United States

When did this study take place?

It began on 03 August 2022 and ended on 13 November 2023.

Who participated in this study?

The study included participants who met the main study requirements:

- Are 12 years of age and older;
- Are immunocompromised;
- Have COVID-19 symptoms and a positive test for COVID-19;
- Are non-hospitalized;
- For the **Rebound Group** only:

  Have recently taken nirmatrelvir/ritonavir for 5 days to treat COVID-19, but they got sick again with COVID-19 within 2 weeks after treatment.

Main Study Group

In total, 156 participants were assigned to a treatment group.

- 72 were men and 84 were women.
- Participants were from 16 to 82 years of age.
- 155 took at least 1 dose of nirmatrelvir/ritonavir and 1 did not receive treatment.
- 140 (90%) finished and 16 (10%) did not finish the treatment period. The most common reason for not finishing the treatment period was the participant left by their choice before the study was over.

Rebound Group

- In total, 2 participants were assigned to a treatment group and took at least 1 dose of nirmatrelvir/ritonavir.
- Both participants finished the treatment period.

How long did the study last?

Study participants were in the study for about 24 weeks. The entire study took about 66 weeks (or 15 months) to complete.

When the study ended in November 2023, the Sponsor reviewed 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?

Was the amount of COVID-19 virus in the body reduced and maintained at low levels after treatment with nirmatrelvir/ritonavir?

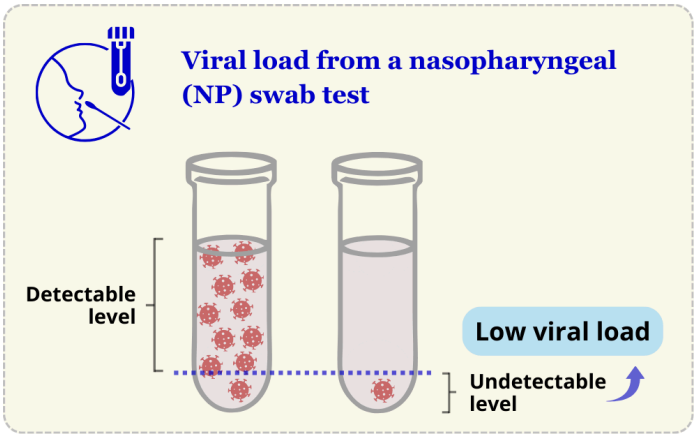
This section describes the results of participants in the Main Study Group.

Participants gave nasopharyngeal (NP) swab samples at scheduled visits during the study: before (baseline) and after starting treatment with nirmatrelvir/ritonavir.

- The NP swab collects a sample from the nasopharynx, which is the area where the back of the nose meets the throat.
- Researchers used the NP swab test to measure the participants' **COVID-19 viral load** throughout the study.

Viral load is the amount of virus particles in the body. Viral load helps doctors understand how severe a virus infection is and how easily a person can spread the virus to others.

The figure below shows what detectable and undetectable viral loads mean.



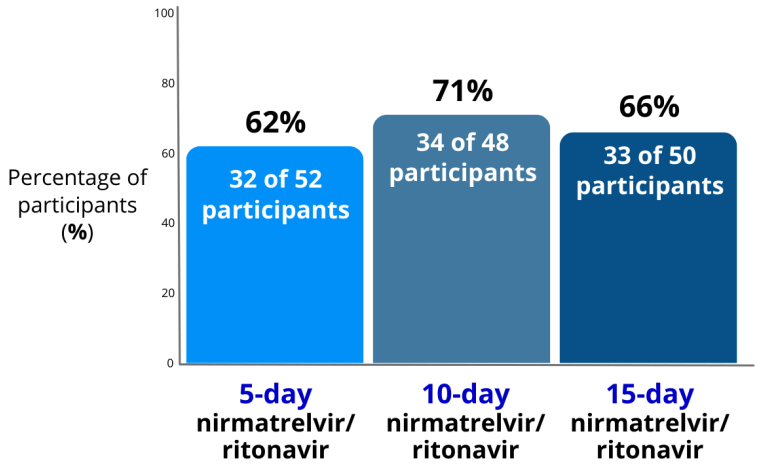
- **Detectable viral load:** The amount of virus in the NP swab sample is **above** the limit of detection.
- **Undetectable viral load:** The amount of virus in the NP swab sample is **low** or **below** the limit of detection.

At baseline, before starting nirmatrelvir/ritonavir treatment, 144 out of 156 participants (**92%**) across the 3 treatment groups had **detectable** COVID-19 viral load.

Researchers checked how many participants were able to maintain a low or undetectable COVID-19 viral load from Day 15 to Day 44 of the study after nirmatrelvir/ritonavir treatment.

After taking nirmatrelvir/ritonavir for 5, 10, or 15 days, **more than 60% of participants** across the 3 treatment groups were able to maintain a **low or undetectable** COVID-19 viral load from Day 15 to Day 44 of the study. The figure below shows these results.

Figure 2. After nirmatrelvir/ritonavir treatment, how many participants were able to maintain a low or undetectable COVID-19 viral load from Day 15 to Day 44 of the study?



The study results mean that taking nirmatrelvir/ritonavir for 5, 10, or 15 days can help keep the COVID-19 virus under control and prevent it from multiplying from Day 15 to Day 44 of the study in most of the immunocompromised participants with COVID-19 infection who are non-hospitalized.

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.

Researchers checked how many participants had medical problems from **Day 1 to Day 44** of the study.

Overall, 1 participant left the study because of a medical problem they had during the study. This participant took 5-day nirmatrelvir/ritonavir and was part of the Main Study Group.

Main Study Group:

The list below shows how many participants had at least 1 medical problem.

- **5-day nirmatrelvir/ritonavir:** 28 of 53 participants (53%)
- **10-day nirmatrelvir/ritonavir:** 34 of 51 participants (67%)
- **15-day nirmatrelvir/ritonavir:** 31 of 51 participants (61%)

Table 1 lists the most common medical problems – those reported by 5% of participants or more – in the Main Study 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 in the Main Study Group during the study. All medical problems reported by 5% of participants or more are listed.
- The **2nd** column tells how many of the 53 participants taking the 5-day nirmatrelvir/ritonavir reported each medical problem. Next to this number is the percentage of the 53 participants taking the 5-day treatment who reported the medical problem.
- The **3rd** column tells how many of the 51 participants taking the 10-day nirmatrelvir/ritonavir reported each medical problem. Next to this number is the percentage of the 51 participants taking the 10-day treatment who reported the medical problem.
- The **4th** column tells how many of the 51 participants taking the 15-day nirmatrelvir/ritonavir reported each medical problem. Next to this number is the percentage of the 51 participants taking the 15-day treatment who reported the medical problem.
- Using these instructions, you can see how many participants had a change in sense of taste:
    - 5-day treatment group: 6 out of 53 participants (11%)
    - 10-day treatment group: 11 out of 51 participants (22%)
    - 15-day treatment group: 14 out of 51 participants (28%)

Table 1. Commonly reported medical problems by participants – Main Study Group			
Medical Problem	**5-day nirmatrelvir/ ritonavir (53 Participants)**	**10-day nirmatrelvir/ ritonavir (51 Participants)**	**15-day nirmatrelvir/ ritonavir (51 Participants)**
Change in sense of taste	6 participants (11%)	11 participants (22%)	14 participants (28%)
Diarrhea	5 participants (9%)	4 participants (8%)	4 participants (8%)
Nausea	1 participant (2%)	2 participants (4%)	5 participants (10%)
Headache	1 participant (2%)	3 participants (6%)	1 participant (2%)
High levels of thyroid-stimulating hormone (TSH)	0 participants (0%)	0 participants (0%)	3 participants (6%)

TSH tells the thyroid gland how much thyroid hormones to make.

Rebound Group:

The medical problems that the 2 participants in the rebound group had during the study are not in this summary. Because of the small number of participants in this group, leaving out this information helps protect their identities.

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.

Main Study Group:

The list below shows how many participants had at least 1 serious medical problem.

- **5-day nirmatrelvir/ritonavir:** 5 of 53 participants (9%)
- **10-day nirmatrelvir/ritonavir:** 1 of 51 participants (2%)
- **15-day nirmatrelvir/ritonavir:** 4 of 51 participants (8%)

Each serious medical problem was reported by no more than 1 participant across treatment groups. None of the serious medical problems were considered by researchers as related to nirmatrelvir/ritonavir.

Rebound Group:

None of the participants in this group had serious medical problems during the study.

Main Study Group and Rebound Group:

No participant died from Day 1 to Day 44 of the study. In the Main Study Group, 2 participants died after Day 44, during or after the long-term follow-up. These participants died due to complications from underlying diseases:

- 1 participant from the 5-day nirmatrelvir/ritonavir group died before the Week 24 long-term follow-up.
- 1 participant from the 15-day nirmatrelvir/ritonavir group died after the Week 24 long-term follow-up.

Where can I learn more about this study?

If you or your child 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 **C4671034**

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

www.clinicaltrials.gov	Use the study identifier **NCT05438602**
www.clinicaltrialsregister.eu	Use the study identifier **2022-001362-35**

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 or your child 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!