PLAIN LANGUAGE SUMMARY OF CLINICAL STUDY RESULTS

Study Sponsor: Gilead Sciences

Gilead Study Number: GS-US-611-6273

Date of Study: November 2022 to November 2023 (the study closed earlier than planned)

Short Study Title: Study of Obeldesivir in Participants With COVID-19 Who Have a High Risk of Developing Serious or Severe Illness

Study Nickname: BIRCH

Date of this Plain Language Summary: July 2024

The information in this summary does not include any information available after this date.

Thank you

Thank you to the participants who contributed to the clinical study for **obeldesivir**, also known as **GS-5245**.

Gilead Sciences sponsored this study. We believe it is important to share the results with study participants and the general public.

If you participated in the study and have questions about the results, please speak with a doctor or staff member at the study site.

Always talk to a doctor or healthcare provider before making any treatment changes.

This document is a short summary of this study written for a general audience. Links to scientific summaries of this study can be found at the end of this document.

What was the purpose of the study?

The purpose of this clinical study was to find out how well the study drug, obeldesivir, worked and how safe it was in treating coronavirus disease (COVID-19) in participants who had a **high risk** of becoming very sick from COVID-19.

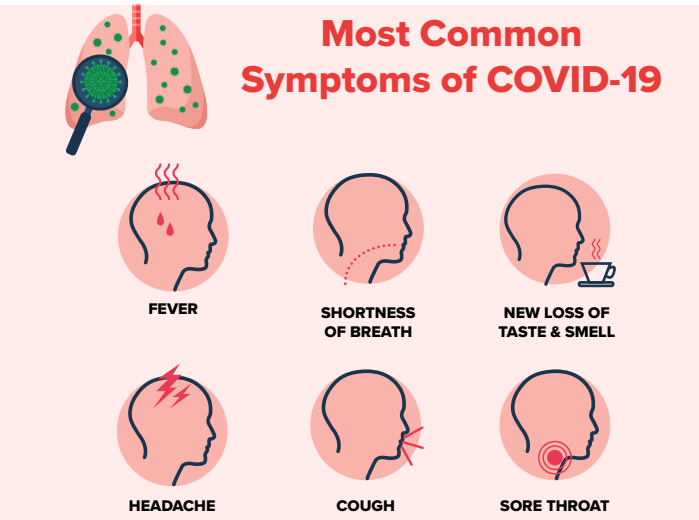
Some of the examples of high risk from COVID-19 include:

- People with serious medical conditions like:
  - Heart, kidney, liver, or lung-related diseases
  - Cancer (uncontrolled cell growth)
  - Weakened immune system
  - High blood pressure
  - History of smoking
  - Overweight or obesity
- People over 50 years of age
- People who underwent organ transplant (organ transplantation is a medical procedure in which an organ is removed from one body and placed into another persons' body, to replace a damaged or a missing organ).

What is COVID-19?

COVID-19 is a respiratory disease caused by a virus called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The virus was the cause of the spread of COVID-19 disease around the world in late 2019. COVID-19 may damage the lungs permanently and also affect other organs. The symptoms range from mild to very bad and may even lead to death. The most common symptoms are shown below. Some of the other symptoms include runny nose, vomiting, muscle or body aches, feeling sick to the stomach (nausea), and diarrhea. COVID-19 has caused millions of deaths worldwide.

Currently, some treatments for COVID-19 are given by injection and that requires a hospital visit to get the injection. However, it might be hard for some people to travel to a clinic or the hospital to get the injection. So, there is a need for a new drug that can be taken orally (by mouth) at home which can help people with COVID-19. Obeldesivir is a pill (tablet). In this study, the researchers wanted to check if obeldesivir could be a treatment option for people with COVID-19 who were at a high risk of becoming very sick and who could not take any other medicine for COVID-19 orally or through an injection.



This is a Phase 3 clinical study. This means that researchers looked at how obeldesivir worked in a large group of people with COVID-19, compared to a **placebo**.

Placebo: A placebo looks like a treatment but does not have any active drug in it. Researchers use a placebo as it helps them compare and see if the new drug works and is safe.

The main questions the researchers wanted to answer in this study were:

- Did obeldesivir help prevent hospitalizations due to COVID-19 or death by Day 29, compared to placebo?
- What side effects did participants have during the study, if any?

Who took part in the study?

- A total of **468 participants** with a high risk of getting very sick due to COVID-19 around the world took part in the study.
- 3 participants left the study before taking study treatment and were not included in the study results.

People could take part in the study if they:

- Were 18 years of age or older
- Had confirmed COVID-19 disease
- Had multiple medical conditions that could increase the risk of getting very sick from COVID-19
- Were not hospitalized

The participants enrolled in the study were between the ages of **18** to **89**.

The table below shows how many study participants were from each country.

Bulgaria	196 **(42%)**	Brazil	8 **(2%)**
Romania	53 **(11%)**	United Kingdom	8 **(2%)**
Mexico	48 **(10%)**	Japan	5 **(1%)**
Taiwan	40 **(9%)**	South Korea	3 **(less than 1%)**
South Africa	31 **(7%)**	Italy	2 **(less than 1%)**
Spain	23 **(5%)**	Turkey	2 **(less than 1%)**
Poland	19 **(4%)**	France	1 **(less than 1%)**
Canada	18 **(4%)**	Hungary	1 **(less than 1%)**
Portugal	9 **(2%)**	Singapore	1 **(less than 1%)**

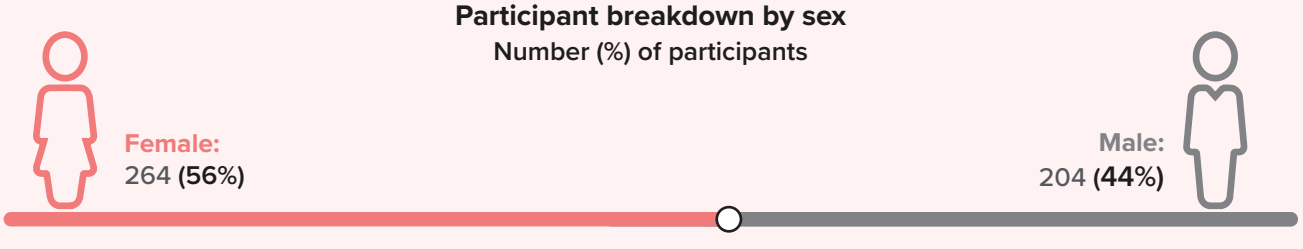
Race of participants is shown below.

White	346 **(74%)**	Black or African American	19 **(4%)**
Asian	56 **(12%)**	Other or more than one race	5 **(1%)**
American Indian or Alaska Native	40 **(less than 9%)**	Native Hawaiian or other Pacific Islander	2 **(less than 1%)**

Ethnicity of participants is shown below.

Not Hispanic Or Latino	389 **(83%)**	Hispanic Or Latino	79 **(17%)**

Participant breakdown by sex
Number (%) of participants



What happened during the study?

The study was **randomized** and **double-blind**.

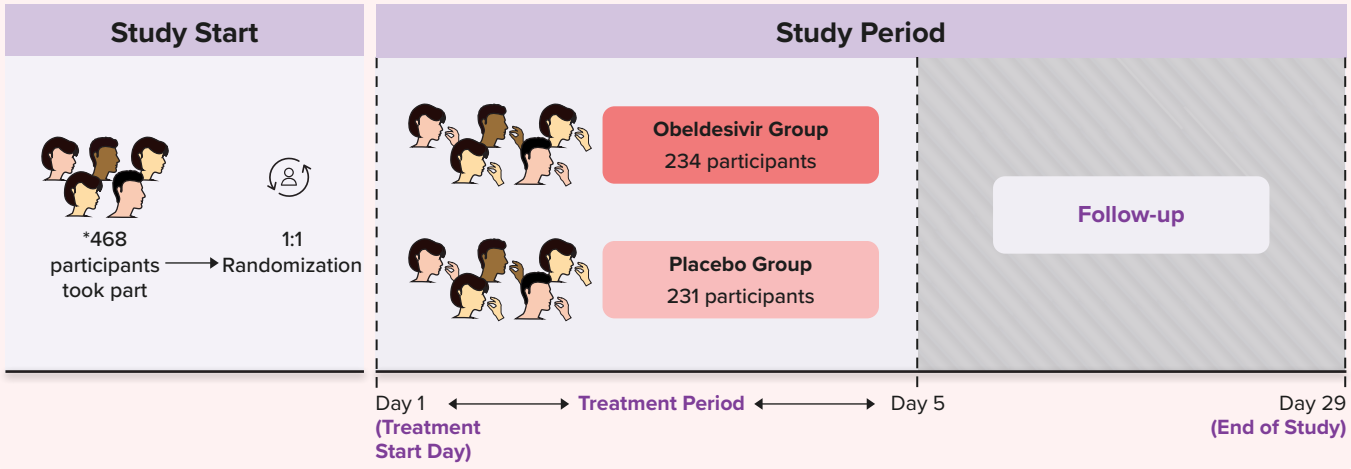
Randomized: This means that the researchers used a computer program to randomly choose the treatment each participant took. This helped make sure the treatments were chosen fairly. In this study, participants had an equal chance of getting obeldesivir or placebo. This is called 1:1 randomization.

Double-blind: This means none of the participants, doctors or other study staff, and the sponsor personnel knew what treatment each participant took. This was done to make sure the study results were not influenced in any way.

The participants took the following treatment:

Obeldesivir Group	Participants took 1 tablet of obeldesivir 350 mg in the morning and 1 in the evening. They did this for 5 days.
Placebo Group	Participants took 1 tablet of placebo in the morning and 1 in the evening. They did this for 5 days. The placebo tablet looked like obeldesivir tablet.

The figure below shows how the study was done.



*Of the 468 participants, 3 participants did not take any study treatment.

Originally, the study aimed to enroll 2300 participants. However, it was stopped early after 468 participants were enrolled. The decision to stop the study ahead of schedule was not due to safety concerns or how obeldesivir worked. Gilead chose to end enrollment of participants early because there were not enough cases of hospitalizations or deaths that occurred by Day 29 in the 468 participants enrolled. Researchers could not prove if obeldesivir helps in preventing hospitalization or death with the limited number of cases.

What were the results of the study?

This is a summary of the main results from this study. The individual results of each participant might be different and are not in this summary. A detailed presentation of the results can be found on the websites listed at the end of this summary.

Did obeldesivir help prevent hospitalizations due to COVID-19 or death by Day 29, compared to placebo?

As the study stopped early, the researchers do not have enough information to know if obeldesivir worked better than placebo in preventing hospitalizations due to COVID-19 or death by Day 29.

What side effects did participants have during the study?

Unwanted medical events can happen to the study participants when they take study treatments. In this summary, **"side effects"** are defined as unwanted medical events that the study doctors thought might be caused by the study treatment. The results from several studies are usually needed to help decide if a treatment actually causes a side effect.

A side effect is considered "serious" if it:

- results in death
- is life-threatening
- is considered by the study doctor to be medically important
- causes lasting problems
- requires hospital care
- causes a birth defect

The table below shows how many participants had side effects during the study.

Overall Side Effects

	Obeldesivir Group (out of 234 participants)	**Placebo Group** (out of 231 participants)	**Total** (out of 465 participants)
	Number of participants (%)		
How many participants had any serious side effects?	1 (less than 1%)	1 (less than 1%)	2 (less than 1%)
How many participants had any side effects?	14 (6%)	11 (5%)	25 (5%)
How many participants stopped taking study treatment because of side effects?	1 (less than 1%)	1 (less than 1%)	2 (less than 1%)

What were the serious side effects?

The **serious side effects** in this study were **dizziness**, which occurred in 1 out of 234 participants (less than 1%) in the obeldesivir group and **vomiting** in 1 out of 231 participants (less than 1%) in the placebo group. **None of the participants died due to any side effects during this study.**

What were the non-serious side effects?

The table below shows the **top 5 most common non-serious side effects** that occurred during the study. These side effects were not serious in nature and did not meet the definition of 'serious side effects' mentioned in the section above in this summary.

Most Common Non-serious Side Effects

	Obeldesivir Group (out of 234 participants)	**Placebo Group** (out of 231 participants)	**Total** (out of 465 participants)
Non-serious side effects	Number of participants (%)		
Feeling sick to the stomach (Nausea)	3 (1%)	3 (1%)	6 (1%)
Frequent loose watery stools (Diarrhea)	4 (2%)	0	4 (less than 1%)
Belly pain (Abdominal pain)	3 (1%)	0	3 (less than 1%)
Upset stomach after eating (Dyspepsia)	1 (less than 1%)	2 (less than 1%)	3 (less than 1%)
Sensation of spinning around and losing one's balance (Dizziness)	0	2 (less than 1%)	2 (less than 1%)

There were other non-serious side effects, but those occurred in fewer participants. Some participants may have had more than 1 non-serious side effect.

How has this study helped researchers?

Even though the study ended early, it helped researchers learn more about the safety of obeldesivir in people with COVID-19 who had a high risk of getting very sick.

The results from several studies are needed to help decide which treatments work and are safe. This summary shows only the main results from this one study. Other studies may provide new information or different results.

Gilead Sciences does plan to have further clinical studies with obeldesivir.

Where can I learn more about this study?

You can find more information about this study on the websites listed below.

Organization (Website)	Study Identifier
Europe Medicines Agency (www.clinicaltrialsregister.eu)	EudraCT number: 2022-002741-18
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	ClinicalTrials.gov ID: NCT05603143
www.gileadclinicaltrials.com	GS-US-611-6273

Please note that information on these websites may be presented in a different way from this summary.

Full Study Title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of GS-5245 for the Treatment of COVID-19 in Participants With High-Risk for Disease Progression

To learn more about clinical trials in general, please visit this **page** on www.clinicaltrials.gov website

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Thank you

Clinical study participants belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

GILEAD