

Summary of Clinical Study Results for General Audience

Plain Language Summary

1. STUDY NAME

A Study to Compare S-217622 With Placebo in Non-Hospitalized Participants With COVID-19 (SCORPIO-HR)

Here is the full study title: A Phase 3, multicenter, randomized, double-blind, 24-week study of the clinical and antiviral effect of S-217622 compared with placebo in non-hospitalized participants with COVID-19

2. WHO SPONSORED THIS STUDY?

This study was sponsored by Shionogi & Co., Ltd./Shionogi Inc./Shionogi B.V. (Shionogi). The other name for this study was “ACTIV-2d”. This was a public-private collaboration between Shionogi and the Accelerating COVID Therapeutic Interventions and Vaccines (ACTIV) group.

3. GENERAL INFORMATION ABOUT THIS STUDY

This study was done to learn about a possible treatment for COVID-19.

The experimental treatment that was studied is called **S-217622**, which is also known as **ensitrelvir**. Ensitrelvir targets the virus that causes COVID-19 and reduces the virus’s ability to reproduce.

The main goal of this study was to learn whether taking ensitrelvir within 3 days of symptom onset could help shorten the time that participants have COVID-19 symptoms. This study was also done to learn about possible side effects of the treatment.

This study was run in these countries:

- United States (732 participants)
- India (416 participants)
- Brazil (207 participants)
- Thailand (162 participants)
- South Africa (129 participants)
- Colombia (100 participants)
- Japan (99 participants)
- Philippines (84 participants)
- Poland (55 participants)
- Pakistan (39 participants)
- Argentina (34 participants)
- Mexico (15 participants)
- Malawi (9 participants)
- Uganda (7 participants)
- Ghana (3 participants)
- Kenya (2 participants)

The study started in August 2022 and ended in March 2024.

4. WHAT PATIENTS WERE INCLUDED IN THIS STUDY?

There were 2,093 patients who took part in this study. Of these participants, 8 left the study before starting treatment.

Among the remaining 2,085 participants, there were 1,155 women and 930 men. Everyone in the study was between 17 and 89 years old when they joined.

All of the participants had COVID-19 but did not need to be hospitalized for treatment at the start of the study.

5. WHICH STUDY DRUGS WERE STUDIED?

The study drugs used in this study were:

- **ensitrelvir**
- **a placebo** – A “placebo” is a dummy treatment that looks like ensitrelvir but does not contain active ingredients of ensitrelvir in it. Using a placebo helps make study results unbiased and fair.

This was a “double-blinded” study. That means that neither the participants nor the study doctors knew who received ensitrelvir and who received the placebo during this study.

Participants in this study were randomly assigned to 1 of these groups to reduce bias between the groups (like picking names from a hat). This means everyone had a fair chance to be in either group.

Of the 2,085 participants who started treatment in this study:

- 1,037 took ensitrelvir
- 1,048 took the placebo

The participants took their study treatment once a day for 5 days. Both treatments were taken orally (by mouth) as tablets.

Participants kept track of their symptoms in a study diary at home for about 1 month. During this month, the participants also had regular healthcare visits at the study clinic, in their home, or in another location.

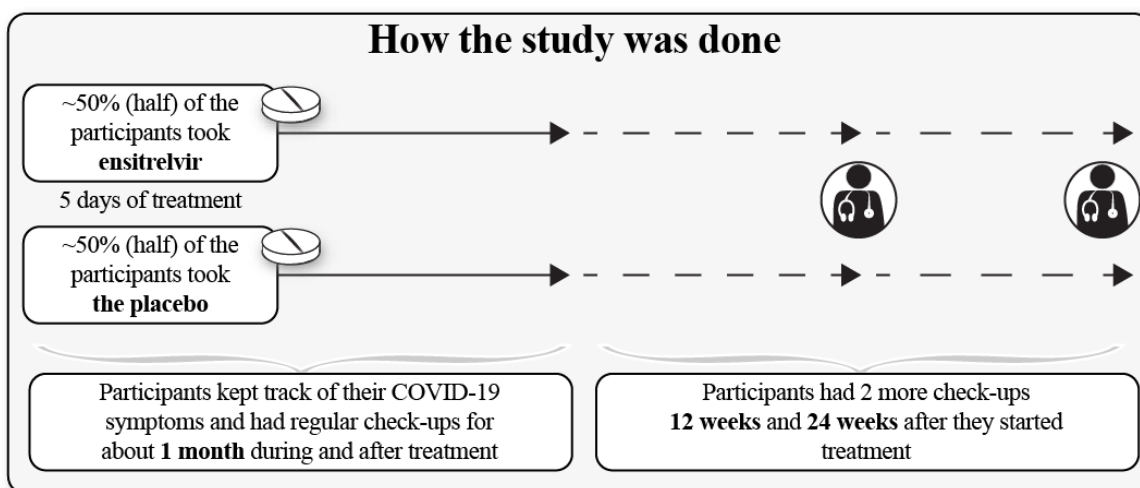
At these healthcare visits, the participants:

- Got a check-up
- Gave blood samples
- Had nasal swabs collected to test for COVID-19

- Told a study doctor about how they were feeling, any symptoms or side effects they were having, and any medications they were taking (including other medications for COVID-19)

The participants had 2 more healthcare visits about 12 weeks (almost 3 months) and 24 weeks (almost 6 months) after they started treatment. These visits were done to check on the participants' longer-term health outcomes.

The figure below shows how the study was done.



6. WHAT WERE THE OVERALL RESULTS OF THIS STUDY?

The main goal of the study was to learn whether taking ensitrelvir within 3 days of symptom onset helped shorten the time that participants had COVID-19 symptoms.

To do this, researchers looked at the participants' study diaries to see how long specific symptoms lasted after participants took their assigned treatment. They looked at 15 symptoms: cough, shortness of breath/difficulty breathing, fever, chills, fatigue, aches and pains, diarrhea, nausea, vomiting, headache, sore throat, stuffy nose, runny nose, loss of taste, and loss of smell.

The researchers first wanted to know how many participants had **sustained resolution** of these symptoms during the first month after treatment without needing to be hospitalized. "Sustained resolution" means their **symptoms resolved** for at least 48 hours.

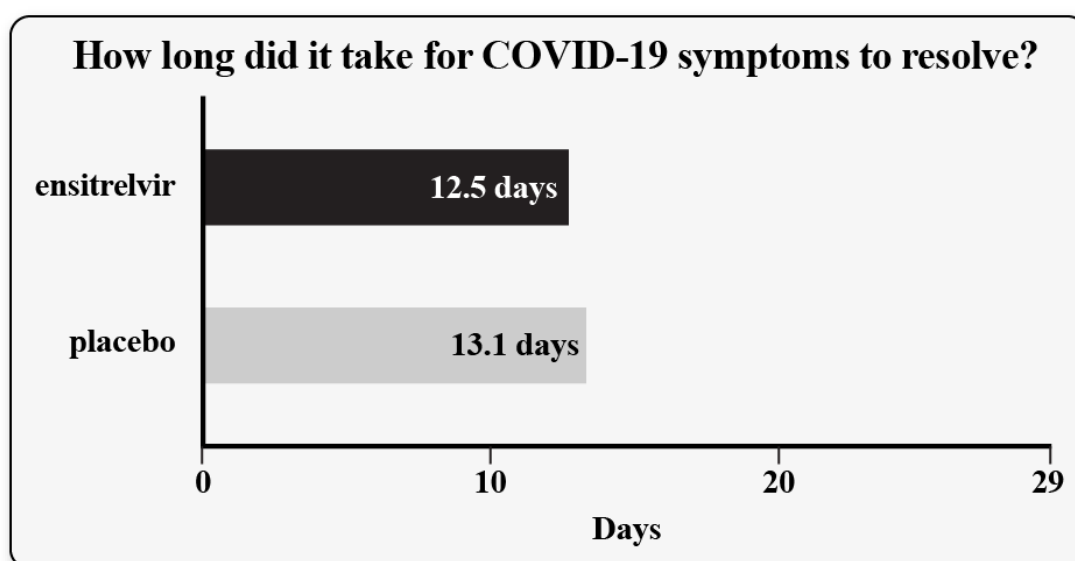
What did it mean for symptoms to "resolve"?

- If a participant developed 1 of these symptoms when they got COVID-19, the symptom was considered resolved only if it went away completely.
- If a participant had any of these symptoms before and the symptom got worse when they got COVID-19, the symptom was considered resolved if it improved.
- If a participant had any of these symptoms before and it did not get worse when they got COVID-19, the symptom was considered resolved as long as it did not get worse.

Of the 2,085 participants who started treatment in this study, there were 1,888 who started treatment within 3 days of the start of their COVID-19 symptoms. This included 945 participants who were assigned to take ensitrelvir and 943 participants who were assigned to take the placebo. Only these participants were included in these results.

Of the 945 participants who were assigned to take **ensitrelvir**, there were 768 (81.3%) who had sustained resolution of all symptoms. The average time until symptoms resolved was **12.5 days**.

Of the 943 participants who were assigned to take the **placebo**, there were 755 (80.1%) who had sustained resolution of all symptoms. The average time until symptoms resolved was **13.1 days**.



Although the average time with symptoms was somewhat shorter among participants who received ensitrelvir, this difference was not “statistically significant”. This means the difference is likely to be by chance rather than a difference caused by the study treatment.

7. WHAT WERE THE SIDE EFFECTS?

A lot of research is needed to know whether a drug causes medical problems. So, when new drugs are being studied, researchers keep track of all medical problems that participants have while they are in the study.

- A “side effect” (unwanted effect) is any medical problem that is judged by the study doctor to be possibly caused by a study drug used in the study.
- A “serious side effect” is a side effect that results in death, is life-threatening, causes lasting problems, needs hospital care, causes birth problems, or is otherwise considered important by a study doctor.

None of the participants in this study had a serious side effect.

Non-serious side effects happened to:

- 87 of 1,037 participants who took ensitrelvir. This was 8% of this group.
- 76 of 1,048 participants who took the placebo. This was 7% of this group.

The most common side effect was abnormally high levels of triglycerides in the bloodstream. Triglycerides are a type of fat that the body uses to store energy. High levels of triglycerides could put someone at risk for heart disease.

There were 50 participants who had this side effect, including 25 who took ensitrelvir and 25 who took the placebo (about 2% of each group).

This was the only side effect that happened to at least 2% of participants in the study. There were other side effects, but they happened to fewer participants.

There were 2 participants (less than 1%) in each treatment group who stopped taking their assigned study treatment because of a side effect.

8. HOW HAS THIS STUDY HELPED PATIENTS AND RESEARCHERS?

The results are limited to the particular participants and cannot be assumed to be true for everybody. Also, only the results of this study are included in this document. New information or different results about the study drug may be given in other studies. However, this research helps future patients and families by helping researchers understand more about the drug being studied.

9. ARE THERE PLANS FOR FURTHER STUDIES?

Other studies of ensitrelvir in participants with COVID-19 are currently ongoing or planned. Future studies will collect more information about ensitrelvir and find out what happens when ensitrelvir is used.

10. WHERE CAN I FIND MORE INFORMATION ABOUT THIS STUDY?

You may find more information about this study:

Website	URL	Identifier
ClinicalTrials.gov	English: https://clinicaltrials.gov/	NCT number: NCT05305547
EudraCT	English: https://www.clinicaltrialsregister.eu/	EudraCT Number: 2021-006504-32
jRCT	Japanese: https://jrct.mhlw.go.jp/	number of clinical trial plan: jRCT2031220353

Contact information for the company that conducted this study:

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The company that conducted this study may be one or more of the above companies.
The above companies are referred to as SHIONOGI.