Clinical Trial Results – Layperson Summary

A study to look at whether bemnifosbuvir worked to improve symptoms in people with COVID-19 who were not hospitalised compared with a 'placebo' – and how safe this medicine was

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of a clinical trial (called a 'study' in this document) – written for:

- members of the public and
- people who took part in the study.

This summary is based on information known at the time of writing (October 2022). More information may now be known.

The study started in April 2021 and stopped early – in December 2021 – because the study organisers decided to change the study plans and how to evaluate the study medicine. Fewer people were included than was planned, which meant that researchers were not able to make strong conclusions from the trial. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.

Contents of the summary

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about COVID-19 and the study medicine.

Key information about this study

- This study was done to test whether the study medicine (called 'bemnifosbuvir') was a safe and effective treatment for people with COVID-19 who were not hospitalised at the start of the study.
- In this study, people were given either bemnifosbuvir or a placebo– it was decided by chance which treatment each person was given.
- This study included 216 people (about 16% of the planned number of people) in 12 countries.
- Fewer people were included than was planned, which meant that researchers were not able to make strong conclusions from the trial.
- The main finding was that bemnifosbuvir did not reduce the time it took for COVID-19 symptoms to improve (or go away) compared with placebo.
- Around 3% of people who were given bemnifosbuvir needed to be hospitalised for their COVID-19 compared with 10% who were given a placebo.
- Around 4% of people (5 out of 141 people) taking bemnifosbuvir had serious side effects, compared to around 10% (7 out of 71 people) taking the placebo.
- This study stopped early because the study organisers decided to change the study plans and how to evaluate the study medicine.

1. General information about this study

Why was this study done?

COVID-19 is a common illness caused by infection with the SARS-CoV-2 virus. It can cause symptoms such as cough, fever, sore throat, being sick and loss of smell or taste.

Most people who catch COVID-19 have mild symptoms, but some people can get seriously ill and may need to be hospitalised. Older people and people with medical conditions (for example, heart disease or cancer) are at higher risk of severe illness.

New medicines are needed to treat COVID-19 and to help stop people from getting seriously ill or dying.

Bemnifosbuvir is a new antiviral (a medicine that treats infections caused by a virus) that may be able to treat COVID-19. This study was done to find out if bemnifosbuvir can be used to treat mild or moderate COVID-19 by reducing symptoms in people who are not hospitalised. Researchers also wanted to find out how safe bemnifosbuvir was.

What was the study medicine?

A medicine called 'bemnifosbuvir' (also called AT-527) was the focus of this study.

- You say this as 'Bem – nee – foz – buh – veer'.
- Bemnifosbuvir works by stopping the virus that causes COVID-19 from multiplying inside the body.
- This may mean that bemnifosbuvir could help people with COVID-19 feel better and stop their illness from getting worse.

Bemnifosbuvir was compared to a 'placebo'.

- You say this as 'plah – see – bo'
- The placebo looked the same as bemnifosbuvir but did not contain any real medicine. This means it had no medicine-related effect on the body.
- Researchers compared the study medicine to a placebo so they could show which benefits or side effects are actually caused by the medicine.

What did researchers want to find out?

- Researchers did this study to compare the study medicine (bemnifosbuvir) with a placebo – to see how well the study medicine worked (see section 4 "What were the results of the study?").
- The researchers also wanted to find out how safe the medicine was – by checking how many people had side effects when taking each of the medicines during this study (see section 5 "What were the side effects?").

The main question that researchers wanted to answer was:

1. How well does bemnifosbuvir work to improve symptoms in people with mild or moderate COVID-19 – who were not hospitalised at the start of the study?

Other questions that researchers wanted to answer included:

2. How many people needed to be hospitalised for their COVID-19?
3. What were the side effects of bemnifosbuvir in people with mild or moderate COVID-19 – who were not hospitalised at the start of the study?

What kind of study was this?

This study was a 'Phase 3' study. This means that bemnifosbuvir had been tested in a smaller number of people with COVID-19 before this study. In this study, a larger number of people with mild or moderate COVID-19 either took bemnifosbuvir or a placebo – this was to find out about the side effects of bemnifosbuvir and if it improved symptoms in people with mild or moderate COVID-19, who were not hospitalised at the start of the study.

The study was 'randomised'. This means that it was decided by chance which of the medicines people in the study would have – like tossing a coin.

This was a 'double-blind' study. This means that neither the people taking part in the study nor the study doctors knew which of the study medicines people were taking.

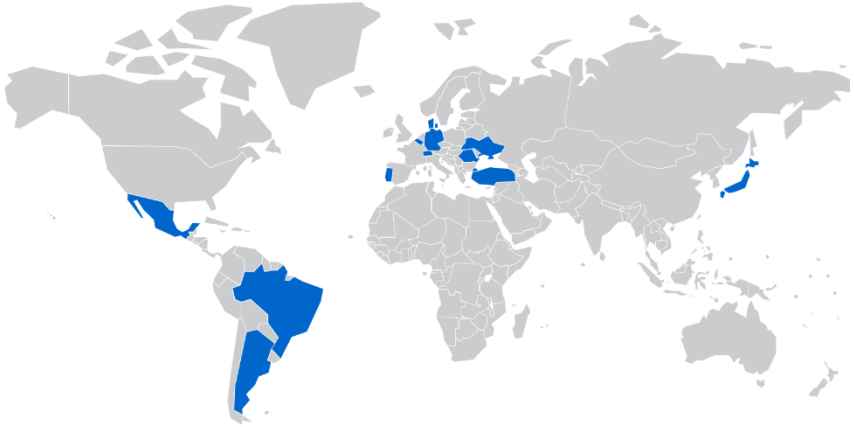
'Blinding' of a study is done so that any effect seen from the medicine is not due to something people expected to happen – if they had known which medicine they were taking.

When and where did the study take place?

The study started in April 2021 and stopped early. This summary presents the results of the study up until it was stopped in December 2021.

The study took place at 50 study centres – across 12 countries in Asia, Europe, and North and South America. The following map shows the countries where this study took place.

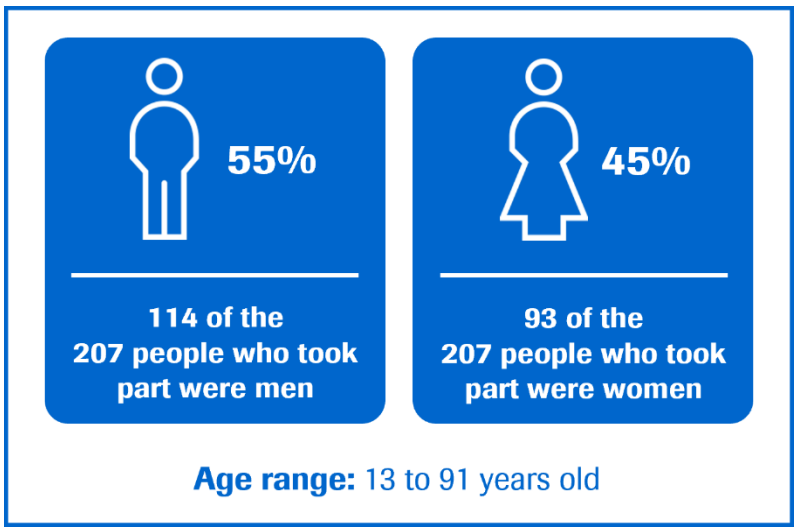
- Argentina
- Belgium
- Brazil
- Denmark
- Germany
- Japan
- Mexico
- Portugal
- Romania
- Switzerland
- Turkey
- Ukraine



2. Who took part in this study?

Fewer people took part in this study than planned because the study stopped early. In this study, 216 people with mild or moderate COVID-19 took part, which was about 16% of the planned number of people.

People who took part in the study were between 13 and 91 years of age. 114 of the 207 people who were given treatment (55%) were male and 93 of the 207 people (45%) were female.



People could take part in the study if they:

- Were at least 12 years old and weighed at least 40 kg
- Had a positive test for COVID-19 no more than three days before screening
- Had at least three mild-to-moderate symptoms of COVID-19 that had started no more than five days before the start of the study

People could not take part in the study if they:

- Had symptoms of severe COVID-19 that led to them being hospitalised before the start of the study
- Had been treated with other medicines for COVID-19 in the three months before the start of the study
- Were pregnant or breastfeeding

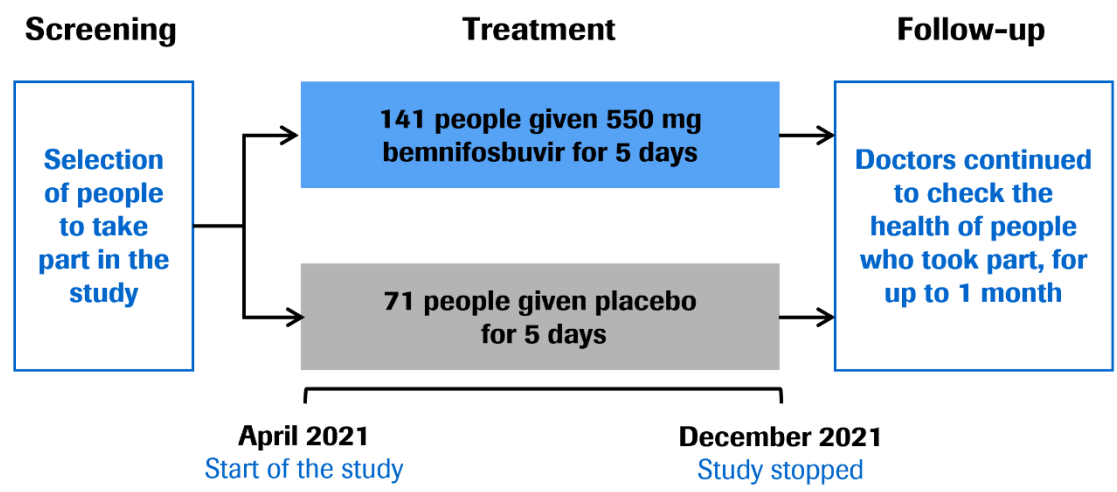
3. What happened during the study?

During the study, people were selected by chance to get one of two treatments. The treatments were selected at random – by a computer.

The treatment groups were:

- **Bemnifosbuvir** (the study medicine) – two tablets taken by mouth twice a day for 5 days.
- **Placebo** – two tablets taken by mouth twice a day for 5 days.

For every two people selected to get bemnifosbuvir, one person was selected to get placebo. After people finished taking their study medicine, they were asked to go back to their study centre for more visits – to check their overall health. Look below to see more information about what happened in the study.

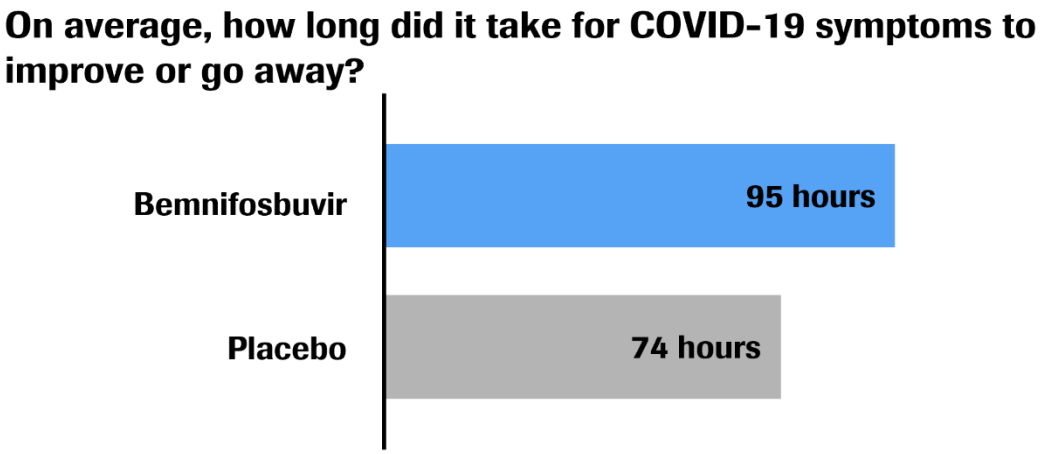


4. What were the results of the study?

Question 1: How well does bemnifosbuvir work to improve symptoms in people with mild or moderate COVID-19 – who were not hospitalised at the start of the study?

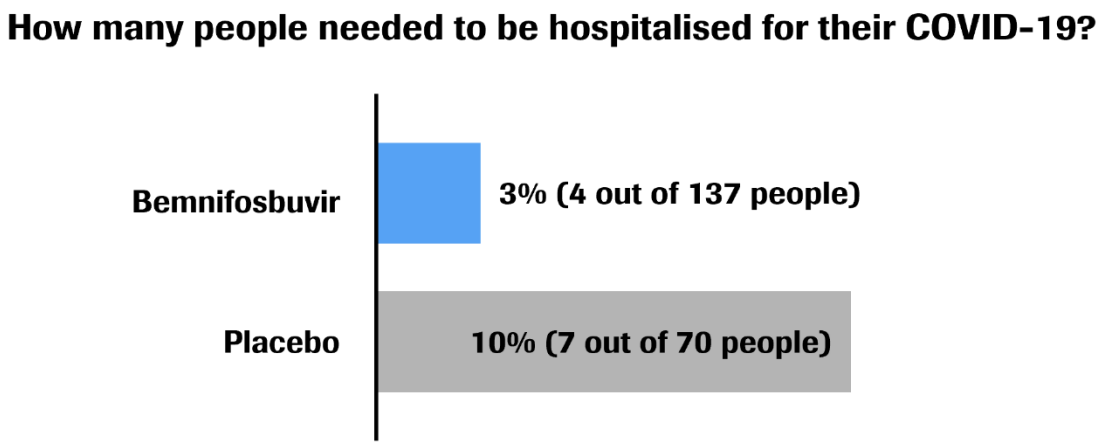
Researchers looked at the time it took for symptoms of COVID-19 to improve (or go away) after people had taken the study medicine – to see if bemnifosbuvir could make symptoms improve faster than a placebo. Symptoms of COVID-19 that were looked at included runny nose, sore throat, cough, shortness of breath, muscle or body aches, feeling tired, headache, chills or sweats, feeling hot or feverish, feeling or being sick to the stomach (feeling nauseated or vomiting), diarrhoea, and reduction or loss of sense of smell or taste.

Bemnifosbuvir did not reduce the time it took for COVID-19 symptoms to improve (or go away) compared with placebo. People who were given bemnifosbuvir had COVID-19 symptoms that lasted around 95 hours (about 4 days). This compares with COVID-19 symptoms that lasted around 74 hours (about 3 days) for people who were given a placebo.



Question 2: How many people needed to be hospitalised for their COVID-19?

Another piece of information that researchers collected was how many people needed to be hospitalised for their COVID-19 after they had taken the study medicine – to see if bemnifosbuvir could reduce this amount better than placebo. About 3% of people needed to be hospitalised for their COVID-19 with bemnifosbuvir compared with 10% who were given a placebo.



This section only shows the key results from the study. You can find information about all other results on the websites listed at the end of this summary (see section 8).

5. What were the side effects?

Side effects (also known as 'adverse reactions') are unwanted medical problems (such as a headache) that happen during the study.

- They are described in this summary because the study doctor believes the side effects were related to the treatments in the study.
- Not all of the people in this study had all of the side effects.

Serious and common side effects are listed in the following sections.

Serious side effects

A side effect is considered 'serious' if it is life-threatening, needs hospital care, or causes lasting problems.

During this study, approximately 6 in every 100 people (6%) had at least one serious side effect. Around 4% of people taking bemnifosbuvir had a serious side effect, compared with around 10% of people taking a placebo. This difference was driven by worsening of COVID-19.

All serious side effects are shown in the following table – these are all of the serious side effects across both treatment groups.

Serious side effects reported in this study	People taking bemnifosbuvir (141 people total)	People taking placebo (71 people total)
Worsening of COVID-19	1% (2 out of 141)	4% (3 out of 71)
COVID-19 pneumonia	Less than 1% (1 out of 141)	6% (4 out of 71)
Bacterial pneumonia	Less than 1% (1 out of 141)	0% (0 out of 71)
Low oxygen in tissues	Less than 1% (1 out of 141)	0% (0 out of 71)
Collapsed lung	Less than 1% (1 out of 141)	0% (0 out of 71)
Respiratory failure	Less than 1% (1 out of 141)	0% (0 out of 71)
Kidney injury that started suddenly or was new to the person	Less than 1% (1 out of 141)	0% (0 out of 71)

There were no deaths reported in this study.

During the study, some people decided to stop taking their medicine because of side effects:

- In the bemnifosbuvir group, 4 out of 141 people (3%) stopped taking their medicine.
- In the placebo group, 5 out of 71 people (7%) stopped taking their medicine.

Most common side effects

During this study, around 11 out of every 100 people (11%) had a side effect that was not considered serious. Around 14.9% of people taking bemnifosbuvir had a side effect that was not considered serious, compared with around 4.2% of people taking a placebo.

The most common side effects are shown in the following table – these are the side effects that happened in at least 2% of people across both treatment groups.

Most common side effects reported in this study	People taking bemnifosbuvir (141 people total)	People taking placebo (71 people total)
Diarrhoea	4% (5 out of 141)	0% (0 out of 71)
Feeling sick (nauseous)	4% (5 out of 141)	1% (1 out of 71)

Other side effects

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see section 8.

6. How has this study helped research?

The information presented here is from a single study of 216 people with mild or moderate COVID-19 who were not hospitalised at the start of the study. These results helped researchers learn more about COVID-19 and bemnifosbuvir.

This study stopped early because study organizers decided to change the study plans and how to evaluate the study medicine. Fewer people were included than was planned, which meant that researchers were not able to make strong conclusions from the trial.

Key findings from this study:

- The main finding was that bemnifosbuvir did not reduce the time it took for COVID-19 symptoms to improve (or go away) compared with placebo.
- About 3% of people needed to be hospitalised for their COVID-19 with bemnifosbuvir compared with 10% who were given a placebo.
- Most serious side effects were worsening of COVID-19 and COVID-19 pneumonia.
- No deaths were reported in this study.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.

7. Are there plans for other studies?

Atea Pharmaceuticals is planning more studies to look at bemnifosbuvir for COVID-19.

8. Where can I find more information?

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

- https://clinicaltrials.gov/ct2/show/NCT04889040
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-005759-18/results
- https://forpatients.roche.com/en/trials/infectious-diseases/covid-19-pneumonia/study-to-evaluate-the-effects-of-ro7496998--at-527--in--47025.html

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/trials/infectious-diseases/covid-19-pneumonia/study-to-evaluate-the-effects-of-ro7496998--at-527--in--47025.html
- Contact a representative at Atea Pharmaceuticals – ateaclinicaltrials@ateapharma.com.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

If you have any questions about future development of bemnifosbuvir for the treatment of COVID-19, please contact Atea Pharmaceuticals at ateaclinicaltrials@ateapharma.com or visit https://clinicaltrials.gov for more information on current and future trials.

Who organised and paid for this study?

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland, and Atea Pharmaceuticals, Inc. who have their headquarters in Boston, USA.

Full title of the study and other identifying information

The full title of this study is: "A Multicenter, Phase III Randomized, Double-Blind, Placebo-Controlled, Outpatient Study to Evaluate the Efficacy, Safety, Antiviral Activity of RO7496998 (AT-527) in Patients with Mild or Moderate COVID-19".

The study is known as 'MORNINGSKY'.

- The protocol number for this study is: CV43043.
- The ClinicalTrials.gov identifier for this study is: NCT04889040.
- The EudraCT number for this study is: 2020-005759-18.