NOVARTIS

The effects and safety of MAS825 in people with COVID-19 pneumonia

Thank you!

Thank you to the participants who took part in the clinical trial for the trial drug **MAS825**. Every participant helped the researchers learn more about MAS825.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public.

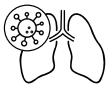
We hope this helps the participants understand their important role in medical research.

Trial information

Trial number: CMAS825F12201
Drug studied: MAS825
Sponsor: Novartis

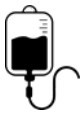
What was the main purpose of this trial?

The main purpose of this trial was to learn if MAS825 could lower the participants' predicted chance of dying from COVID-19 pneumonia in the intensive care unit (ICU).



COVID-19 pneumonia is an infection that causes lung inflammation and fluid in the lungs. It can lead to cough and trouble breathing. COVID-19 pneumonia can be life-threatening.

Inflammation is the immune system's response to infection that brings many cells and proteins to the infected area of the body. Sometimes, the immune system can overreact to an infection and cause inflammation that can damage the body.



MAS825 is a trial drug designed to block certain immune system proteins that cause inflammation. This may prevent the immune system from overreacting to an infection.

The main questions this trial was designed to answer:

- Did MAS825 reduce the predicted chance of dying in the ICU?
- What medical problems did the participants have during this trial?
  Keeping track of the medical problems helped to learn about the safety of MAS825.

Main results: MAS825 did not reduce the predicted chance of dying in the ICU 2 weeks after treatment. The clinical trial team concluded there were no new safety concerns for MAS825.

How long was this trial?

The trial began in June 2020 and ended in April 2021. It was planned for the participants to be in the trial for about 4 months.

Who was in this trial?

140 participants were in this trial – 87 men and 53 women. 138 participants received treatment. 59 participants did not complete this trial. The most common reason that the participants didn't complete this trial is that they died from problems related to COVID-19 pneumonia. The participants were 20 to 92 years old. Their average age was 65.

Every participant in this trial was hospitalized with COVID-19 pneumonia. A person couldn't be in this trial if they had other infections or if a doctor felt they wouldn't survive the next 24 hours, regardless of treatment.

This trial took place in the United States.

Visit novctrd.com for more information about:

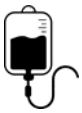
- Who could and could not be in this trial
- The participants in this trial, such as their age, gender, and race
- Reasons why the participants did not complete the trial

Use trial number **CMAS825F12201** to find the scientific summary.

What trial treatments did the participants receive?

Participants were randomly assigned to one of these treatment groups:

- **MAS825** with standard of care
- **Placebo** with standard of care – looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.



Participants received their assigned treatment as 1 intravenous infusion (IV) that lasted 2 hours. An IV gives the treatment into the blood through a thin tube in a vein. Participants received standard of care for at least 14 days.

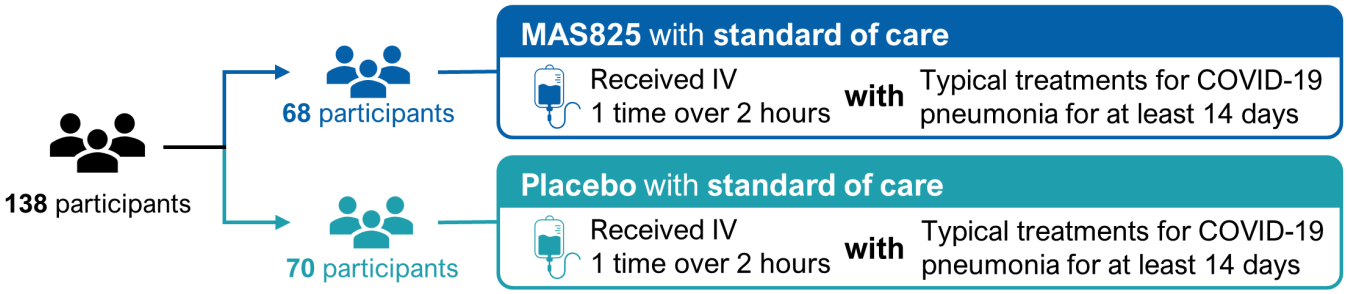
Standard of care included the typical treatments doctors use to treat patients with severe COVID-19 pneumonia, such as:

- Oxygen through a mask
- A ventilator (a machine to help your lungs breathe)
- Medicines that lower inflammation, prevent clotting and treat infection

A computer program was used to randomly assign the treatments. This helped make sure the team compared the results as fairly as possible.

The participants and trial staff did not know what treatment each participant received during the trial. Some trials are done this way because knowing what treatment participants take can influence the results. Not knowing what treatment participants take helps make sure the results are looked at fairly.

The graphic below shows how many participants were in each treatment group.



What were the main results of this trial?

This is a summary of the overall results of this trial. Individual results from each participant may be different and are not included in this summary.

Researchers need many trials to learn if a drug or other treatment is safe and works well. Other trials may provide new information or different results.

Always talk to a doctor before making any changes to your health care.

The **clinical trial team** is a group of experts at Novartis who work together to analyze and determine the results from clinical trial findings.

Did MAS825 reduce the predicted chance of dying in the ICU?

No, MAS825 did not reduce the predicted chance of dying in the ICU 2 weeks after treatment.

To find this out, the clinical trial team compared the APACHE II scores for participants who received MAS825 to those who received the placebo. **APACHE II** (Acute Physiology and Chronic Health Evaluation) is a measure that doctors use to predict a person's chance of dying while in the ICU. APACHE II scores range from 0 to 71. As a participant's score goes down, their predicted chance of dying in the ICU goes down.

The score is based on the participant's:

- Age
- Vital signs, like body temperature, blood pressure, heart rate, and breaths per minute
- Blood oxygen levels
- Blood tests that show signs of disease and organ damage
- Assessment of nervous system health and certain long-term health conditions

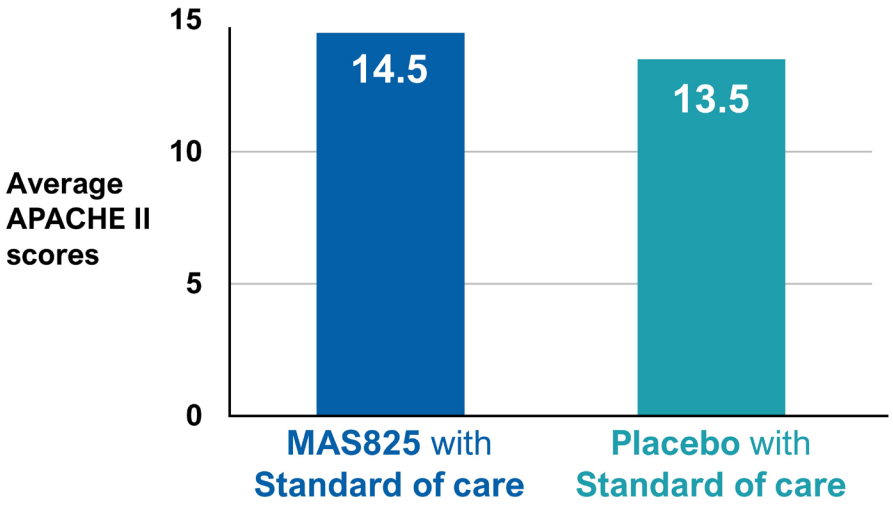
After 2 weeks, the clinical trial team found that the participants who received:

- **MAS825** with **standard of care** had an average score of 14.5
- **Placebo** with **standard of care** had an average score of 13.5

The APACHE II scores for both groups were about the same. The clinical trial team concluded that MAS825 did not reduce the predicated chance of dying in the ICU 2 weeks after treatment.

The participants' APACHE II scores

The participants' average scores 2 weeks after treatment.



What medical problems did the participants have during this trial?

Medical problems that happen during trials are called "adverse events". Trial doctors looked for any adverse events during the trial. The participants also reported adverse events.

Many trials are needed to know if a drug or treatment causes an adverse event. Trial doctors keep track of all adverse events that happen in trials, even if they think the adverse events are not related to the trial treatments.

An adverse event is:

- Any **unwanted sign or symptom** the participants have during a trial
- Considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death

Adverse events **may** or **may not be caused** by treatments in the trial.

The adverse events in this section include those that happened during treatment and up to about 4 months after completing treatment.

More than half of the participants (95 of 138 participants) reported adverse events. 59 participants reported adverse events that were considered serious. 49 of those 59 participants died, mostly from problems related to COVID-19 pneumonia. The adverse events seen in this trial were expected in people with severe COVID-19 pneumonia.

The clinical trial team concluded there were no new safety concerns for MAS825.

What serious adverse events did the participants have?

59 of 138 participants (43%) reported a total of 114 serious adverse events. The table below shows the serious adverse events that happened to **4 or more participants (3%).** Other serious adverse events happened in fewer participants.

	MAS825 with **standard of care** **68** participants	**Placebo** with **standard of care** **70** participants
Lungs suddenly can't get enough oxygen into the blood Acute respiratory failure	16% 11 of 68	11% 8 of 70
Lungs can't get enough oxygen into the blood Respiratory failure	7% 5 of 68	7% 5 of 70
Damage to the kidneys Acute kidney injury	4% 3 of 68	6% 4 of 70
COVID-19 pneumonia that got worse COVID-19 pneumonia	3% 2 of 68	6% 4 of 70
Fluid builds up in the lungs Acute respiratory distress syndrome	9% 6 of 68	0% 0 of 70
Low levels of oxygen Hypoxia	7% 5 of 68	1% 1 of 70
Heart suddenly stops beating Cardiac arrest	3% 2 of 68	4% 3 of 70
Death	31% 21 of 68	27% 19 of 70

Most of the deaths were from problems related to COVID-19 pneumonia. The team concluded that the number of deaths in this trial was similar to what was expected in people with severe COVID-19 pneumonia.

What other adverse events did the participants have?

39 of 138 participants (28%) had adverse events that were not considered serious. The table below shows the adverse events that happened to **7 or more participants (5%)**. Additional adverse events happened in fewer participants.

	MAS825 with **standard of care** **68** participants	Placebo with **standard of care** **70** participants
Damage to the kidneys Acute kidney injury	13% 9 of 68	7% 5 of 70
Fear or worry Anxiety	4% 3 of 68	9% 6 of 70
Low blood pressure Hypotension	7% 5 of 68	4% 3 of 70
Lung infection caused by bacteria Pneumonia bacterial	9% 6 of 68	3% 2 of 70
Irregular heartbeat Atrial fibrillation	6% 4 of 68	6% 4 of 70
Infection in the urinary tract, such as the bladder Urinary tract infection (UTI)	3% 2 of 68	7% 5 of 70
Sign of damage in the liver Transaminases increased	0% 0 of 68	7% 5 of 70

Visit novctrd.com for more information about the adverse events that happened during this trial.

What other results were learned?

The clinical trial doctors looked at blood tests that measure signs of inflammation. These signs went down for both groups after treatment.

They also looked at many measures of COVID-19 pneumonia symptoms. By the end of the study, the clinical team found that both groups were similar in:

- The number of participants who were able to survive without needing a ventilator
- Severity of COVID-19 pneumonia based on the trial doctor's review of their health status

About half of the participants in both groups left the hospital after 2 weeks.

What was learned from this trial?

This was the first trial to learn about MAS825 in participants with COVID-19 pneumonia who also received standard of care. The clinical trial team concluded that MAS825 given one time with standard of care did not meaningfully lower the participants' APACHE II scores.

The team found no new safety concerns for MAS825. They also concluded that the number of deaths during the trial was similar to what was expected in people with severe COVID-19 pneumonia.

The clinical trial team also found that MAS825 had an effect on some signs of inflammation. However, more trials are needed to study the effect of MAS825 with other conditions that involve inflammation. MAS825 did not change other measures of COVID-19 pneumonia, such as the number of participants who survived without using a ventilator.

These are the results of a single trial. Other trials may have different results. This was one of many trials a drug goes through. This type of trial helped researchers to learn about the safety of a trial drug in a small number of participants.

Where can I learn more about this and future trials?

For more information about this trial go to any of these websites:

- **novctrd.com** – search using the study number **CMAS825F12201**
- **clinicaltrials.gov** – search using the number **NCT04382651**

If more trials are planned, they can be found on the public websites above. When there, search for **MAS825.**

? If you participated in the trial and have **questions** about the results, please speak with the trial doctors or staff at your trial site.

Full trial title:
A Phase 2, randomized, placebo-controlled, patient and investigator-blinded, multi-center study to assess efficacy and safety of MAS825 for the treatment of SARS-CoV-2 infected patients with COVID-19 pneumonia and impaired respiratory function.

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