Summary of clinical study results

Title of the study:

Industry Alliance Platform Trial to Assess the Efficacy and Safety of Multiple Candidate Agents for the Treatment of COVID-19 in Hospitalized Patients

Short title of the study:

COVID-19 Multiple Agents and Modulators Unified Industry Members Trial (COMMUNITY)

What was the study about?

To learn whether 3 investigational medications worked and how safe they were. The investigational medications were studied in participants hospitalized with a SARS-CoV-2 infection. SARS-CoV-2 is the virus that causes COVID-19.

Who sponsored the study?

Amgen Inc. supported by its industry partners Takeda Development Center Americas, Inc and UCB Biopharma SRL

What was tested?

There were 3 investigational medications tested: apremilast (marketed in some countries as Otezla®), lanadelumab-IV, and zilucoplan (RA101495).

Thank you to all participants

We would like to thank everyone who took part in this study. Every participant in this study helped the researchers learn more about the treatment of COVID-19.

The sponsor is committed to making research results available to the public. This summary has been provided as part of that commitment and should not be used for any other purpose. It should not be considered to make a claim for any product or to guide treatment decisions.

Some information in this summary involving apremilast may be different from the prescribing information that doctors consider when they give patients this medicine that is approved for unrelated conditions.

About this summary

This summary was completed in April 2022.

Where can I learn more about the study?

You can find more information on the websites listed at the end of this summary.

At a glance

Why was the research needed?

Researchers were looking for a better way to treat people hospitalized with COVID-19. Researchers look at the results of many studies to understand if a medicine might work for a specific condition. It takes a lot of people in many studies all around the world to advance medical science.

Who took part in the study?

Adults aged 18 years or over who were hospitalized with COVID-19 were eligible to take part. A total of 515 people took part across 8 countries.

What study medicine did participants receive?

There were 3 investigational medications studied: apremilast, lanadelumab-IV, and zilucoplan. Participants were assigned to 1 of the 3 investigational medications or a placebo.

A placebo looks like an investigational medication, but has no actual medicine in it. Placebo is used to better see the effects of the investigational medications being tested.

Any of the 3 investigational medications or the placebo may be referred to as the "study medicine".

All participants also received the standard treatment (standard of care) for COVID-19 that was available locally.

What were the main results of the study?

The main question the researchers wanted to answer was:

- Did any of the 3 investigational medications affect the time it took for people in the hospital to recover from COVID-19?

Researchers also wanted to see if, after about a month from starting in the study, any of the 3 investigational medications affected the number of people who:

- improved or were able to leave the hospital
- had improved, been released from the hospital, and who no longer needed extra oxygen
- died.

Overall, researchers found that none of the investigational medications helped people any more than the placebo.

What was learned about safety?

Some participants had unwanted health problems that may have been related to the study medicines. These were called adverse reactions.

Researchers think most of the unwanted health problems reported by people were not related to the investigational medications.

This is because the unwanted health problems seen in people who took 1 of the investigational medicines were similar to those seen in people who took the placebo. They were also similar to those seen in people with COVID-19 who were not in the study.

More details about the results of the study are included on the following pages.

Why was the research needed?

Many people with COVID-19 have mild symptoms such as cough, sore throat, and fever, and get better quickly. In some people, however, symptoms are more severe, and they need to be cared for in a hospital. Some people may even die.

Because there were only a few medications accepted to treat people with COVID-19 at the time that the study took place, it was important to find more options.

Who took part in the study?

Study participants

People could take part in this study if they:

- were 18 years of age or older
- had tested positive for the SARS-CoV-2 virus
- needed to be cared for in a hospital.

A total of 515 people took part in the study. Across all 4 study medicine groups, about 1 in 3 participants (32%–38%) were women, and about 2 in 3 participants (62%–68%) were men. Participants ranged in age from 19 to 90 years.

Other information about the people in the study:

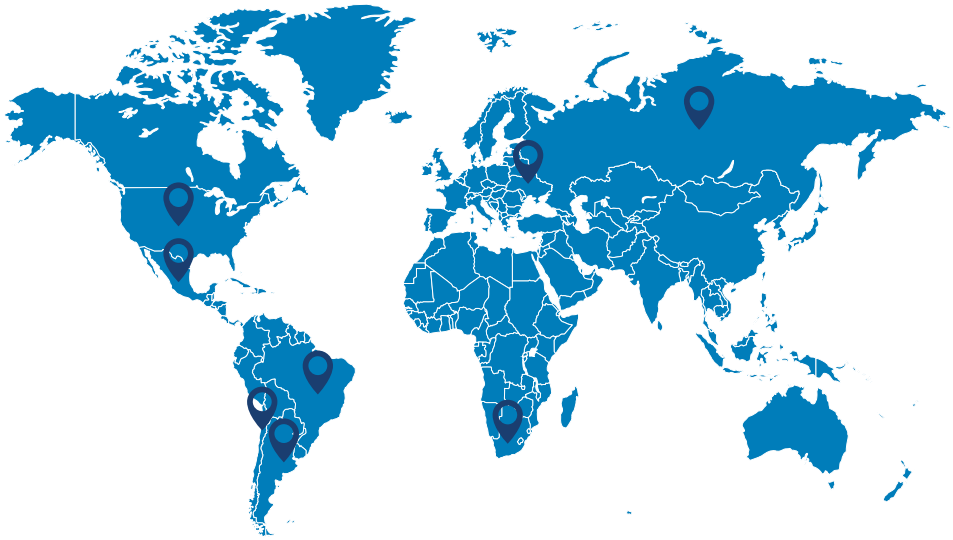
Study centers were in:

- Argentina
- Brazil
- Chile
- Mexico
- Russian Federation
- South Africa
- Ukraine
- United States

About 3 out of 4 participants (about 75%) were white.

Other reported ethnicities included:

- Black
- Asian
- American Indian or Alaska Native
- Native Hawaiian or Pacific Islander
- More than one ethnicity



What was the purpose of the study?

In this study, researchers wanted to know:

- Whether the investigational medications may be used as a potential treatment option when given with the "standard of care". Standard of care is the care that patients would normally receive if they were not in this study
- Whether the investigational medications worked and how safe they were
- The effects of each investigational medication on COVID-19.

The researchers compared each investigational medication (apremilast, lanadelumab-IV, and zilucoplan) with a placebo.

Researchers used a placebo to learn if the study results were due to 1 of the investigational medications, or if the results could be due to some other reason.

All participants also received the usual treatments and care for COVID-19, according to local clinical practice (standard of care).

The main questions the researchers wanted to answer for each of the 3 investigational medications when compared with a placebo were:

- Was the time it took for people in the hospital to recover from COVID-19 affected?
- Was the number of people who showed improvement or who were well enough to leave the hospital affected?
- Was the number of people who had improved, who had been released from the hospital, and who no longer needed extra oxygen affected?
- Was the number of people who died affected?
- What adverse reactions (unwanted health problems) happened during the study?

About the study design

- This study was a double-blinded study.
  - This means that none of the participants, the study doctor, or the study staff knew which study medicine (either the investigational medications or the placebo) each participant received.
- Some studies are "blinded" because knowing what study medicine the participants are receiving can affect the results of the study.
- However, when Amgen and its industry partners looked at the results at the end of the study, they needed to find out which study medicine each participant received to analyze the study results.
- The researchers used a computer program to help randomly choose the study medicine each participant received according to study eligibility criteria. This method is intended to make sure the comparison between the groups is fair and is as accurate as possible.

What study medicine did participants receive?

The participants in the study received either the placebo or 1 of the following investigational medicines:

- Apremilast
- Lanadelumab-IV
- Zilucoplan.

All of the participants also received the locally available standard of care treatment for COVID-19 during the study.

Investigators chose these investigational medications because all of them have been shown in other studies to reduce inflammation. Two of the medicines work to reduce a type of protein, and 1 reduces production of a type of enzyme. Both these proteins and the enzyme play a role in inflammation. It was thought these medicines may help people with COVID-19, because they often will have inflammation in their lungs.

Note: The numbers shown in each results section of this summary may not add up to the total number of people who participated in the study. This is because not everyone who was assigned to take one of the investigational medicines or placebos was able to be included in all of the analyses. For example, some people who were assigned to take a certain medication did not start taking it. Researchers also combined some people from different placebo groups together for analysis.

This table shows the investigational medication that participants were assigned to take:

Investigational medication	Apremilast	Lanadelumab-IV	Zilucoplan
How many participants were assigned to take the investigational medication?	194	28	100
What dose did they take?	30 milligrams	300 milligrams	32.4 milligrams
How was it taken?	By mouth	By intravenous infusion (IV), which is a drip into a vein	By subcutaneous injection, which is a shot or jab under the skin
How often was it taken?	Twice a day for 14 days	Once on the first day and once on the fourth day of the study	Once a day for 14 days
What was it compared with?	190 participants from the pooled placebo group	34 participants from the pooled placebo group	75 participants from the pooled placebo group

What happened during the study?

The study started in November 2020 and ended in August 2021.

Before each participant received study medicine, the study doctor and study staff checked to ensure the study was suitable for them.

Participants were checked daily while they were in the hospital. For participants who went home, they had up to 3 visits by video call. These visits happened about 2 weeks, 4 weeks, and 2 months after they got the first dose of study medicine.

The researchers had planned for the study to last longer and enroll more participants, but:

- Lanadelumab-IV was difficult to administer to some participants, which made it hard to keep people from knowing whether they received the investigational medicine or the placebo.
- Apremilast was not helping the participants as much as expected.
- It was difficult to enroll enough people who were hospitalized with COVID-19 into the zilucoplan group in a timely manner. The sponsor and their industry partners also had some difficulty finding people to enroll in the other medication groups.

Because of the issues noted above, researchers decided to end the study early for all of the investigational medications.

Amgen and its industry partners reviewed the study data collected during the study and created a full report of the results for each investigational medication. This document is a summary of those reports.

What were the main results of the study?

This section is about the main results from each investigational medication in this study. The websites listed at the end of this summary may have additional information about the results of the study.

This summary only shows the results from this one study. Other studies may have different results. Because this study ended early, the number of participants in each study medicine group was smaller than originally expected.

Therefore, the only conclusion that could be drawn was that apremilast did not help people with COVID-19 as much as expected.

No formal conclusions should be drawn from the other results of the study.

Time to recovery from COVID-19

The number of people who had recovered after about 4 weeks was similar for each of the 3 investigational medications and their placebo groups.

"Recovery" was defined as people who were well enough to leave the hospital by 29 days after the start of treatment, and who did not need to be admitted again.

Study medicine	Apremilast	Placebo
Participants who had recovered	133 out of 194 (69%)	136 out of 190 (72%)

Study medicine	Lanadelumab-IV	Placebo
Participants who had recovered	15 out of 25 (60%)	19 out of 30 (63%)

Study medicine	Zilucoplan	Placebo
Participants who had recovered	61 out of 100 (61%)	51 out of 75 (68%)

The question above was the main question researchers wanted to answer.

The results in the remainder of this section are for other questions the researchers wanted to answer.

Number of people who showed improvement or who were well enough to leave the hospital

The number of people who showed improvement or who were well enough to leave the hospital after about 4 weeks was similar for each of the 3 investigational medications compared with their placebo group.

Study medicine	Apremilast	Placebo
Participants who showed improvement	141 out of 194 (73%)	142 out of 190 (75%)
Participants well enough to leave hospital	144 out of 194 (74%)	146 out of 190 (77%)

Study medicine	Lanadelumab-IV	Placebo
Participants who showed improvement	16 out of 25 (64%)	18 out of 30 (60%)
Participants well enough to leave hospital	18 out of 25 (72%)	19 out of 30 (63%)

Study medicine	Zilucoplan	Placebo
Participants who showed improvement	66 out of 100 (66%)	51 out of 75 (68%)
Participants well enough to leave hospital	64 out of 100 (64%)	51 out of 75 (68%)

Number of people who no longer needed extra oxygen

The number of people who had improved, had been released from the hospital and who no longer needed extra oxygen after about 4 weeks was similar for each of the 3 investigational medications when compared with their placebo group.

Study medicine	Apremilast	Placebo
Participants who did not need extra oxygen	116 out of 194 (60%)	121 out of 190 (64%)

Study medicine	Lanadelumab-IV	Placebo
Participants who did not need extra oxygen	13 out of 25 (52%)	17 out of 30 (57%)

Study medicine	Zilucoplan	Placebo
Participants who did not need extra oxygen	54 out of 100 (54%)	45 out of 75 (60%)

The number of people who died

The number of people who had died by 4 weeks after starting a study medicine was similar for the apremilast and lanadelumab-IV groups compared with their placebo groups.

Study medicine	Apremilast	Placebo
Participants who died	34 out of 194 (17%)	33 out of 190 (17%)

Study medicine	Lanadelumab-IV	Placebo
Participants who died	8 out of 25 (32%)	9 out of 30 (30%)

Study medicine	Zilucoplan	Placebo
Participants who died	18 out of 100 (18%)	18 out of 75 (24%)

What adverse reactions happened during the study?

In this study, the study doctors reported all of the unwanted health problems participants had. Study doctors believed some of these unwanted health problems could be related to a study medicine. Unwanted health problems that might be related to a study medicine are called adverse reactions. This section is a summary of the adverse reactions the participants had during the study that were thought to be related to the study medicine.

An adverse reaction can be serious or non-serious. An adverse reaction is considered serious when it is either:

- life threatening
- causes the participant to go to the hospital or stay longer in the hospital
- causes a disability
- causes a death, or
- causes a baby to be born with unwanted effects.

No single clinical study can give a complete picture of the benefits and risks of a medicine. Results from several studies are needed to determine the benefits and risks or if a medicine definitely causes an adverse reaction.

The websites listed at the end of this summary may have additional information about the adverse reactions that happened during the study.

Did any adverse reactions happen?

When reporting adverse reactions in this study, the study doctor did not know which study medicine a participant was receiving.

The adverse reactions seen in the study were similar among people who took 1 of the 3 investigational medications or the placebo, and other people hospitalized with COVID-19.

Were there any serious adverse reactions?

Only one serious reaction was judged by the study doctors to be related to a study medicine. One person who took zilucoplan developed a lung infection caused by aspergillus, a type of fungus.

What other adverse reactions happened?

The tables show how many participants had adverse reactions that could have been caused by the study medicine. Some participants in the study experienced more than 1 adverse reaction.

Study medicine	Apremilast	Placebo
Participants with an adverse reaction considered by the study doctor to be related to the study medicine	20 out of 189 (11%)	15 out of 187 (8%)
Adverse reaction experienced by more than 1 person	• Nausea (8 participants) • Diarrhea (3 participants) • Vomiting (2 participants) • Increases in enzymes called transaminases (2 participants) • Headache (2 participants)	• Increases in an enzyme produced by the liver called alanine aminotransferase (5 participants) • Increases in enzymes called transaminases (4 participants) • Nausea (3 participants)

Study medicine	Lanadelumab-IV	Placebo
Participants with an adverse reaction considered by the study doctor to be related to the study medicine	1 out of 27 (4%)	1 out of 34 (3%)
Adverse reaction experienced	• Nausea (1 participant)	• Diarrhea and dizziness (1 participant)

Study medicine	Zilucoplan	Placebo
Participants with an adverse reaction considered by the study doctor to be related to the study medicine	2 out of 95 (2%)	5 out of 73 (7%)
Adverse reaction experienced	• Bronchopulmonary aspergillosis (a lung infection caused by a fungus) (1 participant) • Increases in an enzyme produced by the liver called alanine aminotransferase (1 participant)	• Nausea (3 participants) • Diarrhea (5 participants) • Increased blood pressure (1 participant) • Raised levels of triglycerides (a type of fat) in the blood (3 participants) • Dizziness (1 participant)

How has this study helped patients and researchers?

This summary shows only the main results from this study. Other studies may provide new information or different results. Because this study ended early, the number of participants in each study medicine group was smaller than originally expected. Therefore, the only conclusion that could be drawn was that apremilast did not help people with COVID-19 as much as expected. No formal conclusions should be drawn from the other results of the study.

The findings from this study may be used to make decisions about further research that may be needed to learn more about COVID-19 and possible treatments.

Where can I find more information about this study?

To learn more, you can find more detailed information on these websites:

- https://clinicaltrials.gov/ct2/show/NCT04590586?term=NCT04590586&draw=2&rank=1
- https://www.amgentrials.com
- https://clinicaltrials.takeda.com/.

Full study title: Industry Alliance Platform Trial to Assess the Efficacy and Safety of Multiple Candidate Agents for the Treatment of COVID-19 in Hospitalized Patients

National Clinical Trial (NCT) identification number: NCT04590586

EudraCT number: 2020-002594-10

If there are more clinical studies with the investigational medications, you can find them on the websites listed above by searching for: SARS-CoV-2, COVID-19, apremilast, lanadelumab-IV, zilucoplan, Otezla®, or RA101495.

If you have any questions, please use the following contact details:

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Queries specific to zilucoplan should be directed to www.ucb.com/UCBCares for country-specific contact information.

Thank you to everyone who took part in this study. Participants in clinical studies belong to a large community of people who take part in clinical research all around the world. They help researchers answer important health questions and find new medical treatments for patients.