Summary of Clinical Trial Results

A study to find out if a new medicine (either astegolimab or efmarodocokin alfa) was safe and effective in patients with severe COVID-19 pneumonia

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).

This summary is written for:

- Members of the public
- People who took part in the study

This summary is based on information known at the time of writing.

The study started in June 2020 and finished in February 2021. 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 answer important questions about astegolimab and efmarodocokin alfa in the treatment of patients with severe COVID-19 pneumonia.

Key information about this study

- This study was done to find out if there was a difference in the time it took for patients to recover from COVID-19 pneumonia when treated with a new medicine in addition to their usual treatment – in comparison to the usual treatment alone.
- In this study, patients were divided into 3 treatment groups: Placebo (sugar pill – no medicine), astegolimab, or efmarodocokin alfa.
- The placebo and study medicines were given on top of the regular treatment for COVID-19 pneumonia.
- This study included 396 patients in 4 countries.
- The main finding was that there was no difference in the time it took for patients to recover (no longer need oxygen or go home from the hospital), whether they got astegolimab, efmarodocokin alfa, or the placebo – in addition to the standard treatment (SOC) for COVID-19.
- Two out of 130 patients who got astegolimab, and 3 out 132 patients who got efmarodocokin alfa, had serious side effects thought to be caused by the study medicine.
- None of the 134 patients who got placebo had any serious side effects thought to be caused by the study treatment.

1. General information about this study

Why was this study done?

In the past 20 years, there have been 3 coronavirus outbreaks caused by a different type of coronavirus each time. All 3 outbreaks caused breathing difficulties in many patients and death in some. The most recent outbreak has been the most severe, widespread, and deadly. It has been called a global pandemic and is currently ongoing.

In the current outbreak, most patients do not have any symptoms or they have mild symptoms – such as fever, cough, and shortness of breath. However, as many as 20% of patients can progress to severe disease that requires hospitalization, and half of these patients require intensive care treatment.

In critically-ill patients, the most common illness is "interstitial pneumonia". This causes air sacs in the lungs to become inflamed. Over time, the disease develops into what is called "acute respiratory distress syndrome" or **ARDS,** a life-threatening lung injury that allows fluid to leak into the lungs and makes breathing difficult. Patients with interstitial pneumonia and ARDS require supplemental oxygen to maintain healthy oxygen levels in the blood and often require prolonged hospitalization.

Many patients with severe COVID-19 develop ARDS. ARDS can progress to "hypoxemic respiratory failure", which means blood oxygen levels drop to a very low level. Complications from ARDS include injury to the kidneys, liver, and heart muscle, multiple organ failure, and even death.

Patients with COVID-19 pneumonia and ARDS have "hyper-inflammatory responses". This is a condition that increases some proteins in the blood, including "**cytokines**", which are signaling proteins. These hyper-inflammatory responses and the virus itself cause damage to the lining of the lungs, making it hard for patients to breath.

A cytokine called "IL-33" causes inflammation in the body. Another cytokine called "IL-22" helps lung cells to repair. Researchers wanted to test if blocking the IL-33 cytokine with a medicine (**astegolimab**) could help patients. They also wanted to know if increasing levels of IL-22 with another medicine (**efmarodocokin alfa**) could help patients. Helping patients with severe COVID-19 means improving their health so they no longer need oxygen and can leave the hospital sooner.

What were the study medicines?

This study looked at 2 medicines – astegolimab and efmarodocokin alfa.

Astegolimab, also known as **MSTT1041A**, is a medicine that has been given to people in other studies and found to be safe for humans. Here is how the medicine works:

- **IL-33** is a protein (a cytokine) that is released by the body during the hyper-inflammatory response in patients with severe COVID-16 pneumonia.
- IL-33 binds to **ST2 receptors** present in the body. Receptors are structures on cells where another protein can dock – just like a lock on a house where a key can go in.
- Astegolimab is a type of medicine known as an "**antibody**" that also binds to ST2 receptors, acting like (mimicking the activity of) IL-33.
- Astegolimab prevents IL-33 from binding to the same receptor. Interfering with the biology of IL-33 in this manner may decrease inflammation and result in improvements in COVID-19 pneumonia and ARDS.

Astegolimab was compared to a "**placebo**".

- In this study, some patients got astegolimab while others got a placebo.
- The placebo looked the same as astegolimab but did not contain any real medicine. Having the placebo allowed researchers to find out if the effect of the treatment was really due to the medicine.

Efmarodocokin alfa, also known as "**UTTR1147A**" was also investigated in this study. This medicine has been given to people in other studies and found to be safe for humans. Here is how the medicine works:

- Efmarodocokin alfa is a medicine made by connecting (fusing) two different proteins – one of which is **IL-22** – and the other is the tail region of an antibody that helps to deliver IL-22 to patients.
- There are receptors for IL-22 present on different cells in the body. Receptors are structures on cells where another protein can dock – just like a lock on a house where a key can go in.
- IL-22 can interact with **IL-22 receptors** on many cells in the body, to repair and heal them – including lung cells.
- It is possible that efmarodocokin alfa will be able to cause lung cells to repair and heal. Therefore, efmarodocokin alfa may be beneficial for patients with COVID-19 pneumonia and ARDS.

Efmarodocokin alfa was compared to a "**placebo**".

- In this study, some people got efmarodocokin alfa while others got a placebo.
- The placebo looked the same as efmarodocokin alfa but did not contain any real medicine. Having the placebo allowed researchers to find out if the effect of the treatment was really due to the medicine.

What did researchers want to find out?

- Researchers did this study to compare response in patients with severe COVID-19 pneumonia treated with astegolimab versus efmarodocokin alfa versus placebo.

The main questions that researchers wanted to answer were:

1. Was astegolimab effective for treating patients with severe COVID-19 pneumonia in comparison to placebo treatments?
2. Was efmarodocokin alfa effective for treating patients with severe COVID-19 pneumonia in comparison to placebo treatments?

Other questions that researchers wanted to answer included:

1. How safe was astegolimab for treating patients with severe COVID-19 pneumonia in comparison to placebo treatments?
2. How safe was efmarodocokin alfa for treating patients with severe COVID-19 pneumonia in comparison to placebo treatments?

What kind of study was this?

There are several ways to describe this study.

- **Phase 2 study**
  Phase 2 studies are carried out to find out if the study medicines are effective for patients. It also means that astegolimab and efmarodocokin alfa had been tested and found to be safe for use in people – in phase 1 studies.
- **Randomized study**
  A computer randomly decided which patient joined which medicine group and which patient joined the placebo group. Researchers and patients had no control over this.
- **Double-blind study**
  The researchers and patients did not know which patient was getting the study medicine and which patient was getting the placebo. That made this a double-blind study.
- **Placebo-controlled study**
  Some patients got the real medicine while others got a placebo. This was done so that all patients got a treatment, and the real effect of the medicine could be compared against the placebo.

When and where did the study take place?

The study started in June 2020 and finished in February 2021. This summary was written after the study had ended.

The study took place at 54 study centers – across 4 countries:

- United States (32 centers)
- Spain (10 center)
- Brazil (7 centers)
- Mexico (5 centers)

2. Who took part in this study?

There were 396 patients with severe COVID-19 pneumonia who took part in this study. They were between the ages of 26 and 94 years. The study included 243 (61%) male and 153 female (37%) patients. Here is a breakdown of patients in the 3 treatment groups:

	Placebo	Astegolimab	Efmarodocokin alfa
Number of patients in this treatment group	134	130	132
Half of the patients in this group were below this age (median age)	57 years	57.5 years	57 years
The youngest patient and oldest patient in this group (age range)	26 years and 89 years	29 years and 94 years	27 years and 86 years
Men and Women	89 men (66%) 45 women (34%)	74 men (57%) 56 women (43%)	80 men (61%) 52 women (39%)

People could take part in the study if:

- They were 18 years or older.
- They were in the hospital with COVID-19 pneumonia.
- Their oxygen levels were low and they required oxygen to have normal oxygen levels.

People could not take part in the study if:

- It looked like the patient was going to die within 24 hours.
- The patient had received other medicines not permitted on this study.
- The patient had medical conditions other than COVID-19 pneumonia that were not allowed on this study. It would not have been safe to give experimental medicines to these patients because to those medical conditions.

3. What happened during the study?

During the study, patients were selected by chance to get one of 3 treatments.

The treatment groups were:

- Placebo
- Astegolimab 700 mg
- Efmarodocokin alfa 90 µg/kg

Whether or not patients required a ventilator to breathe was taken into consideration during randomization. This means that the 3 treatment groups each had a similar number of patients on mechanical ventilators at randomization.

Apart from receiving the placebo and medicines in this study, patients continued to receive all the regular treatments recommended by their doctors for COVID-19 pneumonia.

Patients received the study treatment via intravenous (IV) infusion on Day 1. If they were still in the hospital and needed oxygen on Day 15, then a second dose of the study treatment was given on Day 15.

Patients were followed for up to Day 60.

4. What were the results of the study?

	Placebo	Astegolimab	Efmarodocokin alfa
Number of patients who received one dose	103 (77%)	103 (79%)	107 (81%)
Number of patients who received two doses	31 (23%)	31 (21%)	25 (19%)

Most patients received one dose of the placebo or study medicine. Researchers looked at the number of days it took to recover, have an improvement, come off oxygen, and come off the ventilator. They also compared death rates for each treatment group.

Question 1: Was astegolimab effective for treating patients with severe COVID-19 pneumonia in comparison to placebo treatments?

The study medicine would be effective if it helped patients get better so they no longer needed oxygen and they could go home sooner.

The amount of time it took for patients to get to the point when they did not need oxygen and could go home from the hospital – was similar whether patients got astegolimab or placebo. Therefore, astegolimab did not provide a benefit on top of regular care for COVID-19 when used in the manner indicated in this study – for the type of disease and patients in this study.

Question 2: Was efmarodocokin alfa effective for treating patients with severe COVID-19 pneumonia in comparison to placebo treatments?

The amount of time it took for patients to get to the point when they did not need oxygen and could go home from the hospital – was similar whether patients got efmarodocokin alfa or placebo. Therefore, efmarodocokin alfa was not effective when used in the manner indicated in this study – for the type of disease and patients in this study.

Question 3: How safe was astegolimab for treating patients with severe COVID-19 pneumonia in comparison to placebo treatments

Astegolimab was just as safe as the placebo treatment. Patients in both treatment groups had similar numbers and types of side effects and death rates.

Question 4: How safe was efmarodocokin alfa for treating patients with severe COVID-19 pneumonia in comparison to placebo treatments?

Efmarodocokin alfa was just as safe as the placebo treatment. Patients in both treatment groups had similar numbers and types of side effects and death rates.

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

5. What were the side effects?

- Side effects are medical problems (such as feeling dizzy) that happened 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.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflet(s).
- 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.

There were a few patients with serious side effects thought to be caused by the study medicine. There were several deaths on the study, mostly due to COVID-19 pneumonia.

	Placebo	Astegolimab	Efmarodocokin alfa
Number of patients with a serious side effect thought to be caused by the study medicine	0	2 (1.5%)	3 (2.3%)
Number of deaths on study	23 (17%)	23 (18%)	21 (16%)

During the study, 1 (0.8%) patient in the efmarodocokin alfa treatment group stopped treatment because of a side effect thought to be related to the study medicine.

None of the patients in the astegolimab and placebo groups stopped treatment because of a side effect thought to be related to the study medicine.

Most common side effects

The most common side effects thought to be caused by the study treatment – seen in more than 2 patients in the study – are reported here.

	Placebo	Astegolimab	Efmarodocokin alfa
Total number of patients with at least 1 side effect thought to be caused by the study treatment	15 (11%)	12 (9%)	25 (19%)
Most common side effects:			
Dry skin	5 (3.7%)	3 (2.3%)	7 (5.3%)
Rash	2 (1.5%)	2 (1.5%)	5 (3.8%)
Skin peeling (exfoliation)	2 (1.5%)	0	3 (2.3)
Headache	1 (0.7%)	3 (2.3%)	0
Liver protein (alanine amino-transferase increased)	1 (0.7%)	0	3 (2.3%)
Liver protein (Aspartate amino-transferase increased)	0	0	3 (2.3%)

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 and patients?

The information presented here is from a single study of 396 people with severe COVID-19 pneumonia. These results helped researchers learn more about astegolimab and efmarodocokin alfa. These medicines were not effective when used in the manner indicated in this study – for the type of disease and patients 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.

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- **Always speak to your doctor before making any decisions about your treatment.**

7. Are there plans for other studies?

Studies with astegolimab and efmarodocokin alfa are on-going for other diseases and other patients, and further studies are planned.

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/results/NCT04386616

https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-002713-17/results

https://forpatients.roche.com/en/trials/infectious-diseases/covid-19-pneumonia/a-study-to-evaluate-the-safety-and-efficacy-of-mstt1041-69681.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/About.html
- Contact a representative at your local Roche office.

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.

Who organized and paid for this study?

This study has been funded in whole or in part with Federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority, under OT number: HHSO100201800036C.

This study was also paid for by Genentech, Inc., South San Francisco, CA, USA. Genentech is part of F. Hoffmann-La Roche Ltd., with headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is:

A Phase II, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Safety and Efficacy of MSTT1041A or UTTR1147A in Patients with Severe COVID-19 Pneumonia.

- The protocol number for this study is GA42469.
- The ClinicalTrials.gov identifier for this study is NCT04386616.
- The EudraCT number for this study is 2020-002713-17.