# Summary of Clinical Trial Results

## A study to look at whether a medicine called tocilizumab was safe and worked to treat COVID-19 pneumonia when given to people before they needed ventilator support

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:

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

This study, called EMPACTA, started in May 2020. This summary is based on information available in September 2020. More information may now be known.

One study can't tell us everything about the possible side effects of a medicine and whether a medicine works. It takes a lot 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



### Glossary

- COVID-19 = coronavirus disease 2019
- IL-6 = interleukin 6

## Thank you to the people who took part in this study

The people who took part in this study are helping researchers to answer important questions about how a medicine called tocilizumab works in people with severe COVID-19 pneumonia.

Layperson summary date: October 2020
Veeva: M-XX-00003295

## Key information about this study

- This study was done to look at whether a medicine called tocilizumab is safe and works to treat people with severe COVID-19 pneumonia (an inflammation in the lungs).
- In this study, 377 people in 6 countries were given either tocilizumab or a placebo (looks the same as tocilizumab but does not contain any real medicine). For every 2 people given tocilizumab, 1 person was given placebo. It was decided by chance which treatment each person was given.
- The people in the study did not need a machine called a ventilator to help them breathe at the start of the study. The study showed that people who were treated with tocilizumab were less likely to end up needing a ventilator or die than people treated with a placebo.
- A total of 13% of people given tocilizumab (32 out of 250 people) and 4% of people given a placebo (5 out of 127 people) had a side effect thought to be related to study treatment.
- These side effects were serious in 1% of people given tocilizumab (3 out of 250 people) and none of the people given a placebo (0 out of 127 people).

## 1. General information about this study

### Why was this study done?

Around 20 out of 100 people who get COVID-19 (also called 'coronavirus disease 2019') will develop severe swelling (inflammation) in the lungs called pneumonia. Around 5 out of these 20 people will develop a more severe COVID-19 illness that causes other organs in the body, like the kidney, to stop working. The severe COVID-19 illness also causes very low blood pressure (also called 'septic shock'). Some people with severe COVID-19 develop a life-threatening form of inflammation in the lungs called 'acute respiratory distress syndrome'.

People with severe COVID-19 may need a breathing tube and a machine to help their lungs work (called a 'ventilator').

Most people with severe COVID-19 have high levels of certain proteins made by the immune system – the network of cells and proteins in the body that normally fight infection. The study medicine, tocilizumab, blocks the action of one of these proteins. Studies have shown that tocilizumab is generally safe and works well in people with diseases caused by either inflammation in the body or an overactive or abnormal response by the immune system. Researchers wanted to see if tocilizumab could also work to treat the overactive immune response some people have when they develop severe COVID-19 pneumonia and if it could keep people from needing a ventilator to help them breathe.

This study made it a priority to include people from racial and ethnic minority groups who have been more affected by the COVID-19 pandemic and underserved populations around the world that have not generally been included in clinical trials.

## What is the study medicine?

This study looked at a medicine called **'tocilizumab'** (known by its brand names, Actemra® or RoActemra®)

- You say this as 'toe–si–liz–oo–mab'.
- Tocilizumab works by blocking the action of a protein in the body called 'interleukin 6' (also called 'IL-6'). Too much IL-6 protein can lead to an overactive (abnormal) response of the immune system.
- Tocilizumab is already approved to be given to adults and children with rheumatoid arthritis, some types of juvenile arthritis, giant cell arteritis, and cytokine release syndrome – an overactive immune response caused by a cancer treatment called CAR T-cell therapy.
- Most people with severe COVID-19 pneumonia have high levels of proteins related to inflammation, including IL-6, which can lead to life-threatening serious illness.
- Researchers thought that tocilizumab could help people with severe COVID-19 pneumonia by blocking the action of IL-6.

Tocilizumab was compared with a 'placebo'.

- You say this as 'plah–see–bo'.
- The placebo looked the same and was given in the same way as tocilizumab but did not contain any real medicine. This means it had no medicine-related effects on the body.
- Researchers compared tocilizumab with a placebo so they could show which benefits or side effects were caused by tocilizumab.

## What did researchers want to find out?

- Researchers did this study to compare tocilizumab with a placebo – to see whether tocilizumab works (see section 4 'What were the results of the study?').
- They also wanted to find out if tocilizumab was safe – by checking how many people had side effects (see section 5 'What were the side effects?').

**The main question that researchers wanted to answer was:**

1. How many people needed a ventilator to help them breathe or died within 28 days after receiving study treatment?

**Other questions that researchers wanted to answer included:**

2. How long did it take for people to be sent home or be ready to be sent home from the hospital?
3. How long did it take for people's health condition to improve? ('Health condition' means how sick people were and how much medical care they needed.)
4. How many people had a negative outcome? (A 'negative outcome' means dying, needing a ventilator to breathe, being admitted to the intensive care unit, – or a worsening in health condition if the person was already in the intensive care unit – or leaving the study.)
5. How many people died of any cause (not only COVID-19)?

## What kind of study was this?

This study was a 'Phase 3' study, which means that tocilizumab has been approved to treat other diseases caused by inflammation, and a smaller number of people with severe COVID-19 had received tocilizumab before this study. In this study, a larger number of people with severe COVID-19 pneumonia were given either tocilizumab or a placebo to find out if tocilizumab worked better than a placebo.

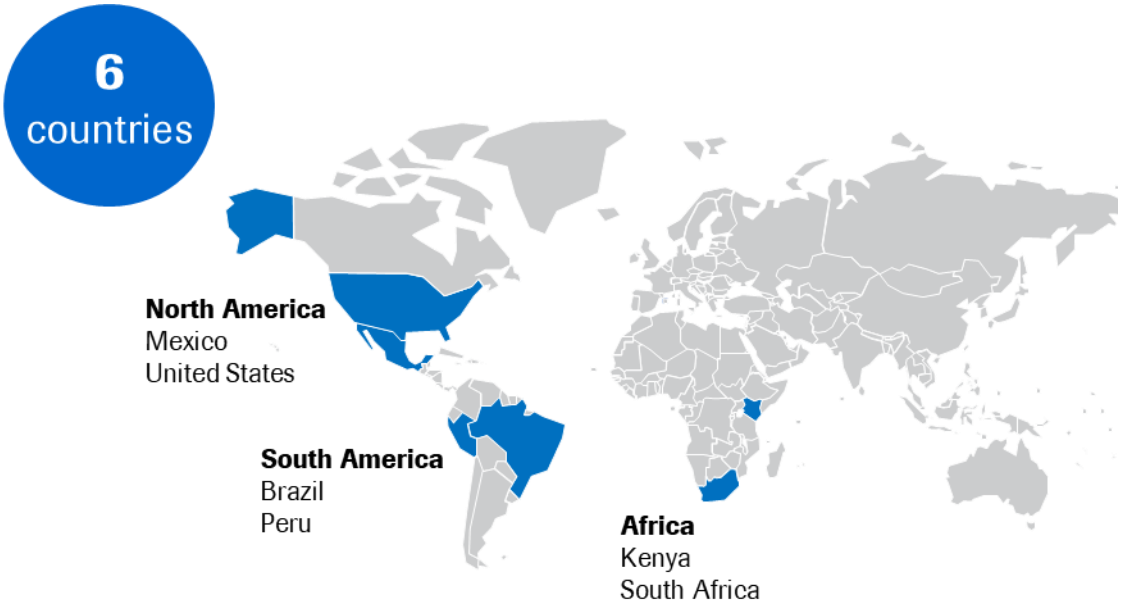
The study was **'randomised'**. This means that it was decided by chance whether people in the study would be given tocilizumab or a placebo – like tossing a coin.

This was a **'double-blind'** study. This means that the people who took part in the study, the study doctors, and the study sponsor did not know whether people were given tocilizumab or a placebo. This 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 people were treated with.

## When and where did this study take place?

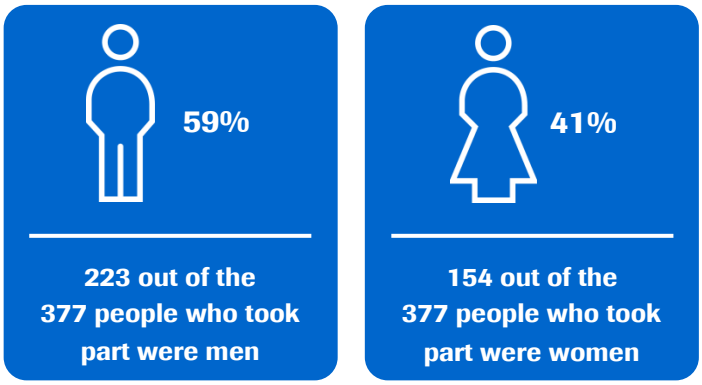
The study started in May 2020. This summary includes the results up until September 2020.

The study took place at 42 study centres in six countries in North America, South America, and Africa. This map shows the countries where this study took place.




## 2. Who took part in this study?

This study included 377 people with severe COVID-19 pneumonia who were given tocilizumab or placebo. Here is more information about the people who took part in the study.




**Age range:** 20 to 95 years old

A total of 87% of people in the study (87 out of every 100 people) were from a racial or ethnic minority group. The racial or ethnic group for all people in this study are listed below:

- 211 out of the 377 people (56%) were Hispanic or Latino
- 56 out of the 377 people (15%) were Black or African American
- 48 out of the 377 people (13%) were American Indian or Alaska Native
- 48 out of the 377 people (13%) were Non-Hispanic White
- 14 out of the 377 people (4%) were another race or the information was not known

People could take part in the study if:

- They were at least 18 years old and
- They had a positive test for SARS-CoV-2 (the virus that causes COVID-19) and
- They had changes to their lungs seen on a chest X-ray or CT scan and low oxygen levels in their blood even while receiving the usual treatment for people with COVID-19 pneumonia and
- They had a blood oxygen level lower than 94%.

People could not take part in the study if:

- They had a known allergic reaction to tocilizumab or similar medication.
- They needed a ventilator or similar machine to breathe.
- They had an active infection like tuberculosis or other infection (other than COVID-19 or well-controlled HIV).
- They had taken a medication that prevents organ rejection or affects the immune system (including tocilizumab) in the 3 months before the study.
- They were pregnant or breastfeeding.

## 3. What happened during the study?

At the start of the study, 389 people had been selected to take part. All of these people were randomly assigned by a computer to be treated with either tocilizumab or a placebo.

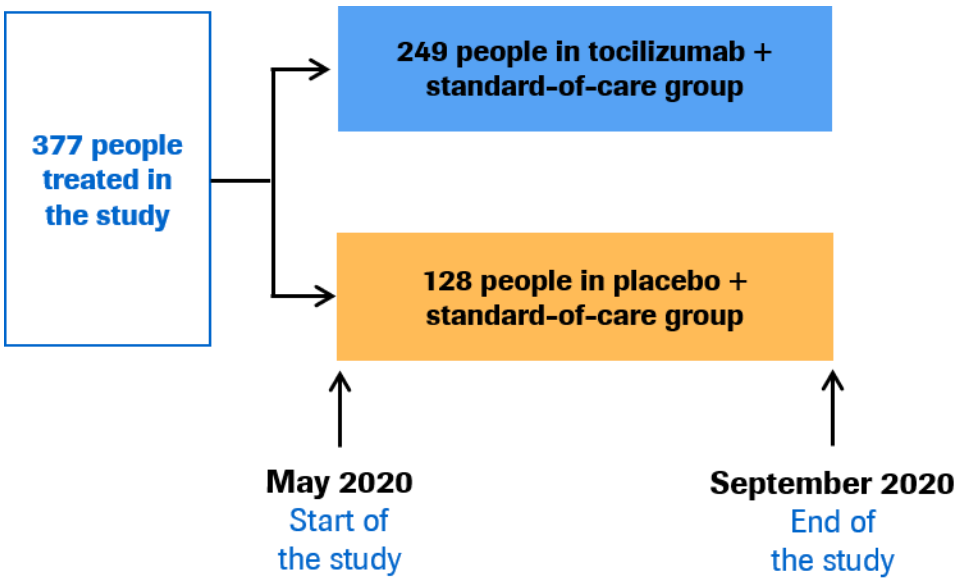
Some of these people left the study before treatment, so only 377 people were given one of the study treatments.

The two treatments were:

- **Tocilizumab** – given by drip (infusion) into a vein. A second infusion could be given after 8 to 24 hours if the person had symptoms that did not improve or got worse.
- **Placebo** – given by infusion into a vein. A second infusion could be given after 8 to 24 hours if the person had symptoms that did not improve or got worse.

**All the people in this study were also given the 'standard-of-care treatment'** (treatment that is given to people based on local guidelines and recommendations for doctors) for severe COVID-19 pneumonia. This could include oxygen and medications that reduced inflammation (steroids) or virus activity in the body (antivirals).

This picture shows what happened in the study.



## 4. What were the results of the study?

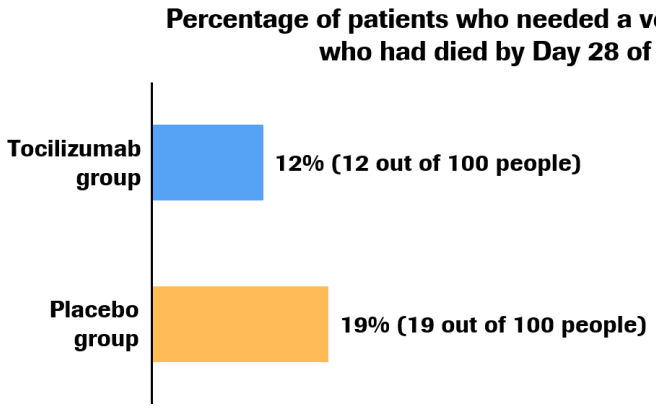
This section shows the key results from this study. You can find information about other results on the websites at the end of this summary (see section 8).

### **Question 1:** How many people needed a ventilator to help them breathe or died within 28 days after receiving the study treatment?

Researchers looked at whether people needed a ventilator to help them breathe or if they had died by Day 28 of the study (28 days after they started getting the study treatment) – this was compared between people who were treated with tocilizumab and people who were treated with placebo.

**People who received tocilizumab treatment were less likely to need a ventilator to breathe or to die during the study than people who received a placebo.**

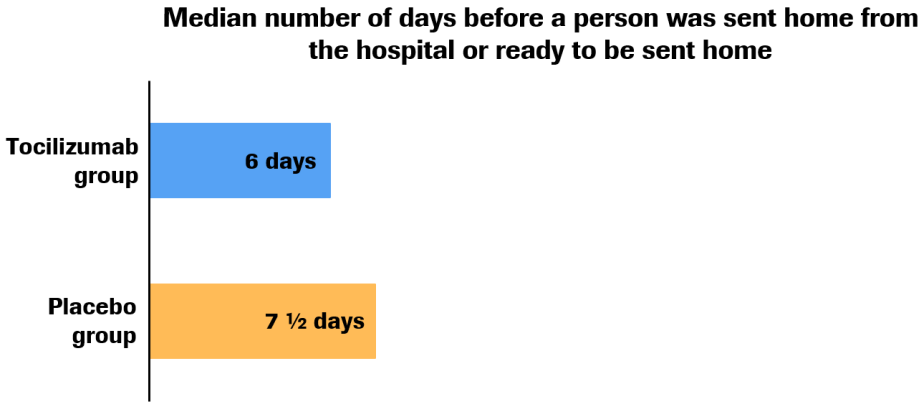
- In the tocilizumab group, 12% of people (12 out of 100 people) needed a ventilator to breathe or died during the study.
- In the placebo group, 19% of people (19 out of 100 people) needed a ventilator to breathe or died during the study.




### **Question 2:** How long did it take for people to be sent home or be ready to be sent home from the hospital?

Researchers also wanted to know how many days it took for people to be sent home or to be ready to be sent home from the hospital up to Day 28 of the study.

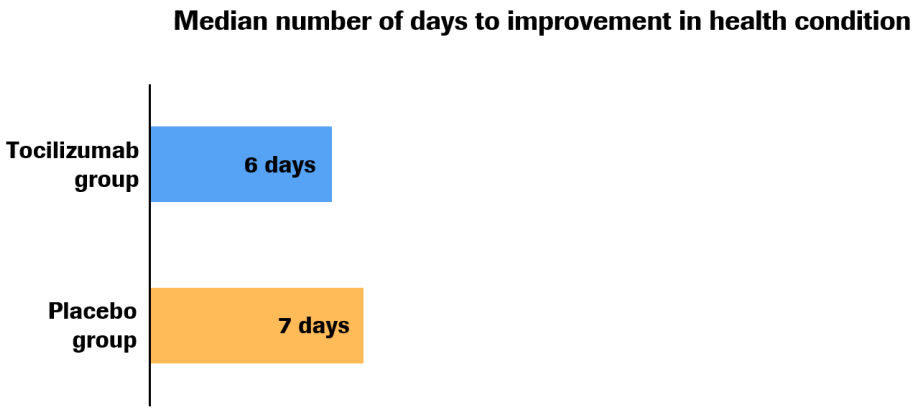
- In the tocilizumab group, the median time it took for people to be sent home or to be ready to be sent home from the hospital was 6 days – the median (a type of average) means that half of the people were sent home or ready to be sent home within 6 days.
- In the placebo group, the median time it took for people to be sent home or to be ready to be sent home from the hospital was 7 ½ days.
- The study researchers do not know if this is a real difference – it could have been caused by chance.




## **Question 3:** How long did it take for people's health condition to improve? ('Health condition' means how sick people were and how much medical care they needed.)

Researchers also looked at how long it took for people's health condition to improve. Health condition was scored on a scale from 1 to 7, with 1 being the best health condition and 7 the worst.

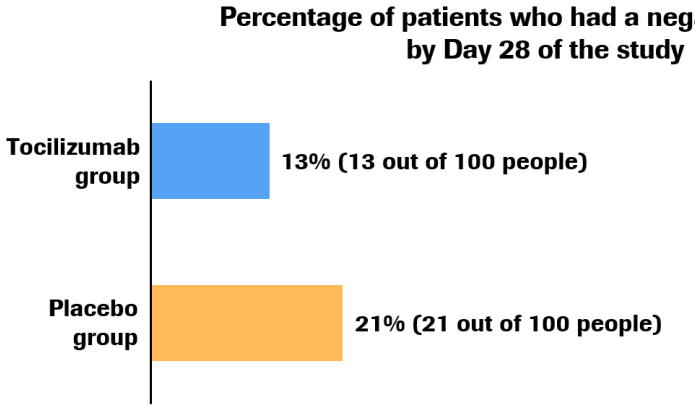
- In the tocilizumab group, the median time to improvement in health condition was 6 days – the median (a type of average) means that half of the people's health condition improved within 6 days.
- In the placebo group, the median time to improvement in health condition was 7 days.
- The study researchers do not know if this is a real difference – it could have been caused by chance.



## **Question 4:** How many people had a negative outcome? (A 'negative outcome' means dying, needing a ventilator to breathe, being admitted to the intensive care unit, – or a worsening in health condition if the person was already in the intensive care unit – or leaving the study.)

Researchers also looked at how many people had a negative outcome by Day 28 of the study. Less than half of the people who were treated with tocilizumab or placebo had a negative outcome.

- In the tocilizumab group, 13% of people (13 out of 100) had a negative outcome by Day 28
- In the placebo group, 21% of people (21 out of 100) had a negative outcome by Day 28




## **Question 5:** How many people died of any cause (not only COVID-19)?

Out of the 377 people who were given either tocilizumab or placebo, 37 people died of any cause as of Day 28 of the study.

- In the tocilizumab group, 26 out of 249 people died. This is 10% or 10 out of 100 people.
- In the placebo group, 11 out of 128 people died. This is 9% or 9 out of 100 people.
- The study researchers do not know if this is a real difference – it could have been caused by chance.

## 5. What were the side effects?

Side effects are medical problems that happen during the study.

- They are described in this summary because the study doctor believed that the side effects were related to the treatments in the study.
- Not all of the people in this study had a side effect.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to know that the side effects reported here are from this one study. This means that the side effects shown here may be different from those seen in other studies, or those that are listed in the tocilizumab information sheet or leaflet.

One person that the computer decided to put in the placebo group was given tocilizumab by mistake. In the results section, the treatment group numbers did not change because the person in the placebo group was supposed to be treated with placebo. But when looking at side effects that may have been related to study treatment, it is important that this person be included in the tocilizumab group.

Because of this reason, **the numbers of people in each group are different than the numbers in the results section above**.

In this side effects section, the number of people who were treated with tocilizumab is 250 and the number of people treated with a placebo is 127.

### Serious side effects

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

During this study, 3 out of 377 people (less than 1%) had at least one serious side effect thought to be related to study treatment.

- In the tocilizumab group, 3 out of 250 people (1%) had a serious side effect.
- No people in the placebo group had a serious side effect.

A total of 4 serious side effects happened during the study. The 4 medical problems were infection in the bloodstream, infection of the gall bladder, infection of a medical device in the body, and lung infection – they were thought to be related to tocilizumab.

### Most common side effects

A total of 37 out of 377 people (10%) had a side effect that the study doctor considered related to the study treatments.

A total of 13% of people given tocilizumab (32 out of 250 people) had a side effect, and 4% of people given a placebo (5 out of 127 people) had a side effect.

This table shows the five most common side effects that people in the study had. Some people had more than one side effect. This means that they are counted in more than one row in the table.

| **Most common side effects considered related to study treatment** | **People treated with tocilizumab** (250 people total) | **People treated with a placebo** (127 people total) |
|---|---|---|
| Problems with the stomach and intestines | **3%** (7 out of 250 people in this treatment group) | **2%** (3 out of 127 people in this treatment group) |
| Abnormal (not normal) change in laboratory test results | **3%** (8 out of 250) | **1%** (1 out of 127) |
| Infections | **2%** (5 out of 250) | **0%** (0 out of 127) |
| Problems with the nervous system | **1%** (3 out of 250) | **2%** (2 out of 127) |
| General problems | **2%** (4 out of 250) | **0%** (0 out of 127) |

### 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 in this summary is from one study of 377 people with severe COVID-19 pneumonia who were treated with tocilizumab or a placebo. These results have helped researchers learn more about tocilizumab treatment for severe COVID-19 pneumonia.

**The study showed that among people who did not need a ventilator to help them breathe at the start of the study, those who were treated with tocilizumab were less likely to need a ventilator or die by Day 28 than people treated with a placebo.**

The results may help people and their doctors make decisions about which treatments to use for COVID-19.

**All of the medical problems seen in people who were treated with tocilizumab in this study have been seen in other studies of tocilizumab or are known to be effects of COVID-19.**

One study can't tell us everything about whether a medicine works and how safe it is. It takes a lot 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?

Other studies looking at the safety and effects of tocilizumab in people with COVID-19 pneumonia are happening now. Some of these studies are looking at the use of tocilizumab in different situations, for example, together with other treatments.

## 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/NCT04372186
- https://forpatients.roche.com/en/trials/infectious-diseases/covid-19-pneumonia/a-study-to-evaluate-the-efficacy-and-safety-of-tocilizu-42486.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/a-study-to-evaluate-the-efficacy-and-safety-of-tocilizu-42486.html
- Contact your local Roche/Genentech office.

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

- Speak to 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 organised and paid for this study?

This study was organised and paid for by Genentech, Inc., who have their headquarters in South San Francisco, California, United States.

### Full title of the study and other identifying information

The full title of this study is: 'A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Tocilizumab in Hospitalized Patients With COVID-19 Pneumonia.'

The study is known as 'EMPACTA'.

- The protocol number for this study is: ML42528.
- The ClinicalTrials.gov identifier for this study is: NCT04372186.