Summary of Clinical Trial Results

A study to look at whether a medicine called tocilizumab works and is safe in people with 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) – written for:

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

This study, called COVACTA, started in April 2020. This summary is based on information collected in June 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
- ICU = intensive care unit
- 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.

Key information about this study

- This study was done to look at whether a medicine called tocilizumab works and is safe in people with severe COVID-19 pneumonia.
- In this study, 438 people in 9 countries were given either tocilizumab or a placebo (a medicine that looked the same as tocilizumab but did not contain any real medicine). It was decided by chance which treatment each person was given.
- The study suggested that some people who were treated with tocilizumab may have done better and been sent home from the hospital sooner than some people treated with a placebo, but this could have happened by chance.
- A total of 18% of people given tocilizumab (54 out of 295 people) had a side effect, and 18% of people given a placebo (26 out of 143 people) had a side effect.

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 (called 'critical') 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 immune system response. 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.

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 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. What was the health condition of people on Day 28 of the study? ('Health condition' meant how sick people were and how much medical care they needed.)

Other questions that researchers wanted to answer included:

2. How many people died?
3. How long did it take for people to be sent home or be ready to be sent home from the hospital?
4. How many days did people stay in the intensive care unit – also known as the ICU?
5. If people did not need a breathing tube and ventilator when they started the study, how likely were they to need a breathing tube and ventilator during the study?

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.

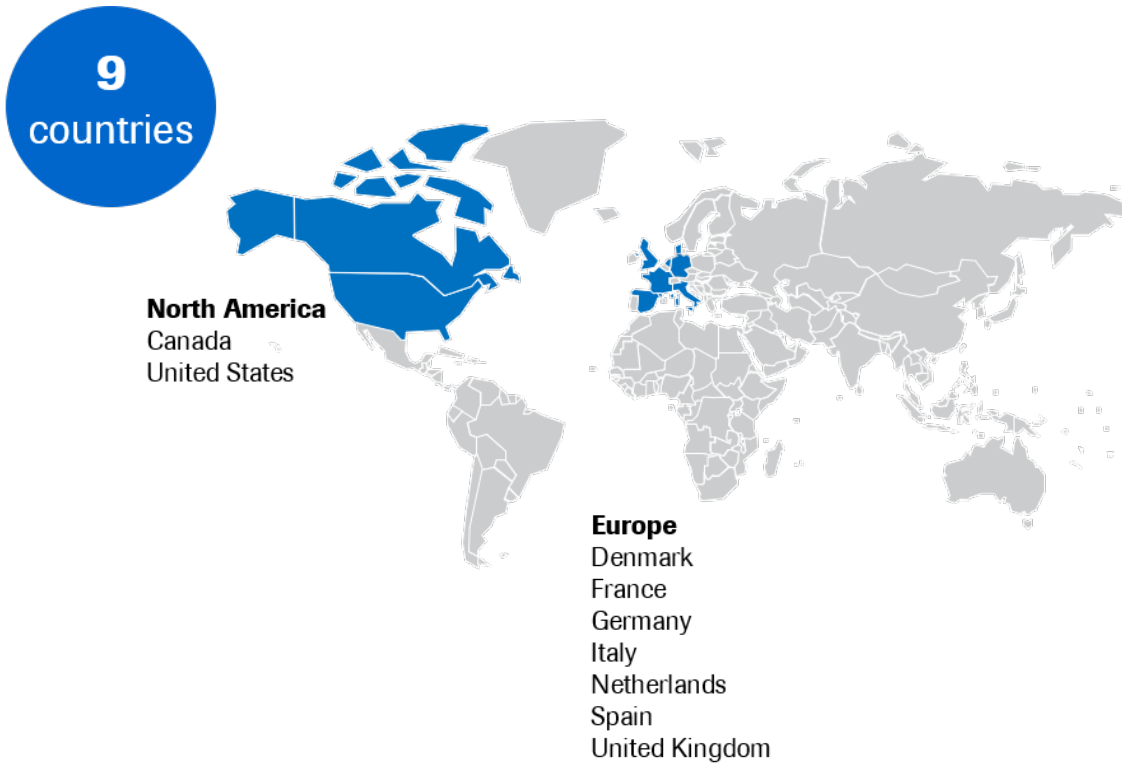
The study was '**randomised**'. This means that it was decided by chance whether people in the study would be given tocilizumab or a placebo – like tossing a coin.

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.

When and where did this study take place?

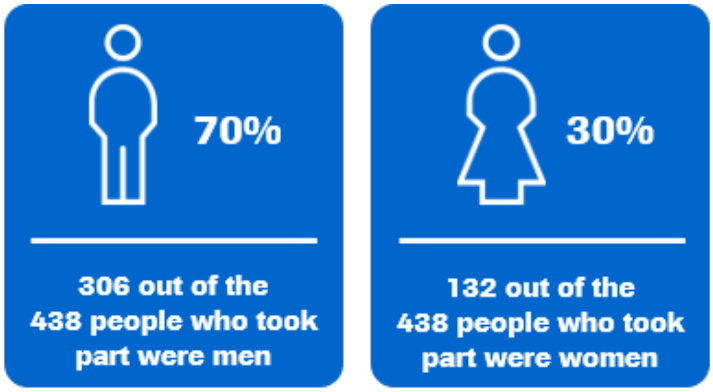
The study started in April 2020. This summary includes the results up until June 2020.

The study took place at 62 study centres in nine countries in North America and Europe. This map shows the countries where this study took place.



2. Who took part in this study?

This study included 438 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: 22 to 96 years old

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.

People could not take part in the study if:

- They had a known allergic reaction to tocilizumab or similar medication.
- They had an active infection like tuberculosis or other infection (other than COVID-19).
- 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, 452 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.

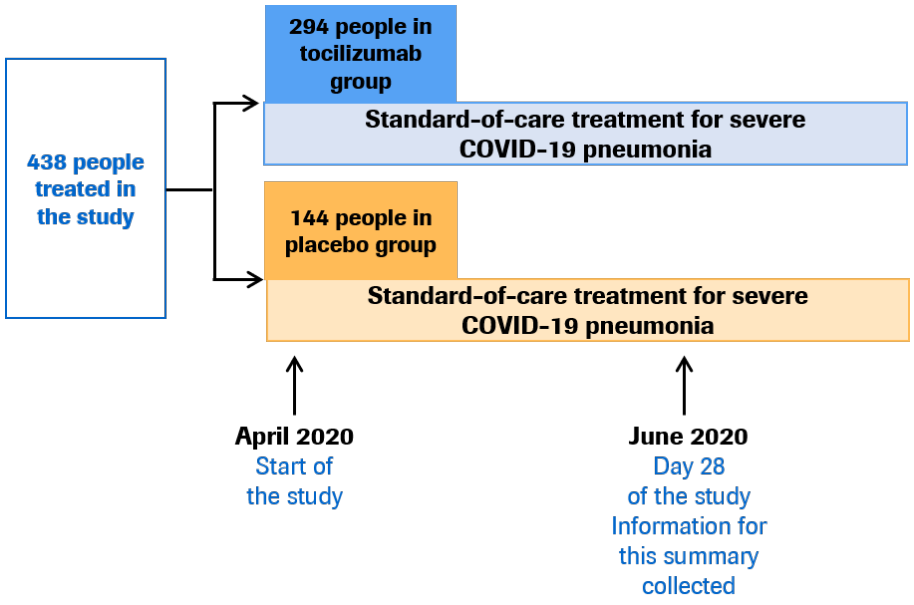
Some of these people left the study before treatment, so only 438 people were given one of the study treatments.

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 picture shows what happened in the study.



4. What were the results of the study?

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

Question 1: What was the health condition of people on Day 28 of the study?

Researchers looked at people's health condition on 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.

Health condition meant how sick people were and how much medical care they needed. This was scored on a scale from 1 to 7, with 1 being the best health condition and 7 the worst. The categories are listed in the table below. **There was no clear benefit in health condition with tocilizumab treatment compared with placebo.**

Researchers looked at the health condition scores of **all** the people in each group to find the middle number of all the scores on the scale of 1 to 7. This middle number is a measure of average called the **median**.

- The median health condition category number in the tocilizumab group was 1.
- The median health condition category number in the placebo group was 2.
- The study researchers do not know if this is a real difference – whether tocilizumab actually caused people to be healthier. It could have been caused by chance.

The percentages of people in each health condition category are listed in this table.

Category number	**Health condition**	**People treated with tocilizumab** (294 people total)	**People treated with a placebo** (144 people total)
1	Discharged (sent home from hospital) or 'ready for discharge'	**56%** (166 out of 294 people in this treatment group)	**49%** (71 out of 144 people in this treatment group)
2	In a non-intensive care unit (non-ICU) part of the hospital and not getting oxygen treatment	**2%** (6 out of 294)	**6%** (8 out of 144)
3	In a non-ICU part of the hospital and getting oxygen treatment	**5%** (14 out of 294)	**3%** (4 out of 144)
4	In ICU or non-ICU, needing breathing support through a mask or high-flow oxygen treatment through a tube in the nose	**2%** (6 out of 294)	**7%** (10 out of 144)
5	In ICU, needing a breathing tube and a ventilator	**9%** (26 out of 294)	**10%** (14 out of 144)
6	In ICU, needing a machine to add oxygen to the blood or a ventilator and treatment to support other organs such as the kidney or heart	**6%** (18 out of 294)	**6%** (9 out of 144)
7	Died	**20%** (58 out of 294)	**19%** (28 out of 144)

Question 2: How many people died?

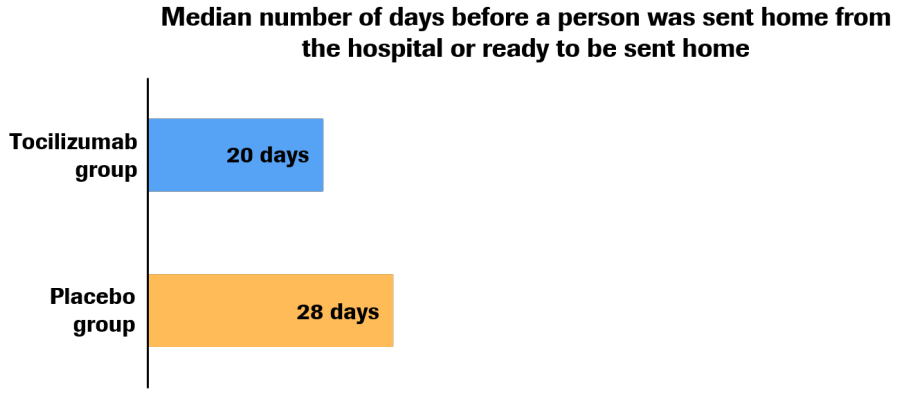
Out of the 438 people who were given either tocilizumab or placebo, 86 people died as of Day 28 of the study. **There was no decrease in death with tocilizumab treatment compared with placebo**.

- In the tocilizumab group, 58 out of 294 people died. This is 20% or 20 out of 100 people.
- In the placebo group, 28 out of 144 people died. This is 19% or 19 out of 100 people.

Question 3: 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.

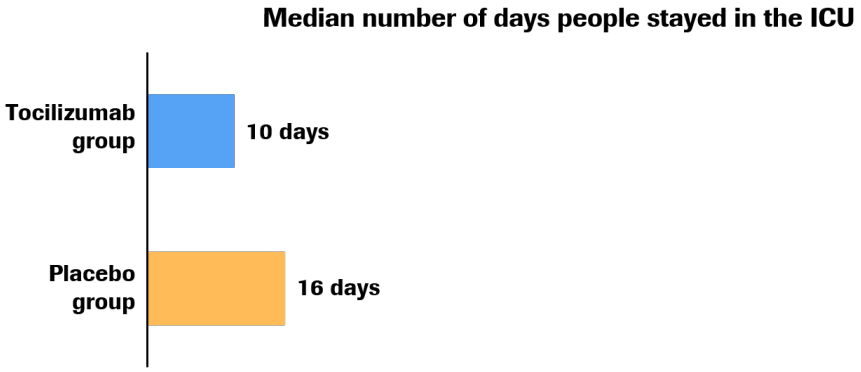
- In the tocilizumab group, the median (middle value – a measure of average) time it took for people to be sent home or to be ready to be sent home from the hospital was 20 days.
- In the placebo group, the median time it took for people to be sent home or to be ready to be sent home from the hospital was 28 days.



Question 4: How many days did people stay in the intensive care unit – also known as the ICU?

Researchers also looked at the number of days that people stayed in the ICU up to Day 28.

- In the tocilizumab group, people stayed in the ICU for a median (middle value – a measure of average) of 10 days
- In the placebo group, people stayed in the ICU for a median of 16 days
- The study researchers do not know if this is a real difference – it could have been caused by chance.



Question 5: If people did not need a breathing tube and ventilator when they started the study, how likely were they to need a breathing tube and ventilator during the study?

At the start of the study, 183 in the tocilizumab group and 90 people in the placebo group were not on a ventilator. Researchers looked at how many of these people needed a breathing tube and ventilator up to Day 28 of the study.

- In the tocilizumab group, 51 out of 183 people (28%) needed a ventilator.
- In the placebo group, 33 out of 90 people (37%) needed a ventilator.
- 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 be aware 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 mistakenly given tocilizumab. It is important that this person be included in the tocilizumab group when looking at side effects that may have been related to a study treatment.

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 295 and the number of people treated with a placebo is 143.

Most common side effects

A total of 80 out of 438 people (18%) had a side effect that the study doctor considered related to study treatments when the information from this study was collected.

When looking at each treatment group, 18% of people given tocilizumab (54 out of 295 people) had a side effect, and 18% of people given a placebo (26 out of 143 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 type of side effects considered related to study treatment	**People treated with tocilizumab** (295 people total)	**People treated with a placebo** (143 people total)
Infections	**5%** (15 out of 295 people in this treatment group)	**10%** (15 out of 143 people in this treatment group)
Abnormal (not normal) change in laboratory test results	**6%** (19 out of 295)	**3%** (4 out of 143)
Problems with the blood and other body fluids such as lymph	**5%** (15 out of 295)	**3%** (4 out of 143)
Problems with the stomach and intestines	**2%** (5 out of 295)	**1%** (2 out of 143)
Problems with the blood vessels and blood circulation	**1%** (4 out of 295)	**1%** (2 out of 143)

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 patients and research?

The information in this summary is from one study of 438 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 some people who were treated with tocilizumab may have done better and been sent home from the hospital sooner than some people treated with a placebo, but the study researchers don't know if this happened by chance. The side effects were similar in each group.

The results did not show a clear benefit to patients treated with tocilizumab. The results may help patients 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:

- In people at a different stage of the disease
- 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/NCT04320615
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=2020-001154-22
- https://forpatients.roche.com/en/trials/infectious-diseases/covid-19-pneumonia/a-study-to-evaluate-the-safety-and-efficacy-of-tocilizu-41434.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-safety-and-efficacy-of-tocilizu-41434.html
- Contact your local Roche 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 F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland. The study was also partially funded by 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.

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 safety and efficacy of tocilizumab in patients with severe COVID-19 pneumonia'.

The study is known as 'COVACTA'.

- The protocol number for this study is: WA42380.
- The ClinicalTrials.gov identifier for this study is: NCT04320615.
- The EudraCT number for this study is: 2020-001154-22.