NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects and safety of hydroxychloroquine given alone and in combination with azithromycin in participants who required hospitalization for moderate to severe COVID-19

Protocol number: CJWT629A12301

Thank You!

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. Thank you for taking part in this trial for the drugs hydroxychloroquine and azithromycin. You helped researchers learn more about the safety and effects of hydroxychloroquine and azithromycin in people with moderate to severe COVID-19.

As a clinical trial participant, you belong to a large community of people around the world. Your invaluable contribution to medicine and healthcare is greatly appreciated.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings. Researchers and health authorities, such as the Food and Drug Administration (FDA) in the United States and the European Medicines Agency (EMA) in Europe, look at the results of many clinical trials to understand which drugs work and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

How long was this trial?

This trial was designed so that an individual participant could take part for one and a half months. The trial started in May 2020 and ended in July 2020. The entire duration, from enrolling the first participant to the last participant completing the trial was about 3 months.

The researchers could not complete the trial as planned. It was ended early due to low number of participants enrolling in this trial. When the trial ended, the researchers collected information on the trial treatments and created a report of the trial results. This summary is based on that report.

Why was the research needed?

Coronavirus disease (COVID-19) is a highly infectious disease, which is caused by a virus. People infected with COVID-19 may experience no symptoms or mild to severe respiratory problems. Some of the most common symptoms are dry cough, runny nose, fever, chills, body aches, headache, diarrhea, sudden loss of taste or smell, chest pain, and difficulty in breathing.

Participants in this trial had moderate to severe COVID-19. Participants who had moderate COVID-19 had a normal amount of oxygen in their blood, but required hospitalization to manage other symptoms associated with COVID-19. Participants who had severe COVID-19 had less oxygen in their blood and required hospitalization for oxygen support. However, none of the participants needed admission to the intensive care unit (ICU) or a machine to help them breathe. At the time of this trial, there was no approved treatment for COVID-19.

In this trial, researchers wanted to find out if hydroxychloroquine taken orally (as a pill), either alone or together with azithromycin, could treat participants with moderate to severe COVID-19 and was safe to use.

Trial drugs

The drugs given in this trial were:

- **Hydroxychloroquine (HCQ):** A drug that is approved for oral use in treating malaria, rheumatoid arthritis, and lupus. It has shown anti-viral effects against COVID-19 virus in non-human and laboratory experiments.
- **Azithromycin (AZI):** A drug that is approved for oral use to treat infections caused by bacteria. It is thought to be able to reduce inflammation in the lungs caused by COVID-19.

Placebo: This looked like the trial drug, but did not have any medicine in it. Using a placebo helps researchers better understand the effect of a trial drug by making sure that any changes observed were not happening by chance.

Trial purpose

The main question the researchers wanted to answer in this trial was:

How many participants showed response to treatment by Day 15?

The other questions researchers wanted to answer in this trial were:

- How many participants tested negative for the virus by Day 10?
- How many participants were discharged from the hospital by Day 15?
- How many participants did not require oxygen support by Day 15?

Who was in this trial?

The participants could take part in this trial if they:

- were 18 years or older in age,
- had moderate to severe COVID-19 infection before the start of the trial, and
- required hospitalization or were already hospitalized, but did not need admission to the ICU or a machine to help them breathe.

A total of 19 participants from 9 centers in the United States participated in this trial.

The average age of participants was 54 years. Participants' age ranged from 35 to 73 years.

Percentage of men and women in this trial

What kind of trial was this?

This was a double-blind trial. This means that none of the participants, trial doctors, or trial staff knew what treatment participants were receiving. Some trials are done this way because knowing what treatment each patient is getting can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness towards all treatments.

What happened during this trial?

During Screening

To find out if participants could take part in this trial, researchers conducted certain tests:

- a full body check-up,
- a COVID-19 test,
- an electrocardiogram (often called ECG) to measure the heart's electrical activity, and
- blood and urine tests.

During Treatment

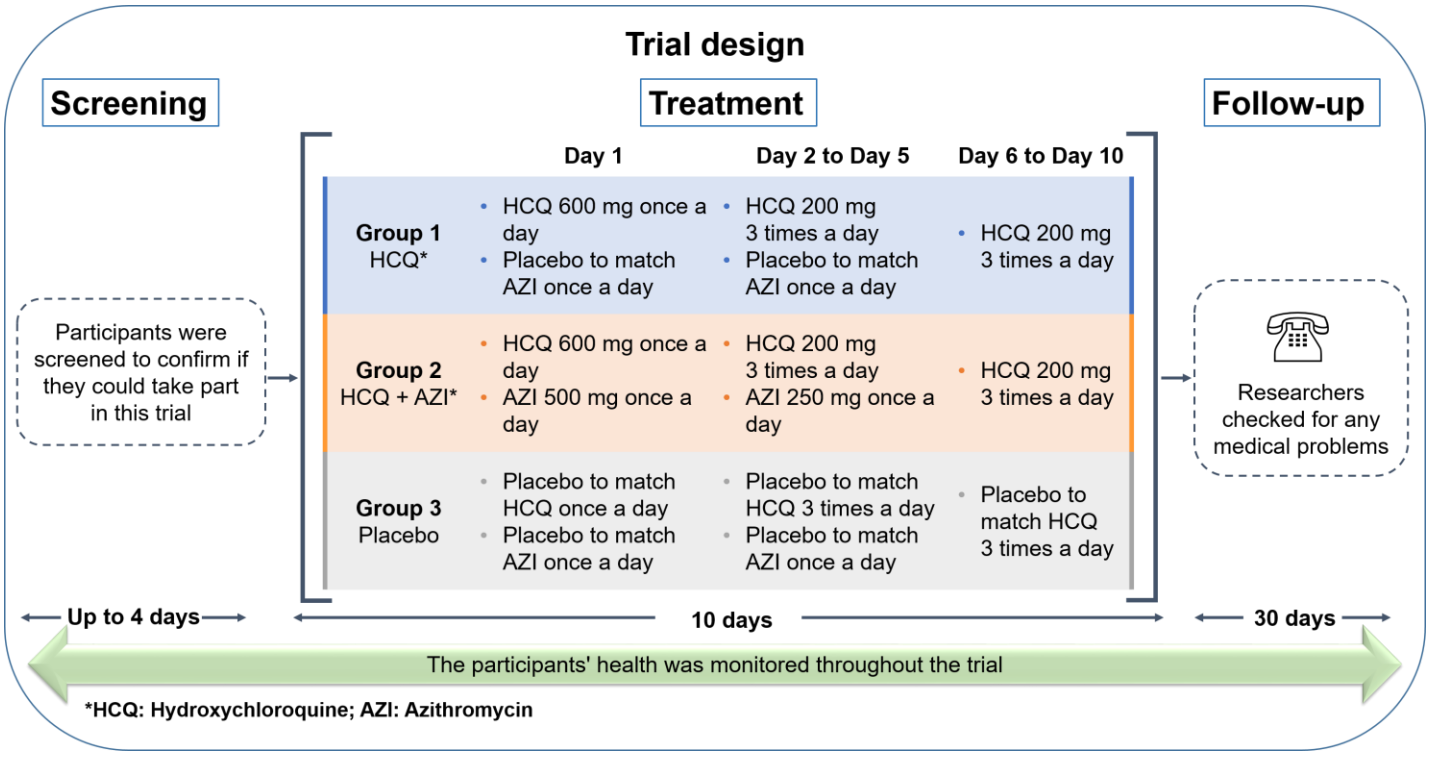
On Day 1, eligible participants were randomly assigned to 1 of the 3 groups to receive:

- **hydroxychloroquine alone (Group 1)**
- **hydroxychloroquine together with azithromycin (Group 2)**
- **placebo (Group 3)**

This process is called randomization. This means that each participant had an equal chance of being assigned to any group.

This trial was terminated early due to the low number of participants enrolling in the trial. When the decision was made to stop this trial, a total of 20 participants were enrolled and 19 participants had received the trial treatment.

On Day 6 and Day 10, the researchers collected nasal swab samples from the participants to check if they were still infected with the COVID-19 virus or not. Throughout the trial, researchers monitored the health of the participants.

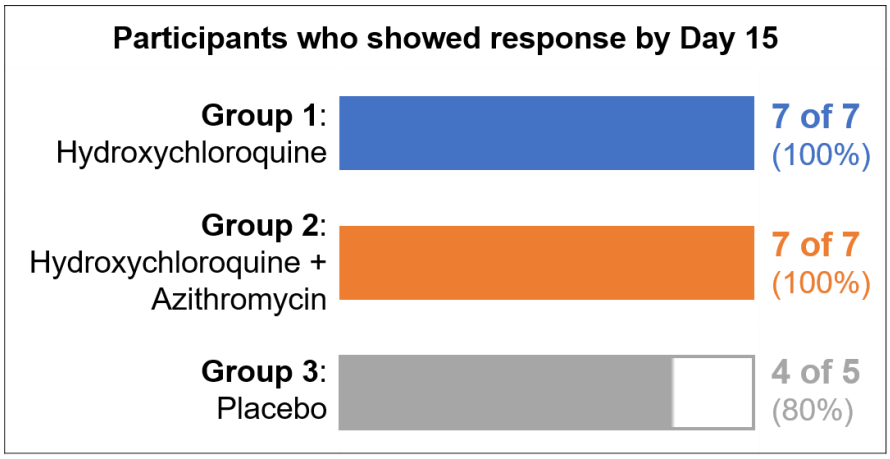


What were the key results of this trial?

This is a summary of the results for all participants in different treatment groups. It does not show the results of each individual participant. Results of individual participants could be different from the results of the total group of participants. A detailed presentation of the results can be found on the websites listed at the end of this summary.

How many participants showed response to treatment by Day 15?

In **Group 1** (**hydroxychloroquine**) and **Group 2** (**hydroxychloroquine plus azithromycin**) all the participants showed response to treatment by Day 15. In **Group 3** (**placebo**), **4** out of **5** participants (**80%**) showed a response by Day 15. Since this trial was ended earlier than planned, researchers could not confirm the effects of hydroxychloroquine alone or together with azithromycin.



How was this measured?

To answer this question, the researchers checked for the number of participants who:

- were discharged from the hospital after getting better, or
- did not require oxygen to manage their COVID-19 symptoms.

What were the other results of this trial?

How many participants tested negative for the virus by Day 10?

By Day 10, **2** out of **7** participants (**29%**) in **Group 1** (**hydroxychloroquine**), **3** out of **7** participants (**43%**) in **Group 2** (**hydroxychloroquine plus azithromycin**) and **3** out of **5** participants (**60%**) in **Group 3** (**placebo**) tested negative for the virus.

How many participants were discharged from the hospital by Day 15?

In **Group 1** (**hydroxychloroquine**) and **Group 2** (**hydroxychloroquine plus azithromycin**) all the participants were discharged from the hospital by Day 15. In **Group 3** (**placebo**) **4** out of **5** participants (**80%**) were discharged from the hospital by Day 15.

How many participants did not require oxygen support by Day 15?

All the participants in **Group 1** (**hydroxychloroquine**), **6** out of **7** participants (**86%**) in **Group 2** (**hydroxychloroquine plus azithromycin**), and **4** out of **5** participants (**80%**) in **Group 3** (**placebo**) did not require oxygen support by Day 15.

What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called "adverse events".

A lot of research is needed to know whether a drug causes an adverse event. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug. When new drugs are being studied, researchers keep track of all adverse events participants have.

This section is a summary of the adverse events that happened during this trial. The websites listed at the end of this summary may have more information about all the adverse events that happened in this trial.

An adverse event is an unwanted sign, symptom, or disease that participants have during a trial

An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial drug

How many participants had adverse events?

13 out of 19 participants (68%) had 1 or more adverse events. During the trial, 2 out of 19 participants (11%) stopped the drug early because of adverse events. Serious adverse events happened in 3 out of 19 participants (16%) in the trial. 1 participant who needed a machine to help them breathe after the trial began died during this trial because of a **heart attack** (cardiac arrest).

Number of Participants (%) With Adverse Events

	Group 1 Hydroxychloroquine (Out of 7 participants)	**Group 2** Hydroxychloroquine + Azithromycin (Out of 7 participants)	**Group 3** Placebo (Out of 5 participants)
At least 1 adverse event	5 (71%)	5 (71%)	3 (60%)
At least 1 serious adverse event	1 (14%)	0 (0)	2 (40%)
Stopped drug due to adverse event	1 (14%)	1 (14%)	0 (0)
Death	0 (0)	0 (0)	1 (20%)

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 20% (20 out of 100) of the participants in any group are presented below:

	Group 1 Hydroxychloroquine (Out of 7 participants)	**Group 2** Hydroxychloroquine + Azithromycin (Out of 7 participants)	**Group 3** Placebo (Out of 5 participants)
Cough	**1** (14%)	**2** (29%)	**0** (0)
Diarrhea	**0** (0)	**3** (43%)	**0** (0)
Decreased appetite	**0** (0)	**2** (29%)	**0** (0)
Feeling sick to the stomach (Nausea)	**0** (0)	**2** (29%)	**0** (0)
Feeling tired (Fatigue)	**1** (14%)	**1** (14%)	**1** (20%)
Headache	**0** (0)	**2** (29%)	**0** (0)
High cholesterol (Hypercholestrolemia)	**0** (0)	**0** (0)	**1** (20%)
Increase in liver test value of alanine aminotransferase in the blood* (Alanine aminotransferase increased)	**0** (0)	**2** (29%)	**1** (20%)
Increase in liver test value of aspartate aminotransferase in the blood* (Aspartate aminotransferase increased)	**0** (0)	**2** (29%)	**1** (20%)

*An increase in the level of alanine aminotransferase and/or aspartate aminotransferase in the blood may indicate that the liver may be inflamed or injured

What were the serious adverse events?

The serious adverse events that happened in any group are shown below:

	Group 1 Hydroxychloroquine (Out of 7 participants)	**Group 2** Hydroxychloroquine + Azithromycin (Out of 7 participants)	**Group 3** Placebo (Out of 5 participants)
Abnormally rapid breathing (Tachypnea)	**0** (0)	**0** (0)	**1** (20%)
Decreased oxygen supply (Hypoxia)	**1** (14%)	**0** (0)	**0** (0)
Decreased kidney function (Acute kidney injury)	**0** (0)	**0** (0)	**1** (20%)
Heart attack (Cardiac arrest)	**0** (0)	**0** (0)	**1** (20%)

How many participants stopped trial drug due to adverse events?

During the trial, **1** out of **7** participants (**14%**) in **Group 1** (**hydroxychloroquine**) stopped the trial drug early because the **heart muscle took longer than normal to recharge between beats** (QT prolongation). **1** out of **7** participants (**14%**) in **Group 2** (**hydroxychloroquine plus azithromycin**) stopped the trial drug early due to adverse events of **feeling sick to the stomach** (nausea) and **diarrhea**.

How was this trial useful?

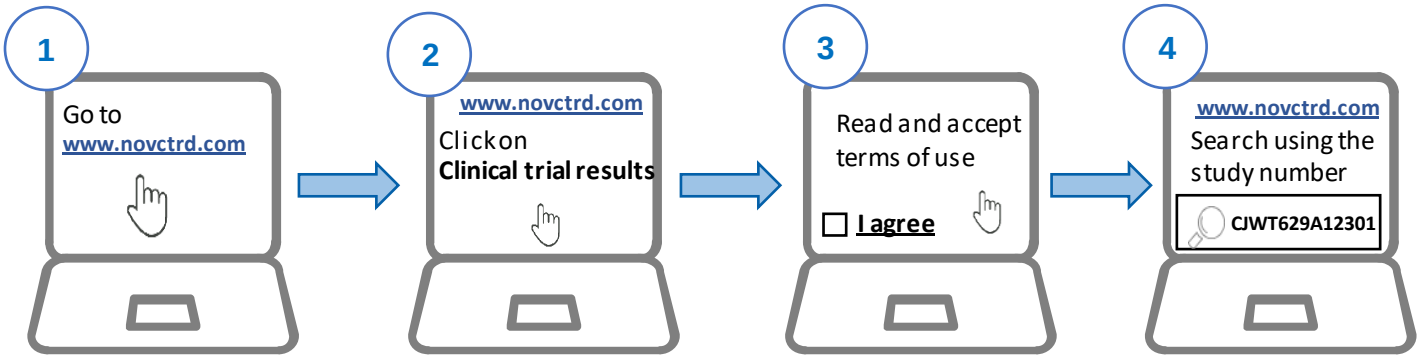
From this trial researchers wanted to learn about the effects and safety of hydroxychloroquine alone and together with azithromycin, in participants with moderate to severe COVID-19. Since this trial was terminated early, researchers could not confirm the effect of hydroxychloroquine alone or together with azithromycin.

Results from this trial may be used in other clinical trials for people with COVID-19.

If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com).



You can find more information about this trial on the following website:

- www.clinicaltrials.gov Use the NCT identifier NCT04358081 in the search field.

Full clinical trial title: A multi-center, randomized, double-blinded, placebo-controlled study to evaluate the safety and efficacy of hydroxychloroquine monotherapy and in combination with azithromycin in patients with moderate and severe COVID-19 disease.

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of people around the world. You helped researchers answer important health questions and test new medical treatments.

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Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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www.novartisclinicaltrials.com