NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects and safety of ruxolitinib in participants with COVID-19

Protocol number: CINC424J12301

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 drug INC424, also known as ruxolitinib. You helped researchers learn more about the effects and safety of ruxolitinib in people with 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 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 about a month. The trial started in May 2020 and ended in October 2020. The entire duration, from enrolling the first participant to the last participant completing the trial, was about 5 and a half months.

The researchers completed this trial as planned. When the trial ended, the researchers collected information on the trial treatments, ruxolitinib (pronounced as ruxO-li-ti-nib) and placebo, and created a report of the trial results. This summary is based on that report.

Why was the research needed?

Coronavirus disease 2019 (COVID-19) is a highly infectious disease, which is caused by a virus known as SARS-CoV-2. People infected with COVID-19 may experience no symptoms or may experience mild to severe respiratory problems requiring hospitalization and oxygen support. Some of the most common symptoms are dry cough, runny nose, fever, chills, body aches, headache, diarrhea, sudden loss of taste, smell and/or appetite, chest pain, and difficulty in breathing.

In this trial, participants were hospitalized for severe respiratory disease due to COVID-19. Currently, there is no treatment available for COVID-19.

In this trial, researchers wanted to find out effects and safety of ruxolitinib in treating participants with severe respiratory disease due to COVID-19.

Trial drugs

The drugs given in this trial were:

- **Ruxolitinib:** It is approved in many countries for the treatment of a type of blood cancer (myelofibrosis) and a blood disorder (polycythemia vera) in adults. It is also approved in the United States for the treatment of a condition that occurs when donor immune cells attack the recipient after a transplant (acute graft versus host disease) in adults and children above 12 years of age. Ruxolitinib exerts its effects and interacts with the body's immune system by blocking a protein called Janus kinase (JAK).
- **Placebo:** It looked like the trial drug, but did not have any active medicine in it. Using a placebo helps researchers better understand the effect of a trial drug by making sure that the changes were not happening by chance.

Along with either of the 2 trial drugs, participants also received standard treatment for management of signs and symptoms of COVID-19 according to their trial doctor's judgement. These medications could include anti-viral drugs, anti-inflammatory drugs, antibiotics, and/or anti-fungal drugs, among others.

Trial purpose

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

How many participants died, had respiratory failure or required intensive care by Day 29 after receiving ruxolitinib and standard treatment compared to placebo and standard treatment?

Participants who had respiratory failure were defined as those needing a machine to help them breathe.

The other question researchers wanted to answer in this trial was:

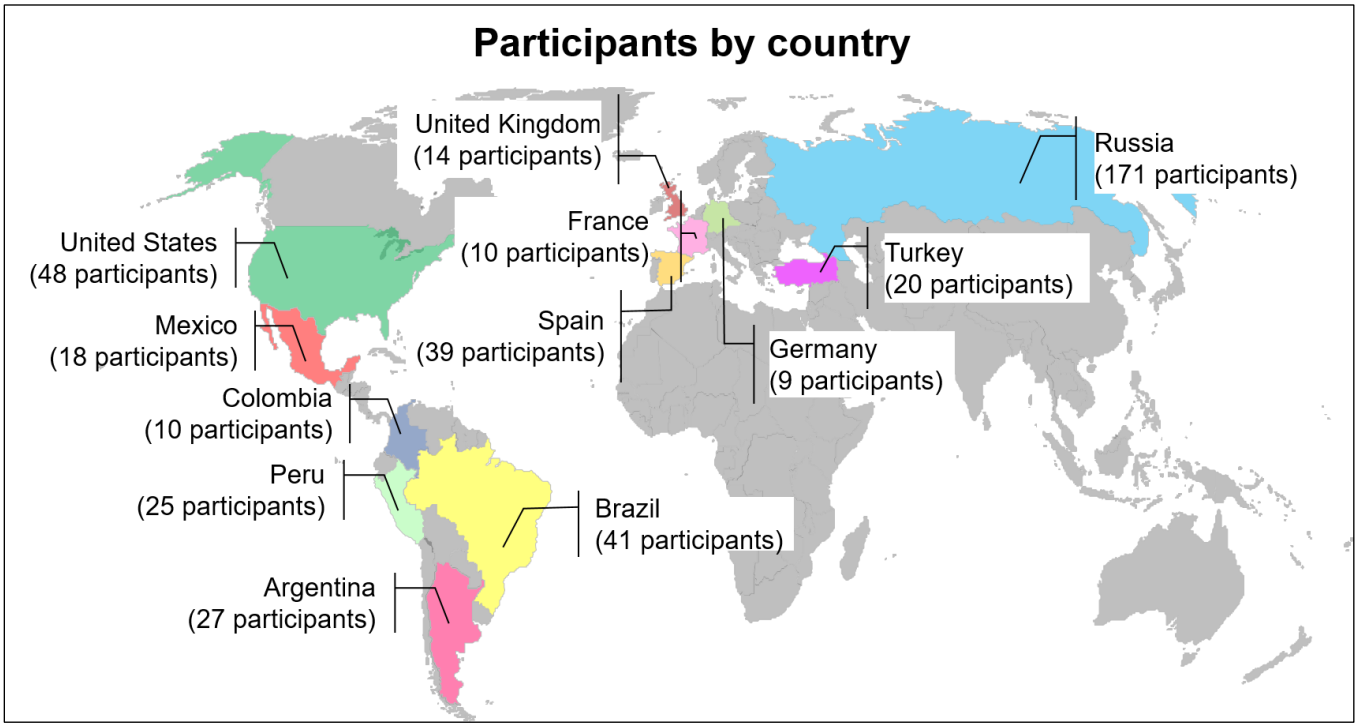
- Was there a difference in the health status of the participants who received ruxolitinib and standard treatment compared with placebo and standard treatment?

Who was in this trial?

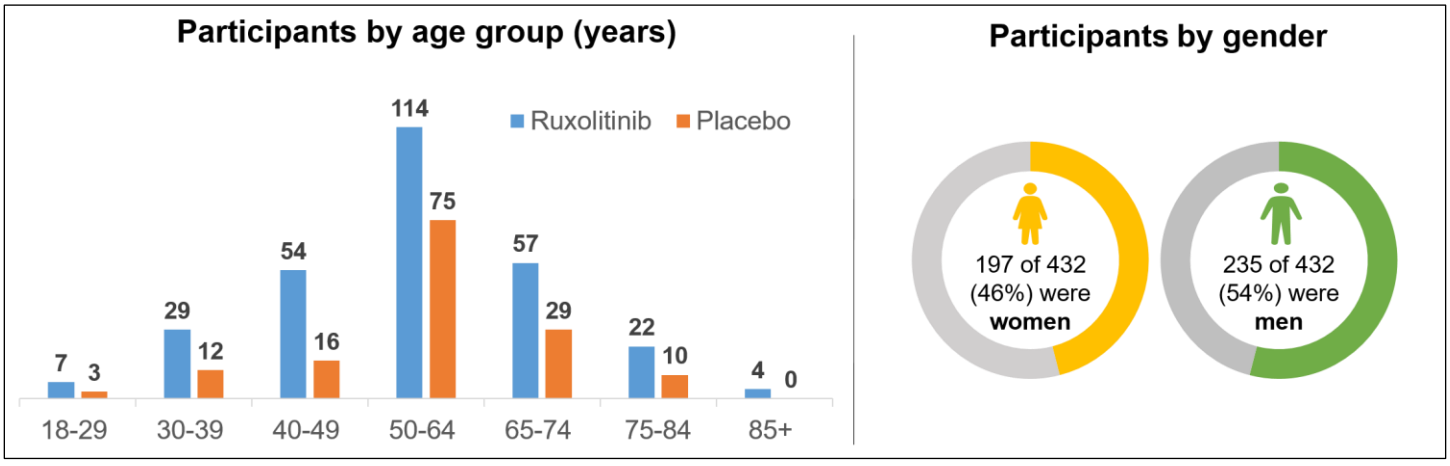
The participants could take part in this trial if they:

- were 12 years or older in age,
- had confirmed COVID-19 infection,
- either had lung infection (pneumonia) confirmed by chest scan or chest X-ray, were breathing rapidly, or had low level of oxygen in the blood requiring oxygen support, and
- were hospitalized before the start of the trial.

A total of 432 participants from 12 countries participated in this trial.



The average age of participants was 57 years. Participants' age ranged from 20 to 90 years. A higher percentage of participants were men, 235 out of 432 (54%).



This trial allowed recruitment of participants from the age of 12 years, however, none of the participants were below the age of 20 years.

The majority of participants, 428 out of 432 (99%), had lung infection (pneumonia).

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 such as:

- a full body checkup,
- a COVID-19 test (if not done already),
- a chest X-ray or chest scan to check the severity of infection caused by COVID-19,
- an Electrocardiogram (often called ECG) to measure the heart's electrical activity, and
- a blood test.

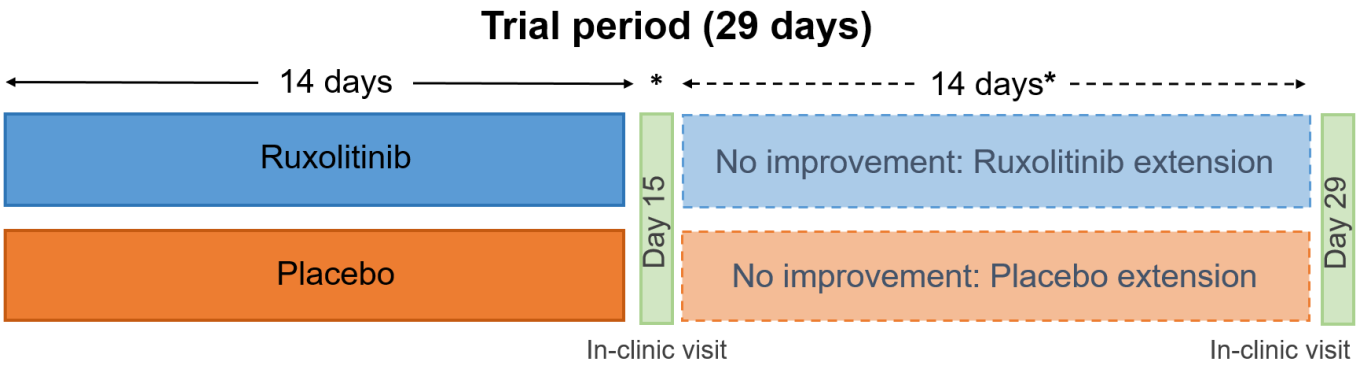
Trial period

On Day 1 of the trial, eligible participants were randomly assigned to receive ruxolitinib 5 milligram (mg) or placebo. This process is called randomization. Participants had double the chance to be assigned to the ruxolitinib group than to the placebo group.

In this trial, 287 participants received 5 mg ruxolitinib, 2 times a day and 145 participants received placebo, 2 times a day. Participants received the trial treatment for 14 days. If there was no improvement in their health status after 14 days of treatment, then the participant's doctor could determine whether trial treatment should be given for an additional 14 days. All participants received standard treatments (anti-viral drugs, anti-inflammatory drugs, antibiotics, and/ or anti-fungal drugs, etc.) for management of signs and symptoms of COVID-19 along with the trial treatment.

During the trial period, researchers conducted frequent checks on the overall health of the participants including the oxygen level in their blood.

Researchers also monitored the health of the participants who were discharged from the hospital every day by a phone call or by in-clinic visits.



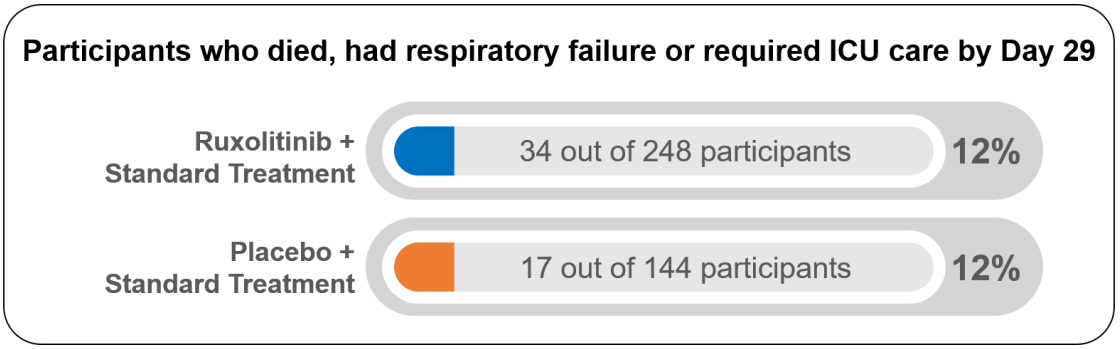
* Participants had in-clinic visits or phone calls every day until Day 29. Visits on Day 15 and Day 29 for all participants were in-clinic visits. Those whose condition did not improve after 14 days of treatment could, upon their doctor's decision, receive the same treatment for an additional 14 days.

- Participants received standard treatment for management of signs and symptoms of COVID-19 throughout the trial.
- Participants' health was monitored throughout the trial.

What were the key results of this trial?

This is a summary of the average 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 died, had respiratory failure or required intensive care by Day 29 after receiving ruxolitinib and standard treatment compared to placebo and standard treatment?



As there was no notable difference between the two treatment groups, researchers could not determine if ruxolitinib provides any benefits over and above standard treatment.

What were the other results of this trial?

Was there a difference in the health status of the participants who received ruxolitinib and standard treatment compared with placebo and standard treatment?

In this trial, researchers checked participants' hospital status, checked for any change in blood oxygen levels and the need for oxygen support, and identified high-risk participants. After treatment, researchers could not find any notable difference in the health status of the participants in the **ruxolitinib** plus standard treatment group compared with participants in the **placebo** plus standard treatment group.

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?

266 out of 424 (63%) participants had 1 or more adverse events. During the trial, 22 out of 424 (5%) participants stopped the trial drug early because of these adverse events. Serious adverse events happened in 46 out of 424 (11%) participants in the trial.

Number of Participants (%) With Adverse Events

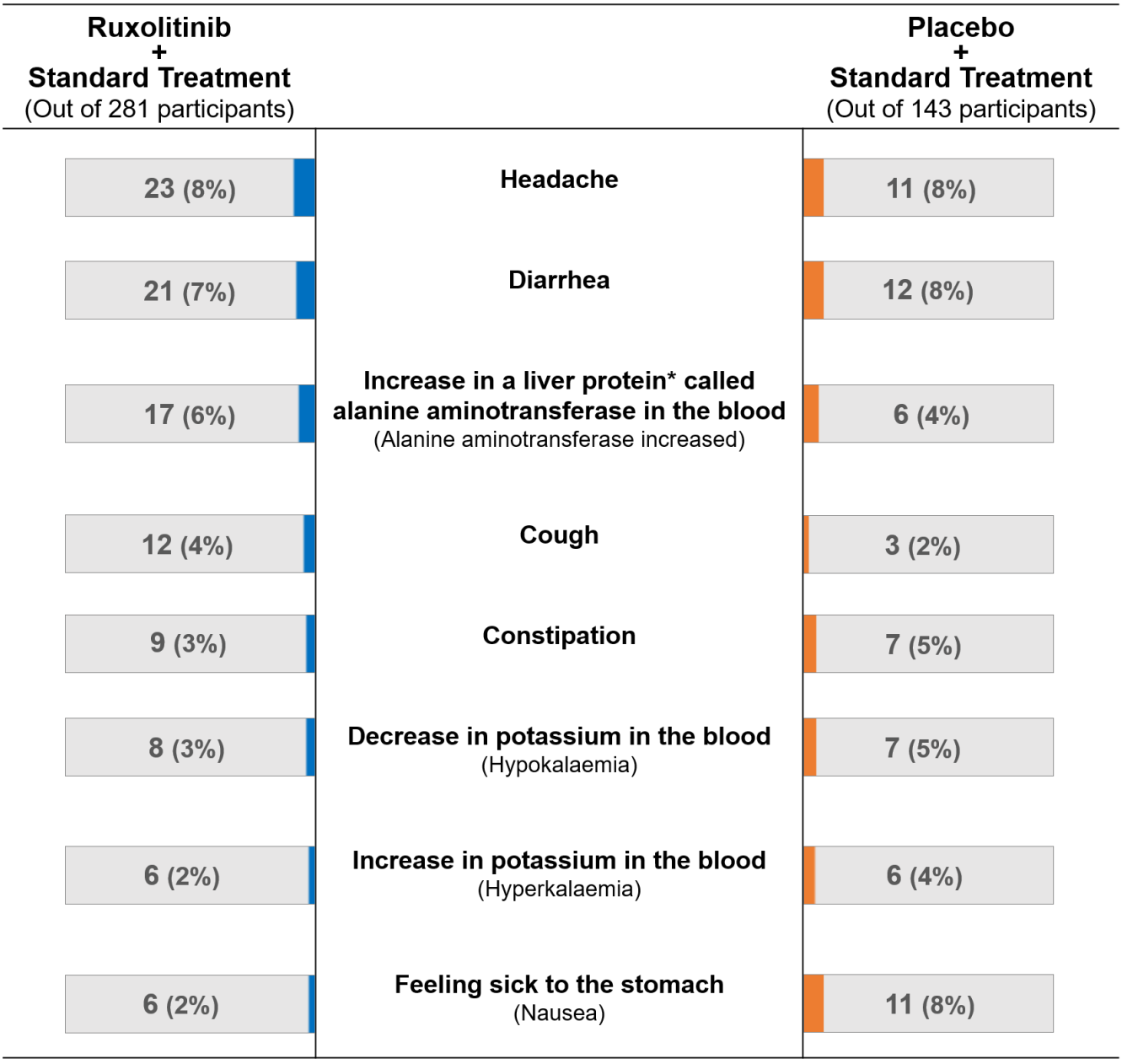
	Ruxolitinib + Standard Treatment (Out of 281 participants)	**Placebo + Standard Treatment** (Out of 143 participants)
At least 1 adverse event	173 (62%)	93 (65%)
At least 1 serious adverse event	31 (11%)	15 (11%)
Stopped drug due to adverse event	16 (6%)	6 (4%)
Death	9 (3%)	3 (2%)

12 out of 424 (3%) participants died during this trial. The average age of participants who died in the **ruxolitinib** plus standard treatment group was 72 years (ranging from 47 years to 84 years) and in the **placebo** plus standard treatment group was 67 years (ranging from 58 years to 72 years). The most common adverse events that led to death were **worsening of COVID-19** (COVID-19) and **insufficient oxygen in the lungs** (respiratory failure).

When an adverse event occurs during a trial, it does not necessarily mean it was due to the trial drugs. In this trial, the adverse event could also be due to COVID-19 or another underlying condition or to another medication the patient was taking at the same time. The same is true if a patient dies during the trial.

What were the most common non-serious adverse events?

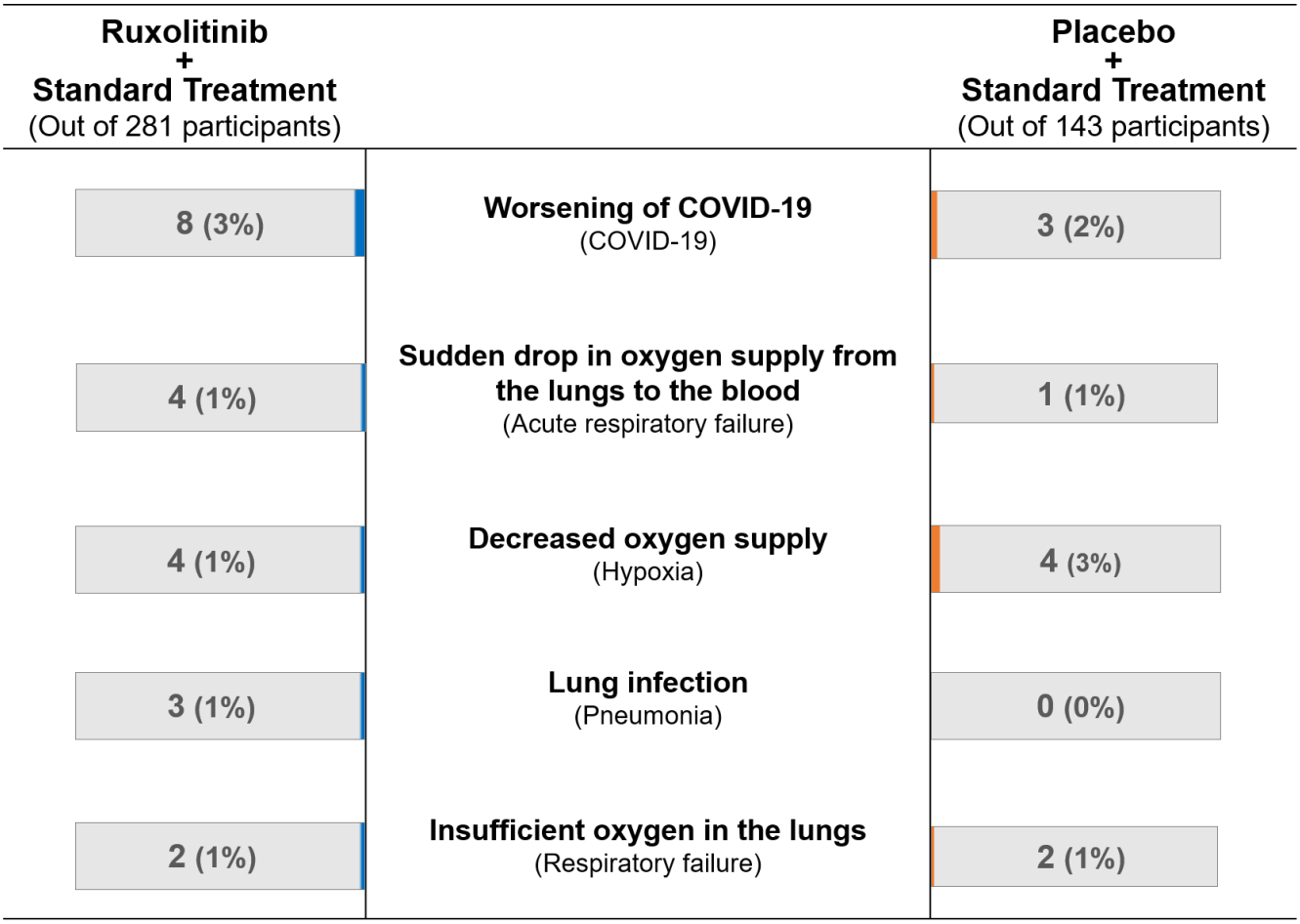
The most common non-serious adverse events that happened in at least 4% (4 out of 100) of participants in any group are presented below:



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

What were the most common serious adverse events?

The most common serious adverse events that happened in at least 2 participants in any group are shown below:



What were the most common adverse events due to which participants stopped the trial drug?

The most common adverse events that led to participants stopping the trial treatments early were **increases in a laboratory test value for a liver protein called alanine aminotransferase** (alanine transferase increased) and **a laboratory test value for liver proteins called transaminases** (transaminases increased) in the blood. An increase in the level of either of these in the blood may indicate that the liver may be inflamed or injured.

How was this trial useful?

This trial helped researchers learn about the effects and safety of ruxolitinib when given along with standard treatment for management of signs and symptoms of COVID-19, in participants with severe respiratory disease from COVID-19.

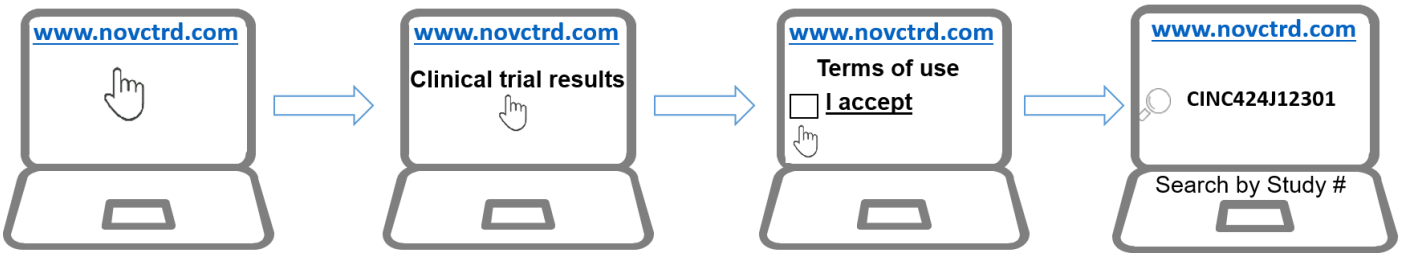
After completion of the trial, the researchers determined ruxolitinib could not help participants with COVID-19. Researchers also found that the adverse events that happened during this trial were those events that are commonly seen in people with COVID-19.

Results and lessons from this trial may be used to help design 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 additional information about this trial on the following websites:

- www.clinicaltrials.gov Use the NCT identifier NCT04362137 in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search/search Use the EudraCT identifier 2020-001662-11 in the search field.

Full clinical trial title: Phase 3 randomized, double-blind, placebo-controlled, multi-center study to assess the efficacy and safety of ruxolitinib in patients with COVID-19 associated cytokine storm (RUXCOVID)

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