AstraZeneca

Clinical Study Results

Research Sponsor: Acerta Pharma B.V., a member of the AstraZeneca group

Drug Studied: Acalabrutinib

Study Purpose: This study was done to learn about the safety of acalabrutinib and how it works in participants with COVID-19 who need hospital care

Protocol Number: D822FC00003

Thank you

Thank you for taking part in the clinical study for the study drug acalabrutinib.

You and all of the participants helped researchers learn more about acalabrutinib to help people with COVID-19 who need hospital care.

Acerta Pharma B.V. sponsored this study and believes it is important to share the results of the study with you and the public. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you. We hope it helps you understand and feel proud of your important role in medical research.

If you participated in the study and have questions about the results, please speak with the study doctor or staff at your study site.

Overview of this study

Why was the research needed?

Researchers are looking for a better way to treat people who have COVID-19 and need hospital care. Before a drug can be approved for people to get, researchers do clinical studies to find out how safe it is and how it works.

What treatments did the participants get?

The participants in this study got either:

- acalabrutinib and "best supportive care", also called BSC
- BSC only

What were the results of this study?

The main questions the researchers wanted to answer in this study were:

- **What signs and symptoms did the participants have during this study?**

  The most common signs or symptoms that the participants had during this study were headache and difficulty sleeping, also called insomnia.

- **Did acalabrutinib when added to BSC help the participants stay alive and breathe without help?**

  No. Overall, the researchers found that acalabrutinib when added to BSC did not help the participants stay alive and breathe without help.

- **What medical problems did the participants have during this study?**

  There were 23.3% of participants who got acalabrutinib with BSC who had medical problems that the study doctors thought might be related to acalabrutinib during the study. The most common medical problem was headache.

More details about the results of this study are included later in this summary.

Where can I learn more about this study?

You can find more information about this study on the websites listed on the last page. When a full report of the study results is available, it also can be found on these websites.

Who took part in this study?

The researchers asked for the help of men and women with COVID-19 who needed hospital care. The participants in this study were 23 to 80 years old when they joined.

The study included 62 participants in the United States.

Why was the research needed?

Researchers are looking for a better way to treat COVID-19 in people whose infection is severe enough that they need hospital care. Before a drug can be approved for people to get, researchers do clinical studies to find out how it works and how safe it is.

In this study, the researchers wanted to find out about the safety of acalabrutinib in a small number of participants with COVID-19 who needed hospital care. They also wanted to find out how acalabrutinib worked for these participants.

COVID-19 is an infectious disease that can cause swelling in the airways and lungs. This can lead to lung damage, difficulty breathing, and other medical problems. If the swelling is severe, people who have COVID-19 may need a breathing tube and a ventilator to help them breathe.

The study drug, acalabrutinib, is used to treat certain types of cancer. But in animal studies, researchers have found that acalabrutinib may also reduce swelling in the lungs. Based on the results from these animal studies, researchers thought that acalabrutinib might be able to decrease swelling in the lungs and airways in patients who have COVID-19.

What was the purpose of this study?

The main questions the researchers wanted to answer in this study were:

- What signs and symptoms did the participants have during this study?
- Did acalabrutinib when added to BSC help the participants stay alive and breathe without help?
- What medical problems did the participants have during this study?

The answers to these questions were important to know before doing other studies to find out if acalabrutinib helps improve the health of people with COVID-19.

What treatments did the participants get?

The participants in this study got either:

- acalabrutinib and "best supportive care", also called BSC
- BSC only

BSC was decided for each participant by their study doctor. The participants who got acalabrutinib took it as a capsule by mouth. The doses of acalabrutinib were measured in milligrams, also known as mg.

This was an "open-label" study. This means the participants, researchers, study doctors, and other study staff knew what each participant was getting.

A computer program was used to randomly choose the treatment each participant got. This helps make sure the groups are chosen fairly. Researchers do this so that comparing the results of each treatment is as accurate as possible.

The participants got study treatment while they were already in the hospital because of COVID-19.

The chart below shows the treatments the researchers planned to study.

	Acalabrutinib and BSC	BSC only
	31 participants	31 participants
	• 100 mg of acalabrutinib as capsules by mouth • BSC as decided by the study doctors	• BSC as decided by the study doctors
	• acalabrutinib twice a day for 10 days • BSC as decided by the study doctors	• BSC as decided by the study doctors

What happened during this study?

The participants were in the study for about 3 months. But, the entire study took 5 months to finish.

The study started in June 2020 and ended in November 2020.

The COVID-19 pandemic did not affect the way the study was done, the results of the study, or the conclusions of the researchers.

The chart below shows what happened during the study.

Before the participants got study treatment

1 visit

The study doctors:

- checked the health of the participants to make sure they could join the study
- did physical exams and asked about the participants' medications and any medical problems
- took blood and urine samples
- checked the participants' lung health using CT or X-ray scans
- checked the participants' heart health using an ECG, and using an echocardiogram for some participants
- did a test to check if the participants had COVID-19

Up to 1 week

While the participants got study treatment

Up to 10 visits from the study doctors while the participants were in the hospital

The study doctors:

- did physical exams and asked about the participants' medications and any medical problems
- checked the participants' lung health using CT or X-ray scans for some participants
- took blood and urine samples
- checked the participants' heart health using an ECG, and using an echocardiogram for some participants

The participants:

- got study treatment

10 days

After the participants got study treatment

1 visit from the study doctors each day while the participants were in the hospital, and then up to 4 visits by the participants to a study site

The study doctors:

- did physical exams and asked about the participants' medications and any medical problems at some visits
- checked the participants' lung health using CT or X-ray scans while they were in the hospital
- took blood and urine samples at some visits
- checked the participants' heart health using an echocardiogram while they were in the hospital

The participants:

- got BSC while they were in the hospital

Up to 12 weeks

What were the results of this study?

This is a summary of the main results from this study overall. The results each participant had might be different and are not in this summary. A full list of the questions researchers wanted to answer can be found on the websites listed at the end of this summary. When a full report of the study results is available, it can also be found on these websites.

Researchers look at the results of many studies to decide which treatments work best and are safest. Other studies may provide new information or different results. Always talk to a doctor before making any treatment changes.

What signs and symptoms did the participants have during this study?

To answer this question, the study doctors did tests and measurements before the participants got treatment, and throughout the study.

The study doctors:

- did physical exams and tested the participants' blood and urine samples to check their overall health
- used CT or X-ray scans to check the participants' lung health
- checked the participants' heart health using ECGs, and using echocardiograms for some participants

Overall, the researchers found that there were some small changes in the results of these tests and measurements. But, the researchers did not consider these changes to be relevant to the results of the study.

The study doctors also kept track of the "adverse events" that the participants had. An adverse event is any sign or symptom that participants have during a study. Doctors keep track of all the adverse events that happen in studies, even if they do not think the adverse events might be related to the study treatment.

Later in this document, there will be a summary of the adverse events that the study doctors thought might be related to acalabrutinib. This section is a summary of all the adverse events, whether they might be related to the study treatment or not. An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care.

Adverse events may or may not be caused by the treatments in the study. A lot of research is needed to know whether a treatment causes an adverse event.

There was 1 participant who was planned to get acalabrutinib and BSC, but this participant did not get any acalabrutinib. So, the results below show this participant as part of the group who got BSC only.

	Acalabrutinib and BSC (out of 30 participants)	BSC only (out of 32 participants)
How many participants had adverse events?	56.7% (17)	46.9% (15)
How many participants had serious adverse events?	13.3% (4)	18.8% (6)
How many participants stopped getting acalabrutinib due to adverse events?	13.3% (4)	None of the participants in this group were getting acalabrutinib

The most common serious adverse event was a urinary tract infection.

The most common adverse events were:

- Headache
- Increased levels of a liver protein called ALT, which can be a sign of liver damage
- Increased levels of blood sugar
- Difficulty sleeping, also called insomnia
- Rash

Did acalabrutinib when added to BSC help the participants stay alive and breathe without help?

No. Overall, the researchers found that acalabrutinib when added to BSC did not help the participants stay alive and breathe without help.

To answer this question, the researchers counted the number of participants who were alive and could breathe without help 4 weeks after the study started. They did this for each treatment group. The researchers calculated these numbers as a percentage. Then, they compared the results in the group who got acalabrutinib and BSC to the results in the group who got BSC only.

The researchers found that after 4 weeks of treatment, the percentage of participants who stayed alive and could breathe without help was similar between the 2 groups.

The percentage of participants who were alive and could breathe without help after 4 weeks of treatment was:

- 80.6% of those who were planned to get acalabrutinib with BSC. This was 25 out of 31 participants.
- 83.9% of those who were planned to get BSC only. This was 26 out of 31 participants.

What medical problems happened during this study?

This section is a summary of the medical problems the participants had during the study that the study doctors thought might be related to acalabrutinib. These medical problems are called "adverse reactions". An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or requires hospital care. This summary does not include adverse reactions for the participants who got BSC only.

These adverse reactions may or may not be caused by acalabrutinib. A lot of research is needed to know whether a drug causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for acalabrutinib.

The websites listed at the end of this summary may have other information about adverse reactions or other medical problems that happened during this study.

Did any adverse reactions happen during this study?

There were 23.3% of participants who got acalabrutinib and BSC who had adverse reactions. This was 7 out of 30 participants.

There were 6.7% of participants who got acalabrutinib and BSC who stopped getting acalabrutinib due to adverse reactions. This was 2 out of 30 participants.

What serious adverse reactions happened during this study?

None of the participants who got acalabrutinib and BSC had serious adverse reactions.

What adverse reactions happened during this study?

The most common adverse reaction was headache.

The table below shows the adverse reactions thought to be related to acalabrutinib that happened in the participants who got acalabrutinib with BSC during this study.

Adverse reactions

Adverse reaction	Acalabrutinib and BSC (out of 30 participants)
Headache	6.7% (2)
Bile reflux	3.3% (1)
Decreased levels of platelets, a type of blood cell that helps form blood clots to stop bleeding	3.3% (1)
Increased levels of a liver protein called ALT, which can be a sign of liver damage	3.3% (1)
Indigestion	3.3% (1)
Mouth ulcer	3.3% (1)
Rash	3.3% (1)
Shingles	3.3% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about the safety of acalabrutinib and how it works in patients with COVID-19 who need hospital care.

Researchers look at the results of many studies to decide which treatments work best and are safest. This summary shows only the main results from this one study. Other studies may provide new information or different results.

Further clinical studies with acalabrutinib in people who have COVID-19 are not planned.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. If more information about the study results is available, it can also be found here.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT04380688"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D822FC00003"** into the search box, and click **"Find a Study"**.

Full Study Title: A Phase 2, Open Label, Randomized Study of the Efficacy and Safety of Acalabrutinib with Best Supportive Care Versus Best Supportive Care in Subjects Hospitalized with COVID-19

Acerta Pharma B.V. Protocol Number: D822FC00003

National Clinical Trials Number: NCT04380688

Acerta Pharma B.V. sponsored this study and has its headquarters at Oss, The Netherlands.

The phone number for the AstraZeneca Information Center is +1-877-240-9479.

Thank you

Clinical study participants and their families belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP is not involved in recruiting participants for clinical studies, nor is it involved in conducting clinical studies.

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