AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: Acalabrutinib

Study Purpose: This study was done to learn more about how acalabrutinib acts in the blood in healthy participants when given in different ways

Protocol Number: D8223C00005

Thank you!

Thank you for taking part in the clinical study for the study drug acalabrutinib. AstraZeneca AB sponsored this study and believes it is important to share the results. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you.

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

Who took part in this study?

The researchers asked for the help of healthy men and women. The participants in this study were 20 to 54 years old when they joined.

The study included 20 participants in Germany.

Why was the research needed?

Researchers are looking for a way to treat the coronavirus disease, also called COVID-19. Before a drug can be approved for people to take, researchers do clinical studies to find out how safe it is and how it works.

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 have a breathing tube inserted and may not be able to swallow a pill. They may also have increased stomach acid while they have a breathing tube in.

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. The results from these animal studies showed that acalabrutinib might be able to decrease swelling in the lungs and airways.

Acalabrutinib has been available as a capsule for some time. In a capsule medication, the drug is inside a shell that is broken down in the gut to release the drug. Researchers have also now developed acalabrutinib as a tablet. In a tablet medication, the drug is packed in a pill without a shell.

Patients who have a breathing tube are often given antacids known as "proton-pump inhibitors" to reduce stomach acid and prevent ulcers. Earlier studies in healthy participants have shown that when there is less stomach acid, it is harder for acalabrutinib to get into the blood when given as a capsule. Drinking flat Coca-Cola adds some acid to the stomach. This may help acalabrutinib, when given as a capsule, get into the blood. Acalabrutinib as a tablet is expected to be less affected by stomach acid than acalabrutinib as a capsule.

The researchers in this study wanted to learn more about acalabrutinib and its metabolite in healthy participants and whether acalabrutinib as a tablet was affected by stomach acid. A metabolite is a substance that the body makes when it breaks down a drug. The body removes metabolites through fluids, such as urine or sweat.

In this study, the researchers wanted to compare how much acalabrutinib got into the blood:

- when given as a capsule or as a tablet
- when given as a tablet with and without a proton-pump inhibitor called rabeprazole

What was the purpose of this study?

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

- How much of acalabrutinib and its metabolite got into the blood when given as a capsule or as a tablet?
- Did rabeprazole affect how much of acalabrutinib given as a tablet and its metabolite got into the blood?
- What medical problems did the participants have during the study?

The researchers wanted to learn the answers to these questions before doing other studies to learn if acalabrutinib could help people who have COVID-19.

This study was planned to have 2 parts. When Part 1 ended, there was information available from other studies in patients with COVID-19. This information showed that acalabrutinib did not help those patients. So, the researchers did not continue to Part 2 of the study.

What treatments did the participants get?

The participants in this study got acalabrutinib through a tube in the nose and rabeprazole as a tablet by mouth.

This study was a "crossover" study. There were 2 groups of participants. A crossover study means that all of the participants got the same 3 treatments, but the 2 groups got the treatments in a different order.

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

The chart below shows the 3 treatments the researchers studied.

	Treatment 1	Treatment 2	Treatment 3
	• 10 participants in Group 1 • 10 participants in Group 2	• 10 participants in Group 1 • 10 participants in Group 2	• 10 participants in Group 1 • 10 participants in Group 2
	• acalabrutinib as a tablet mixed in water and given as a liquid through a tube in the nose	• acalabrutinib as a capsule mixed in flat Coca-Cola and given as a liquid through a tube in the nose	• acalabrutinib as a tablet mixed in water and given as a liquid through a tube in the nose • rabeprazole as a tablet by mouth
	• acalabrutinib and water 1 time	• acalabrutinib and flat Coca-Cola 1 time	• acalabrutinib and water 1 time • rabeprazole twice each day for 3 days, and then once on the day the participants took acalabrutinib

What happened during this study?

The study started in October 2020 and ended in December 2020.

Before the participants got study treatment, they visited their study site 1 time. This part of the study lasted for up to 4 weeks because the participants joined at different times. At this visit, the study doctors made sure the participants could join the study. They also:

- did a physical exam and asked about the participants' medications and any medical problems they were having
- did a test for COVID-19
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG

The study doctors also did these tests and measurements throughout the study.

While the participants got study treatment, they visited their study site 3 times. Each time, they:

- had a breathing tube inserted
- stayed at their study site overnight for 4 nights
- got a different study treatment

Before visiting their study site to get Treatment 3, the participants also took rabeprazole at home for 2 days.

The participants did not get any treatment for at least 4 days in between visits. This was done so the study treatment could be "washed out" of their bodies before they got the next treatment.

Up to 10 days after the participants got their last study treatment, they visited their study site 1 time. At this visit, the study doctors checked the health of the participants.

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.

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.

The websites listed at the end of this summary may have a full report of the study results.

How much of acalabrutinib and its metabolite got into the blood when given as a capsule or as a tablet?

To answer this question, the study doctors took blood samples from the participants throughout the study.

In these samples, the study doctors measured:

- the average total amount of acalabrutinib and its metabolite in the blood during the study
- the average highest amount of acalabrutinib and its metabolite in the blood during the study

Then, the researchers compared the results when the participants got acalabrutinib as a tablet mixed in water during Treatment 1 with when they got it as a capsule mixed in flat Coca-Cola during Treatment 2.

Overall, the researchers found that both the average total and average highest amounts of acalabrutinib and its metabolite in the blood were similar when the participants got Treatment 1 and Treatment 2.

Did rabeprazole affect how much of acalabrutinib given as a tablet and its metabolite got into the blood?

No. The researchers found that overall, rabeprazole did not affect how much of acalabrutinib and its metabolite got into the blood.

To answer this question, the study doctors measured:

- the average total amount of acalabrutinib and its metabolite in the blood during the study
- the average highest amount of acalabrutinib and its metabolite in the blood during the study

Then, the researchers compared:

- the results when the participants got acalabrutinib as a tablet mixed in water and **did not** take rabeprazole during Treatment 1
- the results when the participants got acalabrutinib as a tablet mixed in water and **did** take rabeprazole during Treatment 3

Overall, the researchers found that both the average total and average highest amounts of acalabrutinib and its metabolite in the blood were similar when the participants got Treatment 1 and Treatment 3. This told them that rabeprazole did not affect how much of acalabrutinib and its metabolite got into the blood.

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.

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 15.0% of participants who had adverse reactions. This was 3 out of 20 participants.

- 5.0% of participants had adverse reactions while they got acalabrutinib as a tablet mixed in water during Treatment 1. This was 1 out of 20 participants.
- 10.0% of participants had adverse reactions while they got acalabrutinib as a capsule mixed in flat Coca-Cola during Treatment 2. This was 2 out of 20 participants.
- None of the participants had adverse reactions while they got acalabrutinib as a tablet mixed in water and rabeprazole during Treatment 3.

None of the participants stopped taking study treatment due to adverse reactions.

What serious adverse reactions happened during this study?

None of the participants had serious adverse reactions during this study.

What adverse reactions happened during this study?

The table below shows the adverse reactions that happened during this study.

Adverse reactions

Adverse reaction	Treatment 1 acalabrutinib with water (out of 20 participants)	Treatment 2 acalabrutinib with Coca-Cola (out of 20 participants)	Treatment 3 acalabrutinib and rabeprazole (out of 20 participants)
Decreased appetite	5.0% (1)	0.0% (0)	0.0% (0)
Diarrhea	0.0% (0)	5.0% (1)	0.0% (0)
Discomfort in the belly	0.0% (0)	5.0% (1)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn more about how acalabrutinib acts in the blood of healthy participants when given in different ways.

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 1 study. Other studies may provide new information or different results.

Further clinical studies with acalabrutinib in the treatment of 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.

- www.clinicaltrials.gov Once you are on the website, type **"NCT04564040"** into the search box and click **"Search"**
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D8223C00005"** into the search box, and click **"Find a Study"**.

Full Study Title: A 2-Part, Phase I, Open-label, Single-dose, Sequential, Randomized, Crossover Study of Acalabrutinib Tablet Suspension Delivered via Nasogastric Tube in Healthy Subjects to Evaluate Relative Bioavailability and Proton-pump Inhibitor (Rabeprazole) Effect

AstraZeneca AB Protocol Number: D8223C00005

National Clinical Trials Number: NCT04564040

AstraZeneca, AB sponsored this study and has its headquarters in Södertälje, Sweden.

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

Thank you!

Clinical study participants 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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