AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: Acalabrutinib

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

Protocol Number: D8220C00018

Thank you!

Thank you for taking part in the clinical study for the study drug acalabrutinib. AstraZeneca 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 21 to 55 years old when they joined.

The study included 54 participants in the United States.

Why was the research needed?

Researchers are looking for a way to treat B-cell lymphoid cancer, also known as B-cell lymphoma. This is a cancer of the white blood cells in the immune system. 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.

B-cell lymphoid cancer is a type of blood cancer that affects B lymphocytes, a type of white blood cell in the immune system. The study drug, acalabrutinib, is used to treat certain types of blood cancers. It works by stopping the cancer cells from growing out of control.

Acalabrutinib is already available as a capsule. Researchers are now studying acalabrutinib in a tablet form.

Some people take antacids, also known as "proton-pump inhibitors" to decrease stomach acid and prevent open sores in part of the intestine. These sores are called "ulcers". Earlier studies in healthy participants have shown that when there is less stomach acid, it is harder for acalabrutinib taken as a capsule to get into the blood. Researchers think that acalabrutinib as a tablet may be less affected by stomach acid than acalabrutinib as a capsule.

Earlier studies in healthy participants have also shown that eating a high-fat meal makes it harder for acalabrutinib taken as a capsule to get into the blood.

In this study, the researchers wanted to learn more about acalabrutinib in healthy participants and to compare how much acalabrutinib got into the blood when taken as a capsule or as a tablet. The researchers also wanted to find out if the particle size of acalabrutinib affected how much acalabrutinib got into the blood.

What was the purpose of this study?

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

- Did taking acalabrutinib as a capsule or as a tablet affect how much got into the blood?
- Did the particle size of acalabrutinib affect how much got into the blood?
- Did the participants find the smell and taste of acalabrutinib tablets mixed with water to be acceptable?
- 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 B-cell lymphoid cancers.

What treatments did the participants take?

There were 2 Parts in this study. In Part 1, the participants took acalabrutinib as a capsule by mouth or as a tablet by mouth. There were 4 different treatment groups in each part. In some treatment groups, the participants did not eat for 10 or more hours before taking treatment.

All of the participants in Part 1 took Treatments 1 and 2. Then, they took either Treatment 3 or 4. For those who took Treatment 4, they also took a proton-pump inhibitor called rabeprazole as a tablet by mouth.

In Part 2, a different group of participants took acalabrutinib as a tablet or as a liquid by mouth. All of the participants in this part took all 4 treatments.

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

This study was a "crossover" study. This means that the participants took similar treatments in a different order. A computer program was used to randomly choose the order in which each participant took their study treatments. 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 chart below shows the treatments in Part 1.

	Treatment 1	Treatment 2	Treatment 3	Treatment 4
	30 participants • All of the participants took Treatment 1 and Treatment 2 • Then the participants also took either Treatment 3 or Treatment 4			
	• Acalabrutinib as a capsule, without eating for 10 hours or more before	• Acalabrutinib as a tablet, without eating for 10 hours or more before	• Acalabrutinib as a tablet, 30 minutes after eating	• Acalabrutinib as a tablet, without eating for 10 hours or more before, and rabeprazole as a tablet 2 hours before taking acalabrutinib
	• Acalabrutinib and water once	• Acalabrutinib and water once	• Acalabrutinib and water once	• Acalabrutinib and water once, and rabeprazole twice each day for 3 days with food, then once on the day the participants took acalabrutinib, without eating before

The chart below shows the treatments in Part 2.

	Treatment 1	Treatment 2	Treatment 3	Treatment 4
	**24 participants** • All of the participants took all 4 treatments			
	• Acalabrutinib as a tablet • Without eating for 10 hours or more before	• Acalabrutinib with small particle size as a tablet • Without eating for 10 hours or more before	• Acalabrutinib with large particle size as a tablet • Without eating for 10 hours or more before	• Acalabrutinib as a liquid • Without eating for 10 hours or more before
	Acalabrutinib and water once			

Each time the participants took a tablet, they also took another pill that measured the acid level in their stomach and the movement of food and water through their intestines.

What happened during this study?

The study started in June 2020 and ended in January 2021.

Before the participants took study treatment, they visited their study site 1 time. This part of the study lasted for up to 4 weeks because the participants joined the study at different times. At this visit, the study doctors made sure that 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. During the study, the participants had a breath test on the first day of each study treatment.

In Part 1, while the participants took study treatment, they visited their study site 3 times. At each visit, they:

- stayed at their study site overnight for 4 nights
- took a different study treatment

During Part 1, each participant took 3 of the 4 study treatments. For the participants who got Treatment 4, they took rabeprazole at home for 3 days before visiting their study site to get Treatment 4.

Between visits to their study site, the participants did not get any treatment for at least 7 days. This was done so that the study treatment could be "washed out" of their bodies before they took the next treatment.

In Part 2, while the participants took study treatment, they visited their study site 4 times. At each visit, they:

- stayed at their study site overnight for 4 nights
- took a different study treatment

During Part 2, the participants took 4 different study treatments.

Between visits to their study site, the participants did not get any treatment for at least 3 days. This was done so that the study treatment could be "washed out" of their bodies before they took the next treatment.

About 7 to 10 days after the participants took their last study treatment, they visited their study site 1 time. At this visit, the study doctors checked the health of the participants and did blood tests for some 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 more information about the study results.

Did taking acalabrutinib as a capsule or as a tablet affect how much got into the blood?

Overall, the researchers found that both the average total and average highest amounts of acalabrutinib in the blood were similar when the participants took acalabrutinib as a capsule or a tablet in Part 1.

To answer this question, the study doctors took blood samples from the participants in Part 1 throughout the study.

In these samples, the study doctors measured:

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

Then, the researchers compared the results from Treatment 1 and Treatment 2 of Part 1. For these treatments, the participants took:

- acalabrutinib as a **capsule** after not eating for 10 hours or more
- acalabrutinib as a **tablet** after not eating for 10 hours or more

Did the particle size of acalabrutinib affect how much got into the blood?

The researchers found that overall, the particle size of acalabrutinib in the tablets did not affect how much acalabrutinib got into the blood.

To answer this question, in Part 2, the study doctors measured:

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

Then, the researchers compared the results from Treatments 1, 2, and 3 when the participants took:

- acalabrutinib with a standard particle size
- acalabrutinib with a small particle size
- acalabrutinib with a large particle size

Did the participants find the smell and taste of acalabrutinib tablets mixed with water to be acceptable?

Overall, the researchers found that the smell of the acalabrutinib tablets mixed with water was acceptable to the participants, but the taste was bitter.

To answer this question, the researchers asked the participants in Part 2 to fill out surveys about the smell and taste of the acalabrutinib tablets when mixed with water. Most participants could not sense any smell. The participants found that the strongest type of taste they could sense was a bitter taste.

The researchers concluded that, in the future, they will not need to change the smell of the acalabrutinib tablets mixed with water, but they might need to change the taste.

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?

In Part 1:

- There were 6.7% of participants who had adverse reactions. This was 2 out of the 30 participants who took any study treatment.
- None of the participants stopped taking study treatment due to adverse reactions.

In Part 2:

- There were 4.2% of participants who had adverse reactions. This was 1 out of the 24 participants who took any study treatment.
- None of the participants stopped taking study treatment due to adverse reactions.

Did any serious adverse reactions happen during this study?

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

What adverse reactions happened during this study?

During the study, the participants did not take all of the study treatments. The safety results in this part of the summary are for the participants who took the indicated study treatments.

In Part 1:

- 3.4% of participants had an adverse reaction of **headache**. This was 1 out of the 29 participants who took Treatment 2.
- 3.4% of participants had an adverse reaction of **increased levels of ALT**, which is a protein made by the liver. This was 1 out of the 29 participants who took Treatment 2.

In Part 2:

- 4.2% of participants had an adverse reaction of **nausea**. This was 1 out of the 24 participants who took Treatment 4.

How has this study helped patients and researchers?

This study helped researchers learn more about how acalabrutinib acts in the blood in healthy participants when taken 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 one study. Other studies may provide new information or different results.

Further clinical studies with acalabrutinib for the treatment of B-cell lymphoid cancer are not currently 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 **"NCT04488016"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D8220C00018"** 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 New Acalabrutinib Maleate Tablet in Healthy Subjects to Evaluate Relative Bioavailability, Proton Pump Inhibitor (Rabeprazole) Effect, Food Effect and Particle Size Effect

AstraZeneca Protocol Number: D8220C00018

National Clinical Trials Number: NCT04488016

AstraZeneca sponsored this study and has its headquarters in Cambridge, UK.

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.

CISCRP | One Liberty Square, Suite 1100 • Boston, MA 02109 | 1-877-MED-HERO | www.ciscrp.org

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