AstraZeneca

Clinical Study Results

Research Sponsor: Acerta Pharma BV, a member of AstraZeneca group of companies

Treatment Studied: Acalabrutinib

Study Purpose: This study was done to learn how acalabrutinib works and about its safety in participants with leukemia

Protocol Number: 15-H-0016

Thank you

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

You and all of the participants helped researchers learn more about acalabrutinib to help people with leukemia.

Acerta Pharma BV, a member of AstraZeneca group of companies 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 leukemia. Before a treatment can be approved for people to take, researchers do clinical studies to find out how it works and how safe it is.

What treatment did the participants take?

The participants in this study took acalabrutinib.

What were the results of this study?

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

- **How many participants responded to treatment with acalabrutinib?**

  Overall, the researchers found that after taking acalabrutinib:

  - **90.3%** of the participants whose leukemia had come back or stopped responding to prior treatment responded to treatment with acalabrutinib. This was 28 out of 31 participants.
  - **87.5%** of the participants who had not received prior treatment for leukemia responded to treatment with acalabrutinib. This was 14 out of 16 participants.

- **What medical problems happened during this study?**

  During the study, there were **100.0%** of participants who had medical problems that the study doctors thought might be related to the study drug. For the participants whose leukemia had come back or stopped responding to prior treatment, the most common medical problem was headache. For the participants who had not received prior treatment for leukemia, the most common medical problems were bleeding under the skin and 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 those websites.

Who took part in this study?

The researchers asked for the help of men and women with chronic lymphocytic leukemia or small lymphocytic leukemia. The participants' leukemia had either:

- come back or stopped responding to prior treatment, which is called "**relapsed/refractory**", or
- been high-risk and never treated before, which is called "**treatment-naïve**"

The participants in this study were 45 to 83 years old when they joined. The study included 48 participants in the United States.

Why was the research needed?

Researchers are looking for a better way to treat leukemia. Before a treatment can be approved for people to take, researchers do clinical studies to find out how it works and how safe it is.

Leukemia is a type of cancer that develops slowly. In people with lymphocytic leukemia, the bone marrow is not able to control the growth of a type of white blood cell called "lymphocytes". This can cause symptoms such as frequent infections, swollen lymph nodes, and tiredness.

In people with **chronic** lymphocytic leukemia, the cancer cells are mostly in the blood and bone marrow.

In people with **small** lymphocytic leukemia, the cancer cells are mostly in the lymph nodes.

Many people with either type of lymphocytic leukemia respond to standard treatment or do not need treatment at all. But, some people have a form of lymphocytic leukemia that does not always respond to standard treatment. This is why researchers are looking for other treatment options that work in different ways. The study treatment, acalabrutinib, is designed to kill blood cancer cells by stopping certain proteins that help these cells live and grow.

In this study, the researchers wanted to find out if acalabrutinib works in a small number of participants with leukemia. They also wanted to find out if the participants had any medical problems during the study.

What was the purpose of this study?

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

- How many participants responded to treatment with acalabrutinib?
- What medical problems happened during this study?

The answers to these questions are important to know before other studies can be done to find out if acalabrutinib helps improve the health of people with leukemia.

What treatments did the participants take?

In this study, the participants took acalabrutinib as a capsule by mouth. The doses of acalabrutinib were measured in milligrams, also known as "mg".

The participants took acalabrutinib either once a day or twice a day.

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

A computer program was used to randomly choose the treatment each participant took. 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 the researchers planned to study.

	Relapsed/Refractory	Treatment-Naïve
	32 participants	16 participants
	• 100 mg of acalabrutinib twice a day, or • 200 mg of acalabrutinib once a day	

What happened during this study?

The participants were in the study until:

- their cancer got worse
- the study doctors thought they should stop taking study treatment
- they left the study for another reason

The entire study took about 5 and a half years to finish. The study started in January 2015 and ended in June 2020.

The chart below shows what happened during the study.

Before the participants took study treatment

1 or more visits

The study doctors:

- checked the health of the participants to make sure they could join the study
- did a physical exam and asked about the participants' medications and any medical problems
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG
- took pictures of the participants' tumors using CT scans
- used a needle to take a sample of some participants' bone marrow
- used surgery to take a sample of some participants' lymph nodes

The participants:

- answered questions about their symptoms and ability to perform daily activities

Up to 1 month

While the participants took study treatment

1 to 2 visits per month for 6 months then 1 visit every 3 months

At some visits, the study doctors:

- did a physical exam and asked about the participants' medications and any medical problems
- took blood and urine samples
- took pictures of the participants' tumors using CT scans
- used a needle to take a sample of some participants' bone marrow
- used surgery to take a sample of some participants' lymph nodes

The participants:

- took their study treatment
- answered questions about their symptoms and ability to perform daily activities

Until the cancer got worse, or another reason

After the participants took study treatment

1 or more visits

The study doctors:

- did a physical exam and asked about the participants' medications and any medical problems
- took blood and urine samples

The participants:

- answered questions about their symptoms and ability to perform daily activities

Until the end of the study

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 that 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.

The results below include only the participants who took acalabrutinib for more than 6 months. One participant from the relapsed/refractory group was not included for this reason.

How many participants responded to treatment with acalabrutinib?

Overall, the researchers found that after taking acalabrutinib:

- **90.3%** of the participants in the **relapsed/refractory** group responded to treatment with acalabrutinib. This was 28 out of 31 participants.

90.3%
28 out of 31 participants

- **87.5%** of the participants in the **treatment-naïve** group responded to treatment with acalabrutinib. This was 14 out of 16 participants.

87.5%
14 out of 16 participants

To answer this question, the study doctors measured many different things to assess the participants' leukemia throughout the study, including:

- size of the lymph nodes, spleen, and liver
- amounts of certain types of cells and proteins in the blood, such as lymphocytes, platelets, hemoglobin, and neutrophils
- health of bone marrow

The study doctors analyzed these different measurements using a set of rules called the International Workshop on Chronic Lymphocytic Leukemia guidelines, also called the "IWCLL" guidelines.

Then, the study doctors determined if each participant had a response to treatment with acalabrutinib. A "response" means that the participant's leukemia symptoms decreased after treatment. According to the IWCLL guidelines, a participant's response to treatment can be either complete or partial. The researchers calculated the percentage of participants who had either a complete or partial response to acalabrutinib.

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 the study treatments. 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 the study treatments. A lot of research is needed to know whether a treatment 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?

	Relapsed/Refractory (out of 32 participants)	**Treatment-Naïve** (out of 16 participants)
How many participants had adverse reactions?	100.0% (32)	100.0% (16)
How many participants had serious adverse reactions?	34.4% (11)	6.3% (1)
How many participants stopped taking acalabrutinib due to adverse reactions?	9.4% (3)	0.0% (0)

What serious adverse reactions happened during this study?

The most common serious adverse reaction was a type of lung infection called pneumonia.

Most common serious adverse reactions		
Serious adverse reaction	**Relapsed/Refractory** (out of 32 participants)	**Treatment-Naïve** (out of 16 participants)
A type of lung infection called pneumonia	6.3% (2)	0.0% (0)
Fever with low numbers of a type of white blood cell called neutrophils	3.1% (1)	0.0% (0)
Bad bruising	3.1% (1)	0.0% (0)
Headache	3.1% (1)	0.0% (0)
Liver failure	3.1% (1)	0.0% (0)
Sudden increase in hepatitis B virus	3.1% (1)	0.0% (0)
Fungal infection in the lungs	3.1% (1)	0.0% (0)
A type of cancer called adenocarcinoma in the lungs	3.1% (1)	0.0% (0)
A type of cancer called myeloma in a type of white blood cell called plasma cells	3.1% (1)	0.0% (0)
A type of cancer called carcinoma in kidney cells	3.1% (1)	0.0% (0)
A type of cancer called carcinoma in a type of skin cell called squamous cells	3.1% (1)	0.0% (0)
Bleeding in the upper part of the stomach and gut	0.0% (0)	6.3% (1)

There was 1 participant who had relapsed/refractory leukemia who died because of a serious adverse reaction. This serious adverse reaction was liver failure.

What adverse reactions happened during this study?

For participants with relapsed/refractory leukemia, the most common adverse reaction was headache.

For participants with treatment-naïve leukemia, the most common adverse reactions were bleeding under the skin and headache.

The table below shows the adverse reactions that happened in more than 20.0% of participants in either group. There were other adverse reactions, but those happened in fewer participants.

Most common adverse reactions		
Adverse reaction	**Relapsed/Refractory** (out of 32 participants)	**Treatment-Naïve** (out of 16 participants)
Headache	59.4% (19)	68.8% (11)
Bleeding under the skin	56.3% (18)	68.8% (11)
High blood pressure	53.1% (17)	31.3% (5)
Muscle pain	43.8% (14)	25.0% (4)
Diarrhea	40.6% (13)	37.5% (6)
Decreased amount of a type of white blood cell called neutrophils	28.1% (9)	12.5% (2)
Infection of the nose and throat	25.0% (8)	37.5% (6)
Weight increase	25.0% (8)	25.0% (4)
Decreased amount of a type of white blood cell called CD4 lymphocytes	21.9% (7)	12.5% (2)
Tiny blood spots under the skin	21.9% (7)	25.0% (4)
Joint pain	18.8% (6)	37.5% (6)
Flu-like sickness	15.6% (5)	37.5% (6)
Low level of red blood cells	0.0% (0)	25.0% (4)
Swelling of the lower legs or hands	12.5% (4)	25.0% (4)
Decreased amount of a type of blood cell called platelets	18.8% (6)	25.0% (4)
Inflammation of the sinuses	15.6% (5)	25.0% (4)

How has this study helped patients and researchers?

This study helped researchers learn more about the safety of acalabrutinib and how it works in participants with leukemia.

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 are planned.

Where can I learn more about this study?

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

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02337829"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"15-H-0016"** into the search box and click **"Find a Study"**.

Full Study Title: A Phase II Study Using ACP-196 (Acalabrutinib) in Patients with Relapsed/Refractory and Treatment-naïve Deletion 17p CLL/SLL: Pharmacodynamic Assessment of BTK Inhibition and Anti-Tumor Response

AstraZeneca Protocol Number: 15-H-0016

National Clinical Trials Number: NCT02337829

Acerta Pharma BV, a member of AstraZeneca group of companies sponsored this study and has its headquarters at Cambridge, United Kingdom.

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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