AstraZeneca

Clinical Study Results

Research Sponsor: Acerta Pharma BV

Treatment Studied: Ceralasertib and acalabrutinib

Study Purpose: This study was done to learn how ceralasertib works and about its safety when taken by itself and with acalabrutinib in participants with chronic lymphocytic leukemia.

Protocol Number: ACE-CL-110, also known as D5330C00008

Thank you

Thank you for taking part in the clinical study for the study drugs acalabrutinib and ceralasertib. Ceralasertib is also known as AZD6738.

Acerta Pharma BV, a member of the AstraZeneca Group of companies, 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 people with chronic lymphocytic leukemia, also known as "CLL".

The participants in this study had refractory or relapsed CLL, which meant that their CLL had either not responded to treatment or gotten worse after treatment. They also had high-risk CLL, which meant that their cancer was more likely to cause more medical problems.

The participants in this study were 53 to 74 years old when they joined.

The study included 11 participants in Poland and the United Kingdom.

Why was the research needed?

Researchers are looking for a better way to treat relapsed or refractory high-risk CLL. 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.

In people with cancer, the body is not able to control the growth of some cells. CLL is a type of blood cancer that affects white blood cells and bone marrow, which is the spongy material found inside some bones. In CLL, the bone marrow produces too many white blood cells, which are not fully developed and do not work properly. Over time, this can cause problems such as a higher risk of infections, fatigue, unusual bleeding or bruising, and swollen glands in the neck, armpits, or groin.

Researchers think that the study drugs, ceralasertib and acalabrutinib, may be helpful in treating certain types of cancer. They are designed to work by stopping the cancer cells from growing out of control.

In this study, the researchers wanted to learn how ceralasertib works and its safety when taken by itself and with acalabrutinib in participants with CLL.

What was the purpose of this study?

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

- Was the amount of ceralasertib that got into the participants' blood different when taken by itself compared to with acalabrutinib?
- What signs and symptoms did the participants have during the study?
- What medical problems did the participants have during the study?

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

What treatments did the participants take?

In this study, all of the participants were planned to take either ceralasertib by itself, or ceralasertib with acalabrutinib.

There were 2 groups in this study:

- Participants in Group 1 took **ceralasertib by itself**
- Participants in Group 2 took **ceralasertib together with acalabrutinib**

The participants who joined the study first were in Group 1. Participants who joined the study later were in Group 2.

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

Acalabrutinib and ceralasertib were both taken by mouth. Acalabrutinib was taken as a capsule, and ceralasertib was taken as a tablet.

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

	Ceralasertib by itself	Ceralasertib and acalabrutinib
	8 participants	3 participants
	Ceralasertib tablets taken either: • twice a day for up to 12 months **or** • twice a day for 2 weeks on, then 2 weeks off, for up to 12 months	Acalabrutinib capsules alone, twice a day for 4 weeks **THEN** • Acalabrutinib capsules twice a day for up to 12 months **and** • Ceralasertib tablets twice a day for 1 week on, then 3 weeks off, for up to 12 months

After 12 months, the participants could continue to take their treatment until their cancer got worse or they left the study for another reason.

What happened during this study?

The study started in November 2017 and ended in September 2021.

Before the participants took study treatment, they visited their study site 1 time. This visit happened up to 1 month before the participants took the study treatment. At this visit, the study doctors made sure the participants could join the study. They also:

- did physical exams and asked about the participants' medications and any medical problems they were having
- took images of the participants' cancer using either CT or MRI scans
- took a small sample of each participant's bone marrow, also known as a bone marrow biopsy and aspirate
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG

While the participants took study treatment, they visited their study site up to 20 times. This part of the study lasted for about 12 months. At these visits, the study doctors did physical exams and ECGs, and took blood and urine samples. After 12 months, the study researchers decided that some participants could continue to take their study treatment until their disease got worse.

After the participants took study treatment, they visited their study site 1 time. This visit happened up to 1 month after the participants stopped taking study treatment. At this visit, the study doctors checked the health of the participants. The study doctors also followed up with the participants after this visit by telephone calls or clinic visits every 3 months.

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.

There was 1 participant who was planned to take ceralasertib with acalabrutinib, but only took acalabrutinib. The data from this participant is included in the results below.

Was the amount of ceralasertib that got into the participants' blood different when taken by itself compared to with acalabrutinib?

To answer this question, the researchers measured the amount of ceralasertib and acalabrutinib in the participants' blood at different times after they had taken each treatment.

Overall, the researchers found that the amount of ceralasertib in the blood was similar when ceralasertib was taken by itself and when ceralasertib was taken with acalabrutinib.

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

To answer this question, the study doctors did tests and measurements before and after the participants took ceralasertib and acalabrutinib.

The doctors did physical exams and tested the participants' blood and urine samples to check their overall health. They also did ECGs to check the participants' heart health. 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 meaningful.

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 the study treatment. 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.

	Ceralasertib by itself (out of 8 participants)	**Ceralasertib and acalabrutinib** (out of 3 participants)
How many participants had adverse events?	100% (8)	100% (3)
How many participants had serious adverse events?	75.0% (6)	33.3% (1)
How many participants stopped taking study treatment due to adverse events?	none	none

The most common serious adverse events that happened in more than 1 participant were:

- Low red blood cell levels
- Low levels of platelets in the blood, which are cells that help blood to clot

The most common adverse events were:

- Low red blood cell levels
- Low levels of platelets in the blood, which are cells that help blood to clot
- Cough
- Diarrhea
- Fatigue
- Nausea
- Upper respiratory tract infection

What medical problems happened during this study?

The medical problems participants have during clinical studies that the study doctors think might be related to the study drugs are called "adverse reactions".

The adverse reactions that happen in a study may or may not be caused by the study drugs. A lot of research is needed to know whether a drug causes an adverse reaction.

The adverse reactions that the participants had during this study are not in this summary. Because there was a very small number of participants, leaving this information out helps protect their identities.

How has this study helped patients and researchers?

This study helped researchers learn more about how ceralasertib works, and its safety when taken by itself and with acalabrutinib, in participants with CLL.

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 ceralasertib and acalabrutinib 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 **"NCT03328273"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2016-003737-15"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"ACE-CL-110"** into the search box and click **"Find a Study"**.

Full Study Title: A Phase 1/2 Proof-of-Concept Study Investigating AZD6738 Monotherapy and Acalabrutinib in Combination with AZD6738 (ATR inhibitor) in Subjects with Relapsed or Refractory High-Risk Chronic Lymphocytic Leukemia (CLL).

Acerta Pharma BV Protocol Number: ACE-CL-110

National Clinical Trials Number: NCT03328273

EudraCT Number: 2016-003737-15

Acerta Pharma BV, a member of the AstraZeneca Group of companies, sponsored this study and has its headquarters in Oss, the Netherlands.

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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