CLINICAL TRIAL RESULTS

Researchers look at the results of many studies to decide which treatments may offer patients improvements in terms of efficacy and safety. It takes people taking part in many studies around the world to help researchers decide this. This summary only shows the results from this study. Other studies might have different results.

Sponsor	**BeiGene, Ltd.**
Medicine(s) Studied	**Zanubrutinib**
Protocol Number	**BGB-3111-305**
Dates of Study	**November 2018 to February 2024**
Title of This Study	**A Study of Zanubrutinib (BGB-3111) Versus Ibrutinib in Participants With Relapsed/Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma (ALPINE)**
Date of This Report	**August 2025**

Thank You!

BeiGene, who managed this study, thanks participants for taking part in the clinical study for a new medical treatment called zanubrutinib, also known as BGB-3111 or Brukinsa. In this study, researchers learned more about the safety and efficacy of zanubrutinib, and how it may work in patients with a type of cancer called relapsed/refractory chronic lymphocytic leukemia (CLL) and small lymphocytic leukemia (SLL).

BeiGene thinks it is important to share the results of the study with the public. If you participated in the study and have questions about the results, please speak with the doctor or staff at your study center.

Why was this study done?

Researchers are working to find better ways to help people with different types of cancer, including chronic lymphocytic leukemia (CLL) and small lymphocytic leukemia (SLL). Lymphocytic leukemia is a type of blood cancer that starts in the bone marrow and affects the white blood cells, which help the body fight infection. In relapsed or refractory lymphocytic leukemia, the cancer has either come back after treatment (relapsed) or no longer responds to treatment (refractory). Lymphocytic leukemia usually develops slowly, and in the early stages, many people may not have any symptoms. Over time, it can cause fatigue, swollen lymph nodes, frequent infections, weight loss, and night sweats. In more advanced cases, lymphocytic leukemia can become harder to control and may need more urgent and personalized treatments.

In this study, researchers wanted to better understand how safe zanubrutinib is and how well it works in people with CLL and SLL. Zanubrutinib blocks a specific protein in cells known as Bruton's Tyrosine Kinase (BTK), which plays a role in cell development and survival. Blocking BTK function can stop cancer cells from growing.

Before a new medical treatment can be approved for people to take, researchers must do clinical studies to learn how safe the treatment is by looking at adverse events, or side effects. Adverse events are unwanted medical problems that study participants can experience that may or may not be caused by the study drug. Researchers also must learn how the treatment works in people with the disease.

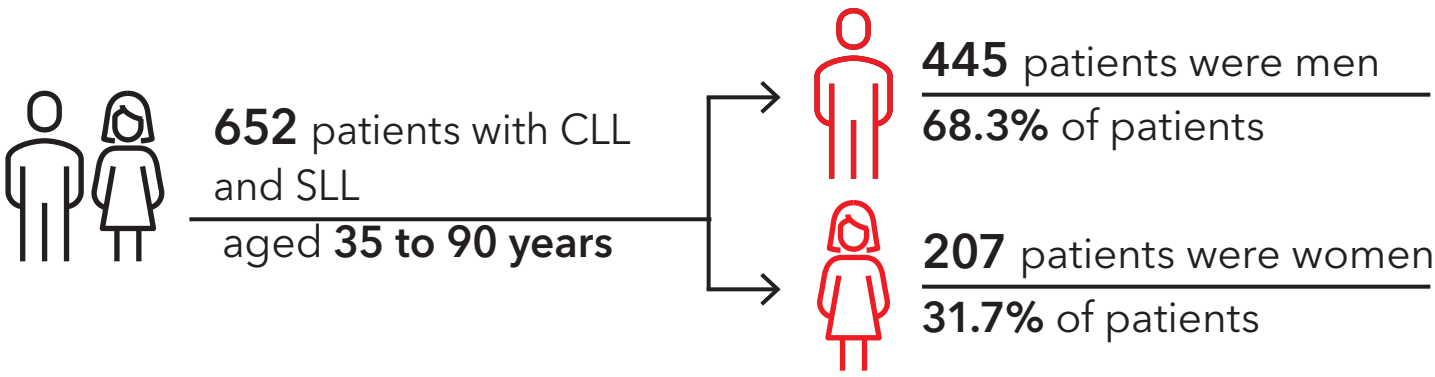
In this study, researchers compared zanubrutinib to ibrutinib, a common treatment for CLL, to see which works better.

Researchers in this study wanted to know:

- What adverse events would patients who took part in this study have?
- How many patients who took part in the study no longer had evidence of cancer or had some improvement in the cancer burden?

Who was in this study?

A total of 652 patients between the ages of 35 and 90 years were in the study. 623 had CLL and 29 patients had SLL. There were 445 men (68.3%) and 207 women (31.7%). All patients had already received at least one prior treatment for their disease. The patients did not have other medical conditions that could affect the study results.



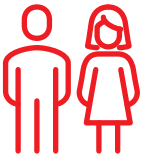
When and where was this study done?

This study started in November 2018 to February 2024. The study was done at 113 study centers in 15 countries, including:

- Australia, with 16 patients
- Belgium, with 1 patient
- China, with 90 patients
- Czech Republic, with 58 patients
- France, with 14 patients
- Germany, with 2 patients
- Netherlands, with 6 patients
- Italy, with 17 patients
- New Zealand, with 42 patients
- Poland, with 216 patients
- Sweden, with 13 patients
- Spain, with 30 patients
- Turkey, with 4 patients
- United Kingdom, with 32 patients
- United States, with 111 patients

How was this study done?

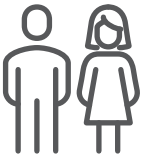
In this study, patients with CLL were randomly placed into one of two treatment groups: one group took zanubrutinib, and the other took ibrutinib. Those in the zanubrutinib group took 160 milligrams (mg) by mouth twice a day, while those in the ibrutinib group took 420 mg by mouth once a day. Treatment continued until the cancer got worse, the side effects became too hard to manage, another cancer treatment was needed, the patient or their doctor decided to stop, a medication that couldn't be used with the study drug was needed, the patient chose to leave the study, or the patient became pregnant. Randomly putting people into groups helps make sure the comparison between treatments is as fair and accurate as possible



327 patients
were assigned to
Zanubrutinib treatment group

324 patients
received
zanubrutinib orally

TWICE DAILY



325 patients
were assigned to
Ibrutinib treatment group

324 patients
received
ibrutinib orally

ONCE DAILY

During the study, the trial doctors:

- Checked patients' overall health and took blood and urine samples
- Asked patients how they were feeling and what medicines they were taking
- Asked patients how well they could move and do their daily activities
- Measured how well patient's hearts were using an electrocardiogram machine
- Took images of patient's bodies with a machine to determine the tumor's status

What adverse events did patients have?

Adverse events are medical problems that may or may not be caused by the study treatment. An adverse event is called "serious" if it causes long-lasting problems, puts the patient in the hospital, is life-threatening, is considered medically important by the study researcher, or leads to death. A total of 648 patients were evaluated for in this study.

Below are the adverse events that patients had in this study. The websites listed at the end of this summary may have more information about the adverse events that occurred in this study.

In this study:

- 99.4% of patients in the zanubrutinib group and 99.7% of patients in the ibrutinib group had at least 1 adverse event
- 53.1% of patients in the zanubrutinib group and 60.5% of the patients in the ibrutinib group had serious adverse events
- 20.1% of patients in the zanubrutinib group and 27.5% of the patients in the ibrutinib group had adverse events that caused them to stop the treatment permanently

What serious adverse events did patients have?

Pneumonia due to COVID-19 was the most common serious adverse event that occurred in the zanubrutinib group.

Serious adverse event	Zanubrutinib (Out of 324 patients)	Ibrutinib (Out of 324 patients)
COVID-19 Pneumonia	10.2% (33 patients)	6.8% (22 patients)
COVID-19	8.6% (28 patients)	6.2% (20 patients)
Pneumonia	7.4% (24 patients)	10.2% (33 patients)
Urinary Tract Infection	2.2% (7 patients)	3.1% (10 patients)

A total of 43 patients (13.3%) in the zanubrutinib group and 41 (12.7%) in the ibrutinib group had adverse events that led to death.

What were the most common adverse events?

COVID-19 infection was the most common adverse event in both groups. The table below shows the most common adverse events that occurred in at least 20% of the patients in this study.

Adverse event	Zanubrutinib (Out of 324 patients)	Ibrutinib (Out of 324 patients)
COVID-19	40.7% (132 patients)	28.1% (91 patients)
Upper respiratory tract infection	29.3% (95 patients)	19.8% (64 patients)
Hypertension	25.6% (83 patients)	22.8 (74 patients)
Neutropenia	25.0% (81 patients)	22.8% (74 patients)
Diarrhoea	18.8% (61 patients)	25.6% (83 patients)

What were the main results of the study?

Below is a summary of the main results of this study. The results for each patient in the study are not shown here and may be different from the overall results shown below.

You can find a full list of the questions for this study on the websites listed on the last page of this summary. If results are already available, they will also be found on these websites.

How many patients who took part in the study no longer had evidence of cancer or had some improvement in the signs and symptoms of cancer?

Measuring overall response rate is one way to determine how well a new cancer treatment works. After up to 45.2 months of follow-up, doctors reported that 83.5% of people with CLL who took zanubrutinib showed no signs of cancer or had improvement in their symptoms, compared to 74.2% of people who took ibrutinib.

How has this study helped patients and researchers?

The results from this study will help researchers understand more about how zanubrutinib works in patients with CLL and SLL.

The results in this summary come from this one study. Other studies may show different results. If you participated in this study and have questions about the results, please speak to the doctor or staff at your study center. You should not make changes to your treatments based on the results of this study.

Where can I found out more about this study?

More information about this study, including any available results, is found below:

The full title of this study is

A Phase 3, Randomized Study of Zanubrutinib (BGB-3111) Compared With Ibrutinib in Patients With Relapsed/Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma

The protocol number is

BGB-3111-305

For information about this study in the United States

Click here

For information about this study in the European Union

Click here

For information about this study in China

Click here

For information about this study from BeiGene

Click here

Clinical study participants help researchers make important discoveries that may lead to new medical treatments worldwide. BeiGene sponsored this study and is thankful for the help of the patients in this study.

For more information about BeiGene:

- Our main office is located in Hopewell, NJ, USA
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- Our email address is ClinicalTrials@beigene.com

BeiGene thanks all the participants for their time and effort that went into making this study possible. Clinical study patients help advance science!