CLINICAL TRIAL RESULTS

Researchers look at the results of many studies to decide which treatments may be best and safest for patients. It takes people taking part in many studies around the world to help researchers make these decisions. 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-AU-003**
Dates of Study	**September 2014 to March 2021**
Title of This Study	**Safety and Efficacy of Zanubrutinib in Patients with B-Cell Lymphoid Cancers**
Date of This Report	**March 8, 2022**

Thank You!

BeiGene, who managed this study, thanks participants for taking part in the clinical study for a new medical treatment called zanubrutinib. In this study, researchers learned more about the safety of zanubrutinib, also called BGB-3111 and Brukinsa, and how it may work in patients with B-cell lymphoid cancers.

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 looking for better ways to help people with **B-cell lymphoid cancers**, also called lymphomas or blood cancers. This type of cancer starts in white blood cells called lymphocytes, which are part of the immune system. Normal B-lymphocytes (B-cells) protect the body from germs by making antibodies. If abnormal B-cells are produced, the unhealthy cells can make it harder to fight off infections.

In this study, researchers wanted to learn more about how safe zanubrutinib is and how it works in people with B-cell lymphoid cancers. Zanubrutinib blocks a specific protein in cells known as **Bruton's tyrosine kinase** (or **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 humans, 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 patients in the study can experience that may or may not be caused by the study drug. Researchers also must learn how well the treatment works in people.

Researchers in this study wanted to know:

- What adverse events did patients have?
- What is the safest dose of zanubrutinib?
- How many people who took part in the study no longer had evidence of cancer or had some improvement in the signs and symptoms of active disease?

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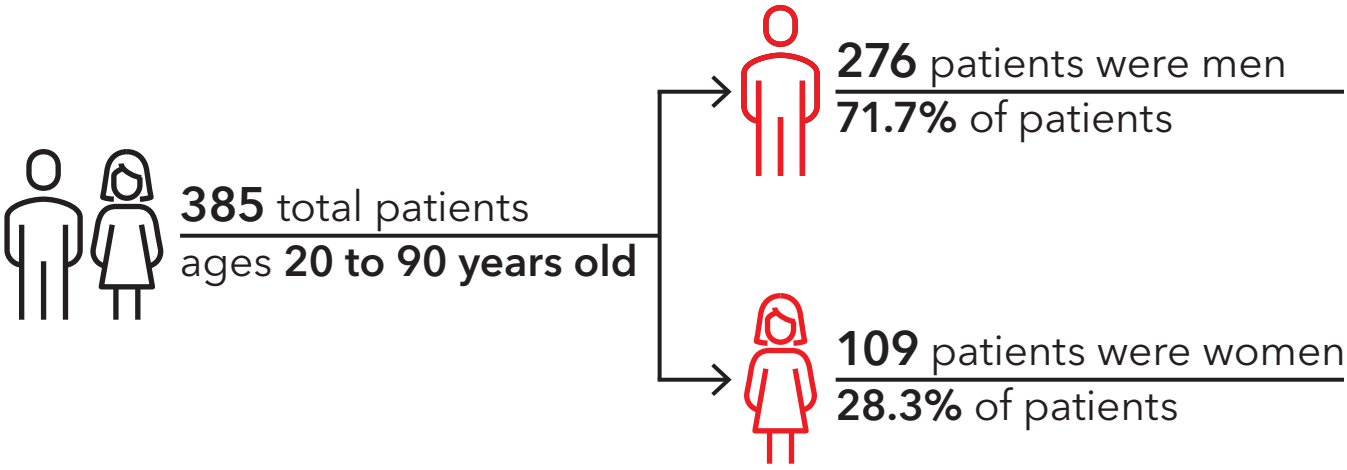
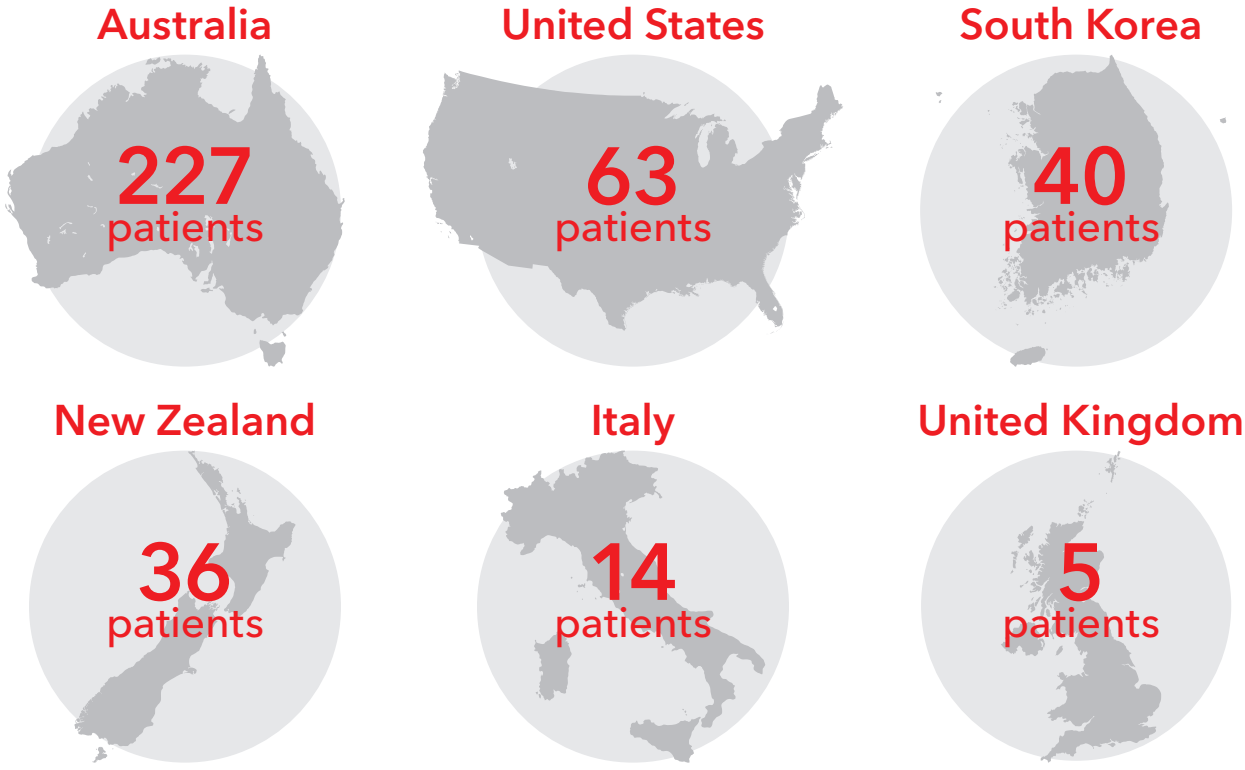
Who was in this study?



All patients had B-cell lymphoid cancers and had acceptable laboratory values specified by researchers. They did not have previous treatment with drugs similar to zanubrutinib or any major transplants.

When and where was this study done?

This study started in September 2014 and ended in March 2021. The study was done in 24 study centers in 6 countries, including:



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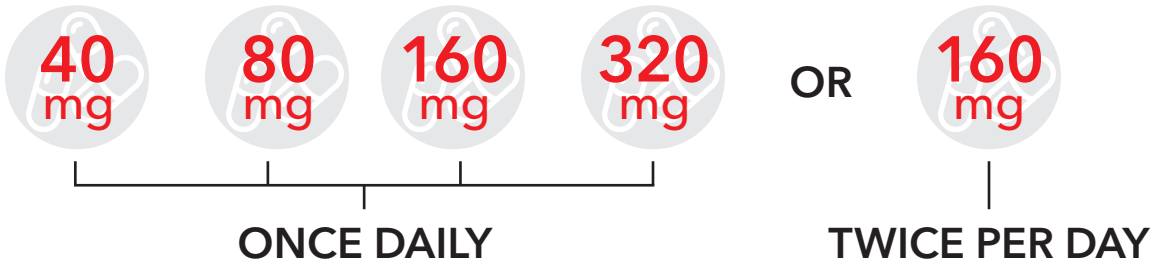
How was this study done?

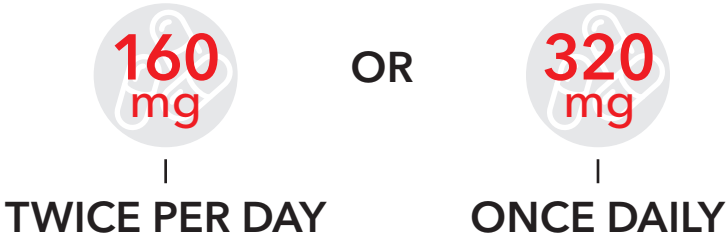
This study was done in 2 parts.

Part 1 Patients were given **different doses** of zanubrutinib in capsule form to find the dose that was **best tolerated**.



Researchers monitored the overall health of patients to check the safety of each dose level.

Part 2 Patients with **different types** of B-cell lymphoid cancers, including **chronic lymphocytic leukemia (CLL)** or **small lymphocytic lymphoma (SLL)**, **Waldenström's macroglobulinemia (WM)**, and **mantle cell lymphoma (MCL)** were assigned to take zanubrutinib at two dosing levels.



Researchers determined how many patients with different types of B-cell lymphoid cancer responded to the treatment. **"Overall response rate"** is the term used to describe whether a patient had a complete or partial response, also called remission. This means that patients no longer had evidence of B-cell lymphoid cancer or there was some improvement in the signs and symptoms of active disease.

What adverse events did patients have?

Adverse events, or **side effects**, are unwanted 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.

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.

98.7% of patients had at least 1 adverse event

54% of patients had serious adverse events

13.8% of patients had adverse events that stopped their treatment

0.5% of patients had adverse events that caused them to leave the study

What serious adverse events did patients have?

Pneumonia was the **most common** serious adverse event. The table at right shows the **most common serious adverse events** that occurred in at least 3% of the patients in this study.

Serious adverse event	Total (385 patients)
Pneumonia	8.6% (33 patients)
Bacterial skin infection	3.4% (13 patients)
Fever	3.4% (13 patients)
Urinary tract infection	3.1% (12 patients)

Twenty-six out of 385 patients had adverse events that led to death. The most common adverse events that led to death were infections that **were not** caused by zanubrutinib.

What were the most common adverse events?

Upper respiratory tract infection (**URTI**) was the most common adverse event. The table at right shows the most common adverse events that occurred in at least 20% of the patients in this study.

Adverse event	Total (385 patients)
URTI	41% (158 patients)
Bruising	36.4% (140 patients)
Diarrhea	27.8% (107 patients)
Cough	27% (104 patients)
Tiredness	21% (81 patients)
Constipation	20.3% (78 patients)
Rash	20.3% (78 patients)

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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.

What is the safest dose of zanubrutinib?

This study showed that it is **safe** for patients with B-cell lymphoid cancers to take **320 milligrams** of zanubrutinib **daily**.

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

Measuring **overall response rate** is one way to determine how well a new treatment works. The percentage of people with different B-cell lymphoid cancer types who **no longer had evidence of cancer** or **had some improvement** in the signs and symptoms of active disease after treatment is shown in the figure below.

Overall Response Rate

95.2%	**Chronic lymphocytic leukemia** or **Small lymphocytic lymphoma**	**119** of **125** patients
95.9%	**Waldenström's macroglobulinemia**	**70** of **73** patients
86.5%	**Mantle cell lymphoma**	**32** of **37** patients

How has this study helped people?

The results from this study will help researchers learn more about how zanubrutinib helps people with different types of B-cell lymphoid cancers. More studies with zanubrutinib are ongoing and planned.

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 find 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 1/2, Open-Label, Multiple-Dose, Dose Escalation and Expansion Study to Investigate the Safety and Pharmacokinetics of the BTK Inhibitor BGB-3111 in Patients With B-Cell Lymphoid Malignancies

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The protocol number is
BGB-3111-AU-003

The study details are found on ClinicalTrials.gov at
https://clinicaltrials.gov/ct2/show/NCT02343120

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 San Mateo, CA, USA
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BeiGene thanks all the participants for their time and effort that went into making this study possible. Clinical study participants help advance science!