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-3111-302**
Dates of Study	**January 2017 to June 2022**
Title of This Study	**Safety and Efficacy of Zanubrutinib Compared to Ibrutinib in Patients with Waldenström's Macroglobulinemia**
Date of This Report	**March 14, 2023**

Thank You!

BeiGene, who managed this study, thanks the patients for taking part in the clinical study for a new medical treatment called zanubrutinib. In this study, researchers learned more about the safety and efficacy of zanubrutinib, also called BGB-3111 and Brukinsa, and how it may work in patients with Waldenström's Macroglobulinemia (WM).

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 WM. WM is a rare, slow-growing type of blood cancer. The bone marrow in patients with WM produces too many abnormal white blood cells that crowd out healthy blood cells. The abnormal white blood cells produce a protein called immunoglobulin M (IgM) that accumulates in the blood and affects circulation, causing health complications.

In this study, researchers compared zanubrutinib and ibrutinib to see how safe these medications are and how well they work in patients with WM. Zanubrutinib and ibrutinib both block the function of a specific protein in cells known as Bruton's tyrosine kinase (or BTK), which plays a role in in how cells grow and survive. Blocking BTK function can stop cancer cells from growing. One of the ways to determine whether the medicine is working is by measuring the levels of IgM in blood.

Before a new medical treatment can be approved for use in patients, 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 can experience that may or may not be caused by treatment. Researchers also must learn how the treatment works in people with the disease.

Researchers in this study wanted to know:

- What adverse events did patients who took part in this study have?
- How many patients had IgM levels in the blood return to normal?

BeiGene

Who was in this study?

201 WM patients
aged **38 to 90 years**

134 patients were men
66.7% of patients

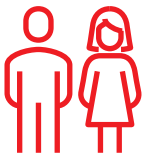
67 patients were women
33.3% of patients

When and where was this study done?

This study started in January 2017 and ended in June 2022. Information collected until July 2022 was used in this analysis. The study was done in 60 study centers in 12 countries, including:

How was this study done?

201 patients with WM were randomly placed in 1 of 2 treatment groups, either zanubrutinib or ibrutinib.

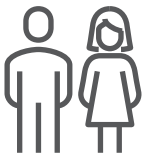


102 patients
were assigned to the
zanubrutinib treatment group

Patients received
zanubrutinib orally at

160 mg

TWICE DAILY



99 patients
were assigned to the
ibrutinib treatment group

Patients received
ibrutinib orally at

420 mg

ONCE DAILY

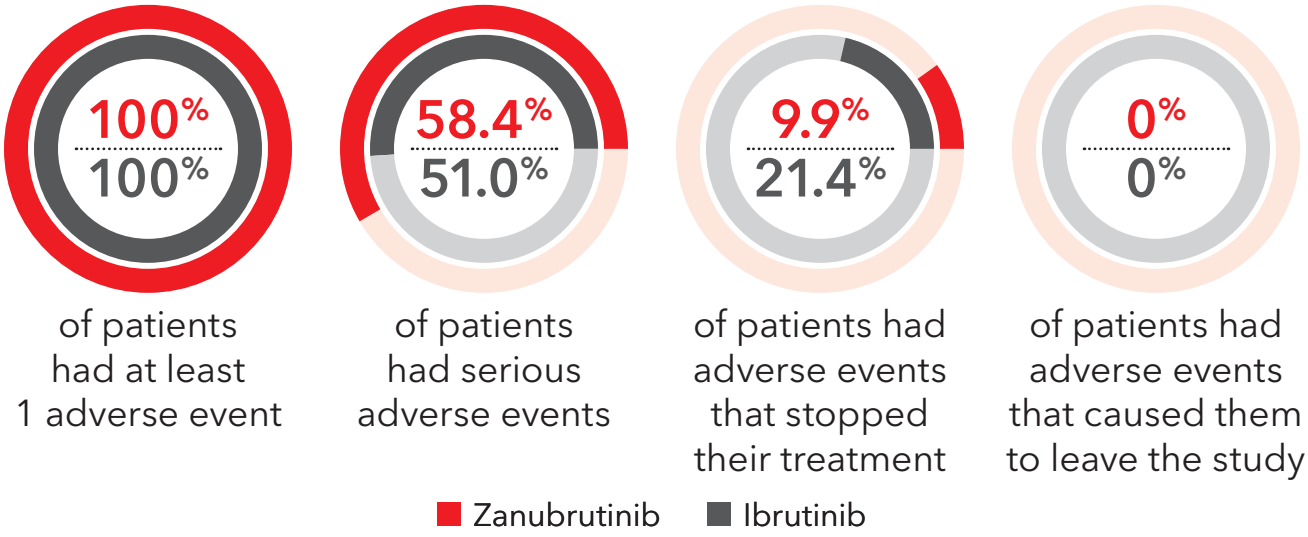
One patient randomized to the zanubrutinib group and one patient randomized to the ibrutinib group did not receive any study medication and were not included in determining adverse events.

During this study, study doctors determined:

- How many patients taking the study medication (either zanubrutinib or ibrutinib) had Complete Response (CR) or Very Good Partial Response (VGPR); a patient is considered to have achieved CR when blood IgM levels return to normal and VGPR is when there is more than 90% reduction in blood IgM levels
- How long patients survived without the disease getting worse while taking the study medication
- How many patients had adverse events

What adverse events did patients have?

Adverse events are unwanted medical problems that may or may not be caused by 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 doctor, 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 happened in this study.

What serious adverse events did patients have?

Pneumonia was the most common serious adverse event. The table below shows the most common serious adverse events that happened in at least 5% of patients in this study.

Serious adverse event	Zanubrutinib (101 patients)	Ibrutinib (98 patients)
Pneumonia	2.0% (2 patients)	14.3% (14 patients)
Irregular rapid heartbeat	2.0% (2 patients)	5.1% (5 patients)

Four (4.1%) patients who took ibrutinib and three (3%) patients who took zanubrutinib had a serious adverse event that led to death. Of the 7 deaths that occurred due to serious adverse events, 4 were considered to be related to the treatment (3 in patients treated with zanubrutinib and 1 in a patient treated with ibrutinib).

What were the most common adverse events?

Diarrhea was the most common adverse event in patients who took ibrutinib. Upper respiratory tract infection (URTI) was the most common adverse event in patients who took zanubrutinib. The table below shows the most common adverse events in this study that happened in at least 20% of the patients in this study.

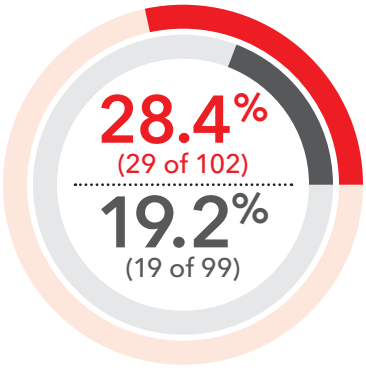
Adverse event	Zanubrutinib (101 patients)	Ibrutinib (98 patients)
URTI	32.7% (33 patients)	32.7% (32 patients)
Pneumonia	5.0% (5 patients)	21.4% (21 patients)
Diarrhea	22.8% (23 patients)	36.7% (36 patients)
Fatigue	25.7% (26 patients)	19.4% (19 patients)
Leg swelling	18.8% (19 patients)	22.4% (22 patients)
Joint stiffness	23.8% (24 patients)	24.5% (24 patients)
Muscle spasms	11.9% (12 patients)	28.6% (28 patients)
Bruising	18.8% (19 patients)	28.6% (28 patients)
Cough	19.8% (20 patients)	20.4% (20 patients)
Nosebleed	17.8% (18 patients)	21.4% (21 patients)
Low white blood cell count	29.7% (30 patients)	16.3% (16 patients)
Low levels of healthy red blood cells	17.8% (18 patients)	22.4% (22 patients)
Irregular heartbeat	6.9% (7 patients)	21.4% (21 patients)
High blood pressure	15.8% (16 patients)	24.5% (24 patients)

What were the efficacy results of the study?

Below is a summary of the efficacy results of this study. The results for each patient are not shown here and may be different from the overall results. You can find a full list of the questions for this study on the websites listed on the last page of this summary. If there are results already available, they will also be found on these websites.

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

Measuring overall response rate is one way to determine how well a new treatment works. The percentage of people with WM who no longer had evidence of cancer in their blood tests or had some improvement in the signs and symptoms of their cancer after treatment is shown in the figure below.



of patients who no longer showed evidence of cancer or had improvements in the signs and symptoms of their cancer after treatment

Zanubrutinib Ibrutinib

How long did the patients survive without the disease getting worse?

Researchers were unable to determine how many months that patients survived without the disease getting worse because there were not enough patients with worsening cancer during the study period to make an accurate conclusion.

How has this study helped patients and researchers?

This study helped researchers understand more about zanubrutinib and ibrutinib in patients with WM and may provide more treatment options for patients in the future.

- Overall, this study showed that zanubrutinib is at least as effective as ibrutinib in treating patients with WM
- Zanubrutinib appeared to be better tolerated with less adverse events compared to ibrutinib. Risk of specific adverse events, such as heart related issues, was lower in patients who took zanubrutinib compared to those who took ibrutinib

The results from this summary will help researchers to compare zanubrutinib with other treatments for people with WM. More studies with zanubrutinib are ongoing.

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 3, Randomized, Open-Label, Multicenter Study Comparing the Efficacy and Safety of the Bruton's Tyrosine Kinase (BTK) Inhibitors BGB-3111 and Ibrutinib in Subjects with Waldenström's Macroglobulinemia (WM)

The protocol number is
BGB-3111-302

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 from BeiGene

Click here

Clinical study patients 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 study patients.

For more information about BeiGene:

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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!