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COMPLETED ⓘ

A Study of Zanubrutinib (BGB-3111) Versus Ibrutinib in Participants With Relapsed/Refractory Chronic Lymphocytic Leukemia (ALPINE)

ClinicalTrials.gov ID ⓘ NCT03734016

Sponsor ⓘ BeiGene

Information provided by ⓘ BeiGene (Responsible Party)

Last Update Posted ⓘ 2024-04-01

Study Details Tab

Study Overview

Brief Summary

This study is designed to compare the overall response rate of zanubrutinib versus ibrutinib in participants with relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma.

Detailed Description

This is a global, Phase 3, randomized study of zanubrutinib versus ibrutinib in 652 participants with relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma.

The primary efficacy endpoint is overall response rate determined by investigator assessment. Participants were randomized in a 1:1 manner to either zanubrutinib or ibrutinib. Treatment with zanubrutinib and ibrutinib was open label.

Official Title

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

Conditions ⓘ

- Chronic Lymphocytic Leukemia
- Small Lymphocytic Lymphoma

Intervention / Treatment ⓘ

- Drug: Zanubrutinib
- Drug: Ibrutinib

Other Study ID Numbers ⓘ

- BGB-3111-305
- 2018-001366-42 (EudraCT Number)
- CTR20190098 (Registry Identifier) (REGISTRY: Center for drug evaluation, CFDA)

Study Start (Actual) ⓘ

2018-11-01

Primary Completion (Actual) ⓘ

2022-08-08

Study Completion (Actual) ⓘ

2024-02-28

Enrollment (Actual) ⓘ

652

Study Type ⓘ

Interventional

Phase ⓘ

Phase 3

Resource links provided by the National Library of Medicine

[MedlinePlus](https://medlineplus.gov/) (<https://medlineplus.gov/>) related topics: [Chronic Lymphocytic Leukemia](https://medlineplus.gov/chroniclymphocyticleukemia.html) (<https://medlineplus.gov/chroniclymphocyticleukemia.html>), [Leukemia](https://medlineplus.gov/leukemia.html) (<https://medlineplus.gov/leukemia.html>), [Lymphoma](https://medlineplus.gov/lymphoma.html) (<https://medlineplus.gov/lymphoma.html>).

[Genetic and Rare Diseases Information Center](https://rarediseases.info.nih.gov/gard) (<https://rarediseases.info.nih.gov/gard>) resources: [Chronic Graft Versus Host Disease](https://rarediseases.info.nih.gov/diseases/10964/chronic-graft-versus-host-disease) (<https://rarediseases.info.nih.gov/diseases/10964/chronic-graft-versus-host-disease>), [Lymphosarcoma](https://rarediseases.info.nih.gov/diseases/6946/lymphosarcoma) (<https://rarediseases.info.nih.gov/diseases/6946/lymphosarcoma>), [Chronic Lymphocytic Leukemia](https://rarediseases.info.nih.gov/diseases/6104/chronic-lymphocytic-leukemia) (<https://rarediseases.info.nih.gov/diseases/6104/chronic-lymphocytic-leukemia>).

[Drug Information](https://dailymed.nlm.nih.gov/dailymed/) (<https://dailymed.nlm.nih.gov/dailymed/>) available for: [Ibrutinib](https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Ibrutinib) (<https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Ibrutinib>), [Zanubrutinib](https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Zanubrutinib) (<https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Zanubrutinib>).

[FDA Drug and Device Resources](https://clinicaltrials.gov/fda-links) (<https://clinicaltrials.gov/fda-links>).

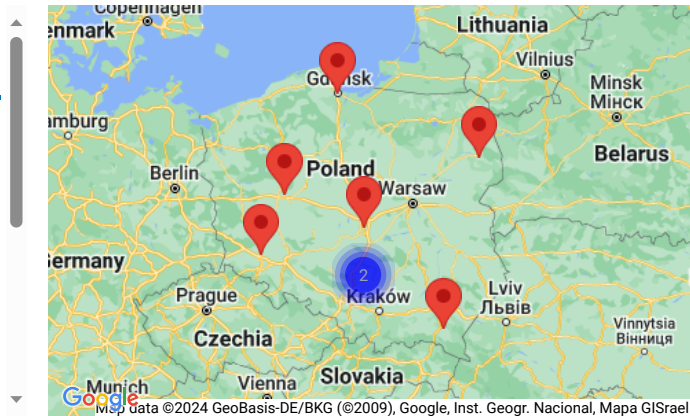
Contacts and Locations

This section provides the contact details for those conducting the study, and information on where this study is being conducted.

This study has 9 locations

Poland

-  **Bialystok, Poland, 15748**
Interhem Opieka Szpitalna
-  **Brzozow, Poland, 36-200**
Szpital Specjalist W Brzozowie, Podkarpacki Ośrodek Onkologiczny
-  **Chorzow, Poland, 41-500**
Samodzielny Publiczny Zakład Opieki Zdrowotnej Zespół Szpitali Miejskich
-  **Gdansk, Poland, 80-952**
Uniwersyteckie Centrum Kliniczne



Participation Criteria

Researchers look for people who fit a certain description, called [eligibility criteria](#). Some examples of these criteria are a person's general health condition or prior treatments.

For general information about clinical research, read [Learn About Studies \(https://clinicaltrials.gov/study-basics/learn-about-studies\)](https://clinicaltrials.gov/study-basics/learn-about-studies).

Eligibility Criteria

Description

Key Inclusion Criteria

1. Confirmed diagnosis of CLL or SLL that meets the 2008 International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria
2. CLL/SLL requiring treatment per 2008 IWCLL criteria
3. Relapsed or refractory to at least 1 prior systemic therapy for CLL/SLL
4. Measurable disease by Computerized Tomography (CT)/magnetic resonance imaging (MRI)
5. Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2
6. Life expectancy $\geq$ 6 months
7. Adequate bone marrow function
8. Adequate renal and hepatic function

Key Exclusion Criteria

1. Known prolymphocytic leukemia or history of, or currently suspected, Richter's transformation
2. Clinically significant cardiovascular disease.
3. Prior malignancy within the past 3 years, except for curatively treated basal or squamous cell skin cancer, non-muscle-invasive bladder cancer, carcinoma in situ of the cervix or breast
4. History of severe bleeding disorder or history of spontaneous bleeding requiring blood transfusion or other medical intervention
5. History of stroke or intracranial hemorrhage within 180 days before first dose of study drug
6. Severe or debilitating pulmonary disease
7. Active fungal, bacterial, and/or viral infection requiring systemic therapy
8. Known central nervous system involvement by leukemia or lymphoma
9. Known infection with HIV or active viral hepatitis B or C infection
10. Moderate or severe hepatic impairment, ie, Child-Pugh class B or C
11. Major surgery within 4 weeks of the first dose of study drug
12. Prior treatment with a (Burton's Kinase) BTK inhibitor
13. Toxicity from prior anticancer therapy that has not recovered to $\leq$ Grade 1
14. Pregnant or lactating women
15. Vaccination with a live vaccine within 35 days prior to the first dose of study drug
16. Hypersensitivity to zanubrutinib, ibrutinib, or any of the other ingredients in either drug
17. Concurrent participation in another therapeutic clinical trial

NOTE: Other protocol defined Inclusion/Exclusion criteria may apply.

Ages Eligible for Study ¹

18 Years and older (Adult, Older Adult)

Sexes Eligible for Study ²

All

Accepts Healthy Volunteers ³

No

Study Plan

This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Primary Purpose ⓘ : Treatment
Allocation ⓘ : Randomized
Interventional Model ⓘ : Parallel Assignment
Masking ⓘ : None (Open Label)

Arms and Interventions

Participant Group/Arm ⓘ	Intervention/Treatment ⓘ
Experimental: Zanubrutinib Participants received 160 mg zanubrutinib orally twice daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy	Drug: Zanubrutinib 160 mg orally twice daily - Other Names: - BGB-3111 - Brukinsa
Active Comparator: Ibrutinib Participants received Ibrutinib 420 mg orally once daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy	Drug: Ibrutinib - Ibrutinib 420 mg orally once daily - Other Names: - Imbruvica

What is the study measuring?

Primary Outcome Measures ⓘ

Outcome Measure	Measure Description	Time Frame
Overall Response Rate (ORR) as Determined by Investigator Assessment	ORR is percentage of participants with partial response (PR) or higher, (defined as Complete response/ Complete response with incomplete bone marrow recovery (CR/CRi) + PR + nodular PR) per investigator assessment using the "modified" 2008 International Workshop on Chronic Lymphocytic Leukemia (IWCLL) guidelines with modification for treatment-related lymphocytosis for participants with CLL and per Lugano Classification for non-Hodgkin lymphoma (NHL)) for participants with Small lymphocytic lymphoma (SLL)	Up to approximately 3 years and 9 months
ORR as Determined by Independent Review Committee (IRC)	ORR is the percentage of participants with PR or higher, (CR/CRi) + PR + nodular PR per IRC assessment using the "modified" 2008 IWCLL guidelines with modification for treatment-related lymphocytosis for	Up to approximately 3 years and 9 months

	participants with CLL and per Lugano Classification for NHL for participants with SLL	
Secondary Outcome Measures ⓘ		
Outcome Measure	Measure Description	Time Frame
Progression-free Survival Determined by Independent Central Review		Up to 51 months
Progression-free Survival Determined by Investigator Assessment		Up to 51 months
Duration of Response Determined by Investigator Assessment		Up to 51 months
Duration of Response Determined by Independent Central Review		Up to 51 months
Time to Treatment Failure		Up to 51 months
Overall Survival		Up to 51 months
Patient Reported Outcomes as Assessed by EORTC-QLQ-C30		Up to 51 months
Patient Reported Outcomes as Assessed by EQ-5D-5L		Up to 51 months
Incidence of Adverse Events as Assessed by CTCAE v4.03 [Safety and Tolerability]		51 months
Rate of Partial Response With Lymphocytosis (PR-L) or Higher Determined by Independent Central Review	Proportion of participants who achieve a CR/CRI + PR + nodular PR + PR-L	Up to 51 months
Overall Response Rate Determined by		51 months

Independent Central
Review

Other Outcome Measures ⓘ

Outcome Measure

Measure Description

Time Frame

Correlation Between
Prognostic and Predictive
Biomarkers and Clinical
Outcomes

Up to 51
months

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor ⓘ

BeiGene

Investigators ⓘ

- Study Director: Study Director, BeiGene

Publications

General

These publications are provided voluntarily by the person who enters information about the study and may be about anything related to the study.

- [Brown JR, Eichhorst B, Hillmen P, Jurczak W, Kazmierczak M, Lamanna N, O'Brien SM, Tam CS, Qiu L, Zhou K, Simkovic M, Mayer J, Gillespie-Twardy A, Ferrajoli A, Ganly PS, Weinkove R, Grosicki S, Mital A, Robak T, Osterborg A, Yimer HA, Salmi T, Wang MD, Fu L, Li J, Wu K, Cohen A, Shadman M. Zanubrutinib or Ibrutinib in Relapsed or Refractory Chronic Lymphocytic Leukemia. N Engl J Med. 2023 Jan 26;388\(4\):319-332. doi: 10.1056/NEJMoa2211582. Epub 2022 Dec 13.](https://pubmed.ncbi.nlm.nih.gov/36511784) (https://pubmed.ncbi.nlm.nih.gov/36511784)
- [Hillmen P, Eichhorst B, Brown JR, Lamanna N, O'Brien SM, Tam CS, Qiu L, Kazmierczak M, Zhou K, Simkovic M, Mayer J, Gillespie-Twardy A, Shadman M, Ferrajoli A, Ganly PS, Weinkove R, Grosicki S, Mital A, Robak T, Osterborg A, Yimer HA, Salmi T, Ji M, Yecies J, Idoine A, Wu K, Huang J, Jurczak W. Zanubrutinib Versus Ibrutinib in Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma: Interim Analysis of a Randomized Phase III Trial. J Clin Oncol. 2023 Feb 10;41\(5\):1035-1045. doi: 10.1200/JCO.22.00510. Epub 2022 Nov 17.](https://pubmed.ncbi.nlm.nih.gov/36395435) (https://pubmed.ncbi.nlm.nih.gov/36395435)

Study Results

These publications are provided voluntarily by the person who enters information about the study and are about the study results.

- [Hillmen P, Brown JR, Eichhorst BF, Lamanna N, O'Brien SM, Qiu L, Salmi T, Hilger J, Wu K, Cohen A, Huang J, Tam CS. ALPINE: zanubrutinib versus ibrutinib in relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma. Future Oncol. 2020 Apr;16\(10\):517-523. doi: 10.2217/fon-2019-0844. Epub 2020 Mar 24.](https://pubmed.ncbi.nlm.nih.gov/32207333) (https://pubmed.ncbi.nlm.nih.gov/32207333)

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

EX2089.0006

Study Registration Dates

First Submitted ⓘ

2018-11-02

First Submitted that Met QC Criteria ⓘ

2018-11-06

First Posted ⓘ

2018-11-07

Results Reporting Dates

Results First Submitted ⓘ

2023-07-07

Results First Submitted that Met QC Criteria ⓘ

2023-07-26

Results First Posted ⓘ

2023-07-27

Study Record Updates

Last Update Submitted that met QC Criteria ⓘ

2024-03-28

Last Update Posted ⓘ

2024-04-01

Last Verified ⓘ

2024-03

More Information

Terms related to this study

Keywords Provided by BeiGene

Chronic Lymphocytic Leukemia
Small Lymphocytic Lymphoma
CLL
SLL
relapsed
refractory

Additional Relevant MeSH Terms

Neoplasms by Histologic Type
Neoplasms
Lymphoproliferative Disorders
Lymphatic Diseases
Immunoproliferative Disorders
Immune System Diseases
Hematologic Diseases
Leukemia, B-Cell
Chronic Disease
Disease Attributes
Pathologic Processes
Lymphoma
Leukemia

Leukemia, Lymphoid
Leukemia, Lymphocytic, Chronic, B-Cell
Tyrosine Kinase Inhibitors
Protein Kinase Inhibitors
Enzyme Inhibitors
Molecular Mechanisms of Pharmacological Action
Antineoplastic Agents
Zanubrutinib
Ibrutinib

Plan for Individual Participant Data (IPD)

Plan to Share Individual Participant Data (IPD)?

Yes

Drug and device information, study documents, and helpful links

Studies a U.S. FDA-Regulated Drug Product

Yes

Studies a U.S. FDA-Regulated Device Product

No

Study Documents ⓘ Provided by BeiGene

- [Study Protocol and Statistical Analysis Plan \(https://cdn.clinicaltrials.gov/large-docs/16/NCT03734016/Prot_SAP_000.pdf\)](https://cdn.clinicaltrials.gov/large-docs/16/NCT03734016/Prot_SAP_000.pdf) [PDF, 2.39MB, 2020-01-31]



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COMPLETED ⓘ

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ClinicalTrials.gov ID ⓘ NCT03734016

Sponsor ⓘ BeiGene

Information provided by ⓘ BeiGene (Responsible Party)

Last Update Posted ⓘ 2024-04-01

Researcher View Tab

Trial Contacts

Contacts	ICMJE
Contact information is only displayed when the study is recruiting subjects	

Study Record Dates

First Submitted	ICMJE
2018-11-02	
First Posted	ICMJE
2018-11-07	
Results First Submitted	ICMJE
2023-07-07	
Results First Posted	ICMJE
2023-07-27	
Last Update Posted	
2024-04-01	
Last Verified *	
2024-03	

Outcome Measures

Change History

[See all versions of this study.](#)

Primary (Current) *

ICMJE

(Submitted: 2023-07-26)

- Overall Response Rate (ORR) as Determined by Investigator Assessment [Time Frame: Up to approximately 3 years and 9 months]
 - ORR is percentage of participants with partial response (PR) or higher, (defined as Complete response/ Complete response with incomplete bone marrow recovery (CR/CRi) + PR + nodular PR) per investigator assessment using the "modified" 2008 International Workshop on Chronic Lymphocytic Leukemia (IWCLL) guidelines with modification for treatment-related lymphocytosis for participants with CLL and per Lugano Classification for non-Hodgkin lymphoma (NHL)) for participants with Small lymphocytic lymphoma (SLL)
- ORR as Determined by Independent Review Committee (IRC) [Time Frame: Up to approximately 3 years and 9 months]
 - ORR is the percentage of participants with PR or higher, (CR/CRi) + PR + nodular PR per IRC assessment using the "modified" 2008 IWCLL guidelines with modification for treatment-related lymphocytosis for participants with CLL and per Lugano Classification for NHL for participants with SLL

Primary (Original) *

ICMJE

(Submitted: 2018-11-06)

- Overall response rate determined by independent central review [Time Frame: 29 months]

Secondary (Current) [*]

ICMJE

(Submitted: 2023-07-26)

- Progression-free Survival Determined by Independent Central Review [Time Frame: Up to 51 months]
- Progression-free Survival Determined by Investigator Assessment [Time Frame: Up to 51 months]
- Duration of Response Determined by Investigator Assessment [Time Frame: Up to 51 months]
- Duration of Response Determined by Independent Central Review [Time Frame: Up to 51 months]
- Time to Treatment Failure [Time Frame: Up to 51 months]
- Overall Survival [Time Frame: Up to 51 months]
- Patient Reported Outcomes as Assessed by EORTC-QLQ-C30 [Time Frame: Up to 51 months]
- Patient Reported Outcomes as Assessed by EQ-5D-5L [Time Frame: Up to 51 months]
- Incidence of Adverse Events as Assessed by CTCAE v4.03 [Safety and Tolerability] [Time Frame: 51 months]
- Rate of Partial Response With Lymphocytosis (PR-L) or Higher Determined by Independent Central Review [Time Frame: Up to 51 months]
 - Proportion of participants who achieve a CR/CRi + PR + nodular PR + PR-L
- Overall Response Rate Determined by Independent Central Review [Time Frame: 51 months]

Secondary (Original) [*]

ICMJE

(Submitted: 2018-11-06)

- Progression-free survival determined by independent central review [Time Frame: 65 months]
- Progression-free survival determined by investigator assessment [Time Frame: 65 months]
- Duration of response determined by independent central review [Time Frame: 65 months]
- Duration of response determined by investigator assessment [Time Frame: 65 months]
- Time to treatment failure [Time Frame: 65 months]
- Overall survival [Time Frame: 65 months]
- Patient reported outcomes as assessed by EORTC-QLQ-C30 [Time Frame: 65 months]
- Patient reported outcomes as assessed by EQ-5D-5L [Time Frame: 65 months]
- Incidence of adverse events as assessed by CTCAE v4.03 [Safety and Tolerability] [Time Frame: 80 months]

Other Pre-specified (Current)

(Submitted: 2023-07-26)

- Correlation Between Prognostic and Predictive Biomarkers and Clinical Outcomes [Time Frame: Up to 51 months]

Other Pre-specified (Original)

(Submitted: 2018-11-06)

- Correlation between prognostic and predictive biomarkers and clinical outcomes [Time Frame: 65 months]

Trial Description

Brief Title *

ICMJE

A Study of Zanubrutinib (BGB-3111) Versus Ibrutinib in Participants With Relapsed/Refractory Chronic Lymphocytic Leukemia

Official Title *§

ICMJE

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

Brief Summary *

This study is designed to compare the overall response rate of zanubrutinib versus ibrutinib in participants with relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma.

Detailed Description

This is a global, Phase 3, randomized study of zanubrutinib versus ibrutinib in 652 participants with relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma.

The primary efficacy endpoint is overall response rate determined by investigator assessment. Participants were randomized in a 1:1 manner to either zanubrutinib or ibrutinib. Treatment with zanubrutinib and ibrutinib was open label.

Study Type *

ICMJE

Interventional

Study Phase *

ICMJE

Phase 3

Study Design *§

ICMJE

Allocation

Randomized

Interventional Model

Parallel Assignment

Masking

None (Open Label)

Primary Purpose

Treatment

Condition *

ICMJE

- Chronic Lymphocytic Leukemia
- Small Lymphocytic Lymphoma

Intervention *

ICMJE

- Drug: Zanubrutinib
 - 160 mg orally twice daily
 - Other Names:
 - BGB-3111
 - Brukina
- Drug: Ibrutinib
 - Ibrutinib 420 mg orally once daily

- Other Names:
 - Imbruvica

Study Arms *

ICMJE

- Experimental: Zanubrutinib
 - Participants received 160 mg zanubrutinib orally twice daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy
 - Interventions:
 - Drug: Zanubrutinib
- Active Comparator: Ibrutinib
 - Participants received Ibrutinib 420 mg orally once daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy
 - Interventions:
 - Drug: Ibrutinib

Publications

(Includes general and study results' publications, and Pubmed publications referencing this study by ClinicalTrials.gov Identifier (NCT Number))

- [Brown JR, Eichhorst B, Hillmen P, Jurczak W, Kazmierczak M, Lamanna N, O'Brien SM, Tam CS, Qiu L, Zhou K, Simkovic M, Mayer J, Gillespie-Twardy A, Ferrajoli A, Ganly PS, Weinkove R, Grosicki S, Mital A, Robak T, Osterborg A, Yimer HA, Salmi T, Wang MD, Fu L, Li J, Wu K, Cohen A, Shadman M. Zanubrutinib or Ibrutinib in Relapsed or Refractory Chronic Lymphocytic Leukemia. N Engl J Med. 2023 Jan 26;388\(4\):319-332. doi: 10.1056/NEJMoa2211582. Epub 2022 Dec 13.](https://pubmed.ncbi.nlm.nih.gov/36511784/) (https://pubmed.ncbi.nlm.nih.gov/36511784/)
- [Hillmen P, Eichhorst B, Brown JR, Lamanna N, O'Brien SM, Tam CS, Qiu L, Kazmierczak M, Zhou K, Simkovic M, Mayer J, Gillespie-Twardy A, Shadman M, Ferrajoli A, Ganly PS, Weinkove R, Grosicki S, Mital A, Robak T, Osterborg A, Yimer HA, Salmi T, Ji M, Yecies J, Idoine A, Wu K, Huang J, Jurczak W. Zanubrutinib Versus Ibrutinib in Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma: Interim Analysis of a Randomized Phase III Trial. J Clin Oncol. 2023 Feb 10;41\(5\):1035-1045. doi: 10.1200/JCO.22.00510. Epub 2022 Nov 17.](https://pubmed.ncbi.nlm.nih.gov/395435/) (https://pubmed.ncbi.nlm.nih.gov/395435/)
- [Hillmen P, Brown JR, Eichhorst BF, Lamanna N, O'Brien SM, Qiu L, Salmi T, Hilger J, Wu K, Cohen A, Huang J, Tam CS. ALPINE: zanubrutinib versus ibrutinib in relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma. Future Oncol. 2020 Apr;16\(10\):517-523. doi: 10.2217/fon-2019-0844. Epub 2020 Mar 24.](https://pubmed.ncbi.nlm.nih.gov/32207333/) (https://pubmed.ncbi.nlm.nih.gov/32207333/)

Recruitment Information

Recruitment Status *

ICMJE

Completed

Enrollment (Actual) *§

ICMJE

(Submitted: 2021-04-27)

652

Original Enrollment (Estimated) *§

ICMJE

(Submitted: 2018-11-06)

400

Study Start Date (Actual) *§

ICMJE

2018-11-01

Primary Completion Date (Actual) *	
2022-08-08 (Final data collection date for primary outcome measure)	
Study Completion Date (Actual) *§	ICMJE
2024-02-28	
Eligibility Criteria *	ICMJE
Key Inclusion Criteria 1. Confirmed diagnosis of CLL or SLL that meets the 2008 International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria 2. CLL/SLL requiring treatment per 2008 IWCLL criteria 3. Relapsed or refractory to at least 1 prior systemic therapy for CLL/SLL 4. Measurable disease by Computerized Tomography (CT)/magnetic resonance imaging (MRI) 5. Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2 6. Life expectancy ≥ 6 months 7. Adequate bone marrow function 8. Adequate renal and hepatic function Key Exclusion Criteria 1. Known polymorphocytic leukemia or history of, or currently suspected, Richter's transformation 2. Clinically significant cardiovascular disease. 3. Prior malignancy within the past 3 years, except for curatively treated basal or squamous cell skin cancer, non-muscle-invasive bladder cancer, carcinoma in situ of the cervix or breast 4. History of severe bleeding disorder or history of spontaneous bleeding requiring blood transfusion or other medical intervention 5. History of stroke or intracranial hemorrhage within 180 days before first dose of study drug 6. Severe or debilitating pulmonary disease 7. Active fungal, bacterial, and/or viral infection requiring systemic therapy 8. Known central nervous system involvement by leukemia or lymphoma 9. Known infection with HIV or active viral hepatitis B or C infection 10. Moderate or severe hepatic impairment, ie, Child-Pugh class B or C 11. Major surgery within 4 weeks of the first dose of study drug 12. Prior treatment with a (Burton's Kinase) BTK inhibitor 13. Toxicity from prior anticancer therapy that has not recovered to ≤ Grade 1 14. Pregnant or lactating women 15. Vaccination with a live vaccine within 35 days prior to the first dose of study drug 16. Hypersensitivity to zanubrutinib, ibrutinib, or any of the other ingredients in either drug 17. Concurrent participation in another therapeutic clinical trial NOTE: Other protocol defined Inclusion/Exclusion criteria may apply.	
Sex/Gender *	ICMJE
Sexes Eligible for the Study: All	
Ages *	ICMJE
18 Years and older (Adult, Older Adult)	
Accepts Healthy Volunteers *§	ICMJE
No	
Location Countries	ICMJE
Poland	
Removed Location Countries	
Australia, Belgium, China, Czechia, France, Germany, Italy, Netherlands, New Zealand, Spain, Sweden, Turkey, United Kingdom, United States	

Administrative Information

NCT Number	ICMJE
NCT03734016	
Other Study ID Numbers [*]	ICMJE
BGB-3111-305 2018-001366-42(EudraCT Number) CTR20190098(Registry Identifier)	
Has Data Monitoring Committee	
Yes	
U.S. FDA-regulated Product *§	
Studies a U.S. FDA-regulated Drug Product Yes Studies a U.S. FDA-regulated Device Product No	
IPD Sharing Statement	ICMJE
Plan to Share IPD: Yes	
Current Responsible Party *	
BeiGene	
Original Responsible Party *	
Same as current	
Current Study Sponsor *	ICMJE
BeiGene	
Original Study Sponsor *	ICMJE
Same as current	
Collaborators	ICMJE
Not provided	
Investigators	ICMJE
Study Director: Study Director BeiGene	
PRS Account	
BeiGene	

Symbol Legend

*

Required

*§

Required if Study Start Date is on or after January 18, 2017

[*]

Conditionally required

No Symbol

ICMJE

Unmarked fields are optional. If no information is provided, fields will be labeled as "not provided"

Data element required by the [International Committee of Medical Journal Editors](https://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html) (<https://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html>), and the [World Health Organization ICTRP](https://www.who.int/clinical-trials-registry-platform) (<https://www.who.int/clinical-trials-registry-platform>).



The U.S. government does not review or approve the safety and science of all studies listed on this website.
Read our full [disclaimer](https://clinicaltrials.gov/about-site/disclaimer) (<https://clinicaltrials.gov/about-site/disclaimer>) for details.

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A Study of Zanubrutinib (BGB-3111) Versus Ibrutinib in Participants With Relapsed/Refractory Chronic Lymphocytic Leukemia (ALPINE)

ClinicalTrials.gov ID ⓘ NCT03734016

Sponsor ⓘ BeiGene

Information provided by ⓘ BeiGene (Responsible Party)

Last Update Posted ⓘ 2024-04-01

Results Posted Tab

Results Overview

Conditions ⓘ

- Chronic Lymphocytic Leukemia Small Lymphocytic Lymphoma

Intervention/Treatment ⓘ

- Drug: Zanubrutinib
- Drug: Ibrutinib

Other Study ID Numbers ⓘ

- BGB-3111-305
- 2018-001366-42 (EudraCT Number)
- CTR20190098 (Registry Identifier) (REGISTRY: Center for drug evaluation, CFDA)

Study Design

- Allocation** ⓘ: Randomized
Interventional Model ⓘ: Parallel Assignment
Masking ⓘ: None (Open Label)
Primary Purpose ⓘ: Treatment

Results Point of Contact

- Name/Title:** Study Director
Organization: BeiGene
Phone: +1-877-828-5568
Email: clinicaltrials@beigene.com



Enrollment (Actual) ⓘ

652

Study Type ⓘ

Interventional

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted ⓘ

2018-11-02

First Posted ⓘ

2018-11-07

Results Reporting Dates

Results First Submitted ⓘ

2023-07-07

Results First Posted ⓘ

2023-07-27

Study Record Updates

Last Update Posted ⓘ

2024-04-01

Last Verified ⓘ

2024-03

Participant Flow ⓘ

Recruitment Details

[Not Specified]

Pre-assignment Details

[Not Specified]

Arm/Group Title	Zanubrutinib	Ibrutinib
Arm/Group Description	Participants received 160 milligrams (mg) zanubrutinib orally twice daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy	Participants received Ibrutinib 420 mg orally once daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy

Arm/Group Title	Zanubrutinib	Ibrutinib
Arm/Group Description	Participants received 160 milligrams (mg) zanubrutinib orally twice daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy	Participants received Ibrutinib 420 mg orally once daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy

Started	327	325
Completed	0	0
Not Completed	327	325

Reason Not Completed

Participants Remaining in the Study	260	240
Death	48	60
Withdrawal by Subject	14	16
Physician Decision	0	7
Lost to Follow-up	3	1
Adverse Event	2	1

Baseline Characteristics ⓘ

Arm/Group Title	Zanubrutinib	Ibrutinib	Total
Arm/Group Description	Participants received 160 mg zanubrutinib orally twice daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy	Participants received Ibrutinib 420 mg orally once daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy	Total of all reporting groups
Overall Number of Baseline Participants	327	325	652
Baseline Analysis Population Description	Intent-to-Treat (ITT) Analysis Set includes all randomized participants		

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Age, Continuous

Mean (Standard Deviation) | Unit of measure: years

Number Analyzed	327 participants	325 participants	652 participants
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	66.7 (10.18)	67.1 (9.18)	66.9 (9.69)
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Sex: Female, Male

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed	327 participants	325 participants	652 participants
Female	114 34.9%	93 28.6%	207 31.7%
Male	213 65.1%	232 71.4%	445 68.3%

Race (NIH/OMB)

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed	327 participants	325 participants	652 participants
American Indian or Alaska Native	0 0.0%	0 0.0%	0 0.0%
Asian	47 14.4%	44 13.5%	91 14.0%
Native Hawaiian or Other Pacific Islander	0 0.0%	0 0.0%	0 0.0%
Black or African American	0 0.0%	0 0.0%	0 0.0%
White	261 79.8%	265 81.5%	526 80.7%
More than one race	0 0.0%	0 0.0%	0 0.0%
Unknown or Not Reported	19 5.8%	16 4.9%	35 5.4%

Outcome Measures

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1. Overall Response Rate (ORR) as Determined by Investigator Assessment

Type: Primary | Time Frame: Up to approximately 3 years and 9 months

Description	ORR is percentage of participants with partial response (PR) or higher, (defined as Complete response/ Complete response with incomplete bone marrow recovery (CR/CRi) + PR + nodular PR) per investigator assessment using the "modified" 2008 International Workshop on Chronic Lymphocytic Leukemia (IWCLL) guidelines with modification for treatment-related lymphocytosis for participants with CLL and per Lugano Classification for non-Hodgkin lymphoma (NHL)) for participants with Small lymphocytic lymphoma (SLL)
Time Frame	Up to approximately 3 years and 9 months
Analysis Population Description	Intent To Treat (ITT) Analysis Set

Arm/Group Title	Zanubrutinib	Ibrutinib
Arm/Group Description	Participants received 160 mg zanubrutinib orally twice daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy	Participants received Ibrutinib 420 mg orally once daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy
Overall Number of Participants Analyzed	327	325
Measure Type: Number (95% Confidence Interval) Unit of Measure: Percentage of participants	83.5 (79.0 to 87.3)	74.2 (69.0 to 78.8)

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Statistical Analysis 1

Statistical Analysis Overview

Comparison Group Selection	Zanubrutinib, Ibrutinib
Comments	[Not Specified]
Type of Statistical Test	Non-Inferiority
Comments	P-value is calculated for noninferiority via stratified test statistic against a null response ratio of 0.8558

Statistical Test of Hypothesis

P-Value	<.0001
Comments	[Not Specified]
Method	stratified test statistic against a null
Comments	[Not Specified]

Statistical Analysis 2

Statistical Analysis Overview

Comparison Group Selection	Zanubrutinib, Ibrutinib
Comments	[Not Specified]
Type of Statistical Test	Superiority
Comments	[Not Specified]

Statistical Test of Hypothesis

P-Value	0.0035
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Comments	P-value is calculated for superiority via stratified Cochran-Mantel-Haenszel test statistic
Method	Cochran-Mantel-Haenszel
Comments	2-sided

2. ORR as Determined by Independent Review Committee (IRC)

Type: Primary | Time Frame: Up to approximately 3 years and 9 months

Description	ORR is the percentage of participants with PR or higher, (CR/CRi) + PR + nodular PR per IRC assessment using the "modified" 2008 IWCLL guidelines with modification for treatment-related lymphocytosis for participants with CLL and per Lugano Classification for NHL for participants with SLL	
Time Frame	Up to approximately 3 years and 9 months	
Analysis Population Description	ITT Analysis Set	
Arm/Group Title	Zanubrutinib	Ibrutinib
Arm/Group Description	Participants received 160 mg zanubrutinib orally twice daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy.	Participants received Ibrutinib 420 mg orally once daily until disease progression, intolerable toxicity, initiation of alternative anticancer therapy, investigator/Sponsor decision, need for prohibited medication, study withdrawal, or pregnancy
Overall Number of Participants Analyzed	327	325
Measure Type: Number (95% Confidence Interval) Unit of Measure: Percentage of participants	86.2 (82.0 to 89.8)	75.7 (70.7 to 80.3)

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Statistical Analysis 1

Statistical Analysis Overview

Comparison Group Selection	Zanubrutinib, Ibrutinib
Comments	[Not Specified]
Type of Statistical Test	Non-Inferiority
Comments	P-value is calculated for noninferiority via stratified test statistic against a null response ratio of 0.8558

Statistical Test of Hypothesis

P-Value	<.0001
Comments	[Not Specified]
Method	stratified test statistic against a null
Comments	[Not Specified]

Statistical Analysis Overview

Comparison Group Selection	Zanubrutinib, Ibrutinib
Comments	[Not Specified]
Type of Statistical Test	Superiority
Comments	P-value is calculated for superiority via stratified Cochran-Mantel-Haenszel test statistic

Statistical Test of Hypothesis

P-Value	0.0007
Comments	2-sided
Method	Cochran-Mantel-Haenszel
Comments	[Not Specified]

3. Progression-free Survival Determined by Independent Central Review

Type: Secondary | Time Frame: Up to 51 months

Description	[Not Specified]
Time Frame	Up to 51 months
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

4. Progression-free Survival Determined by Investigator Assessment

Type: Secondary | Time Frame: Up to 51 months

Description	[Not Specified]
Time Frame	Up to 51 months
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

5. Duration of Response Determined by Investigator Assessment

Type: Secondary | Time Frame: Up to 51 months

Description	[Not Specified]
Time Frame	Up to 51 months
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

6. Duration of Response Determined by Independent Central Review

Type: Secondary | Time Frame: Up to 51 months

Description	[Not Specified]
Time Frame	Up to 51 months
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

7. Time to Treatment Failure

Type: Secondary | Time Frame: Up to 51 months

Description	[Not Specified]
Time Frame	Up to 51 months
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

8. Overall Survival

Type: Secondary | Time Frame: Up to 51 months

Description	[Not Specified]
Time Frame	Up to 51 months
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

9. Patient Reported Outcomes as Assessed by EORTC-QLQ-C30

Type: Secondary | Time Frame: Up to 51 months

Description	[Not Specified]
Time Frame	Up to 51 months
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

10. Patient Reported Outcomes as Assessed by EQ-5D-5L

Type: Secondary | Time Frame: Up to 51 months

Description	[Not Specified]
Time Frame	Up to 51 months
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

11. Incidence of Adverse Events as Assessed by CTCAE v4.03 [Safety and Tolerability]

Type: Secondary | Time Frame: 51 months

Description	[Not Specified]
Time Frame	51 months
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

12. Rate of Partial Response With Lymphocytosis (PR-L) or Higher Determined by Independent Central Review

Type: Secondary | Time Frame: Up to 51 months

Description	Proportion of participants who achieve a CR/CRi + PR + nodular PR + PR-L
Time Frame	Up to 51 months
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

13. Overall Response Rate Determined by Independent Central Review

Type: Secondary | Time Frame: 51 months

Description	[Not Specified]
Time Frame	51 months
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

14. Correlation Between Prognostic and Predictive Biomarkers and Clinical Outcomes

Type: Other Pre-specified | Time Frame: Up to 51 months

Description	[Not Specified]
Time Frame	Up to 51 months
Analysis Population Description	[Not Specified]

Outcome Measure Data Not Reported

Adverse Events

Time Frame

From the date of randomization up to approximately 3 years and 9 months

Adverse Event Reporting Description

[Not Specified]

Arm/Group Title	Zanubrutinib	Ibrutinib
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All-Cause Mortality

Arm/Group Title	Zanubrutinib	Ibrutinib
	Affected / at Risk (%)	Affected / at Risk (%)
Total	48/324 (14.81%)	60/324 (18.52%)

Serious Adverse Events

Arm/Group Title	Zanubrutinib		Ibrutinib	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	136/324 (41.98%)		162/324 (50.00%)	

Blood and lymphatic system disorders

Anaemia ^{†1}	4/324 (1.23%)	7	3/324 (0.93%)	3
Blood loss anaemia ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Febrile neutropenia ^{†1}	1/324 (0.31%)	1	1/324 (0.31%)	1
Haemolytic anaemia ^{†1}	0/324 (0.00%)	0	2/324 (0.62%)	2
Hypoglobulinaemia ^{†1}	1/324 (0.31%)	1	2/324 (0.62%)	3
Immune thrombocytopenia ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Lymphadenitis ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Lymphadenopathy ^{†1}	1/324 (0.31%)	1	2/324 (0.62%)	2
Neutropenia ^{†1}	1/324 (0.31%)	1	1/324 (0.31%)	1
Splenic haematoma ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Splenic haemorrhage ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Splenic infarction ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Thrombocytopenia ^{†1}	1/324 (0.31%)	1	1/324 (0.31%)	3

Cardiac disorders

Acute coronary	1/324 (0.31%)	1	0/324 (0.00%)	0
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Arm/Group Title	Zanubrutinib		Ibrutinib	
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syndrome ^{†1}				
Angina pectoris ^{†1}	0/324 (0.00%)	0	2/324 (0.62%)	2
Atrial fibrillation ^{†1}	1/324 (0.31%)	1	8/324 (2.47%)	8
Atrial flutter ^{†1}	1/324 (0.31%)	1	1/324 (0.31%)	1
Atrial tachycardia ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Cardiac arrest ^{†1}	0/324 (0.00%)	0	3/324 (0.93%)	3
Cardiac failure ^{†1}	1/324 (0.31%)	1	1/324 (0.31%)	1
Cardiac failure acute ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Cardiac failure chronic ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	2
Cardiac failure congestive ^{†1}	1/324 (0.31%)	2	1/324 (0.31%)	2
Congestive cardiomyopathy ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Coronary artery disease ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Myocardial infarction ^{†1}	1/324 (0.31%)	1	3/324 (0.93%)	4
Supraventricular tachycardia ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Ventricular fibrillation ^{†1}	0/324 (0.00%)	0	2/324 (0.62%)	2

Congenital, familial and genetic disorders

Bronchogenic cyst ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
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Ear and labyrinth disorders

Tinnitus ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
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Eye disorders

Cataract ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Cataract nuclear ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Dacryostenosis	1/324 (0.31%)	1	0/324 (0.00%)	0

Arm/Group Title	Zanubrutinib		Ibrutinib	
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acquired ^{†1}				
Keratitis ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Periorbital oedema ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1

Gastrointestinal disorders

Colitis ^{†1}	2/324 (0.62%)	3	0/324 (0.00%)	0
Constipation ^{†1}	0/324 (0.00%)	0	2/324 (0.62%)	2
Crohn's disease ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Diarrhoea ^{†1}	1/324 (0.31%)	1	2/324 (0.62%)	2
Enterocolitis ^{†1}	1/324 (0.31%)	1	1/324 (0.31%)	1
Gastric ulcer perforation ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Gastritis ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Gastrointestinal disorder ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Gastrointestinal haemorrhage ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Inguinal hernia ^{†1}	1/324 (0.31%)	1	2/324 (0.62%)	2
Large intestine polyp ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Mesenteric panniculitis ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Obstructive pancreatitis ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Oesophageal food impaction ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Pancreatitis ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Pancreatitis acute ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Small intestinal obstruction ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Strangulated umbilical hernia ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0

Arm/Group Title	Zanubrutinib	Ibrutinib
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Catheter site haematoma ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Death ^{†1}	2/324 (0.62%)	2	2/324 (0.62%)	2
Drug withdrawal syndrome ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Fatigue ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Malaise ^{†1}	2/324 (0.62%)	3	0/324 (0.00%)	0
Multiple organ dysfunction syndrome ^{†1}	2/324 (0.62%)	2	1/324 (0.31%)	1
Non-cardiac chest pain ^{†1}	1/324 (0.31%)	2	0/324 (0.00%)	0
Pyrexia ^{†1}	2/324 (0.62%)	2	5/324 (1.54%)	6

Hepatobiliary disorders

Cholecystitis ^{†1}	1/324 (0.31%)	1	1/324 (0.31%)	1
Cholecystitis acute ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Cholelithiasis ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Hepatitis ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Jaundice ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0

Infections and infestations

Acinetobacter bacteraemia ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Anal abscess ^{†1}	1/324 (0.31%)	1	1/324 (0.31%)	1
Appendicitis ^{†1}	0/324 (0.00%)	0	2/324 (0.62%)	2
Arthritis bacterial ^{†1}	1/324 (0.31%)	1	1/324 (0.31%)	1
Bacterial sepsis ^{†1}	1/324 (0.31%)	2	1/324 (0.31%)	1
Bronchitis ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Bronchopulmonary aspergillosis ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0

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COVID-19 ^{†1}	18/324 (5.56%)	23	16/324 (4.94%)	24
COVID-19 pneumonia ^{†1}	24/324 (7.41%)	31	13/324 (4.01%)	22
Campylobacter gastroenteritis ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Cellulitis ^{†1}	3/324 (0.93%)	3	1/324 (0.31%)	1
Dacryocystitis ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Encephalitis ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Epstein-Barr virus infection ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	2
Escherichia bacteraemia ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Escherichia urinary tract infection ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Fungal abscess central nervous system ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Gastritis viral ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Gastroenteritis ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Gastroenteritis viral ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Haematoma infection ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Hepatitis B ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Herpes zoster ^{†1}	1/324 (0.31%)	2	2/324 (0.62%)	2
Infection ^{†1}	1/324 (0.31%)	3	2/324 (0.62%)	2
Infective tenosynovitis ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Influenza ^{†1}	0/324 (0.00%)	0	2/324 (0.62%)	3
Large intestine infection ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Localised infection ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1

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Lower respiratory tract infection ^{†1}	3/324 (0.93%)	3	0/324 (0.00%)	0
Lower respiratory tract infection bacterial ^{†1}	1/324 (0.31%)	2	0/324 (0.00%)	0
Lymphadenitis bacterial ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Mastoiditis ^{†1}	0/324 (0.00%)	0	2/324 (0.62%)	2
Meningitis ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Otitis externa ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Otitis media acute ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Paronychia ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Pneumocystis jirovecii pneumonia ^{†1}	1/324 (0.31%)	1	2/324 (0.62%)	2
Pneumonia ^{†1}	18/324 (5.56%)	30	25/324 (7.72%)	34
Pneumonia bacterial ^{†1}	1/324 (0.31%)	3	1/324 (0.31%)	1
Pneumonia cryptococcal ^{†1}	1/324 (0.31%)	3	0/324 (0.00%)	0
Pneumonia fungal ^{†1}	1/324 (0.31%)	2	0/324 (0.00%)	0
Pneumonia klebsiella ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Pneumonia legionella ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	2
Pneumonia pneumococcal ^{†1}	1/324 (0.31%)	2	1/324 (0.31%)	1
Pneumonia pseudomonal ^{†1}	1/324 (0.31%)	2	0/324 (0.00%)	0
Pneumonia respiratory syncytial viral ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Post procedural infection ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Pulmonary tuberculosis ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1

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Respiratory tract infection ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Sepsis ^{†1}	4/324 (1.23%)	6	1/324 (0.31%)	1
Septic shock ^{†1}	0/324 (0.00%)	0	2/324 (0.62%)	3
Sinusitis ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Skin bacterial infection ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Soft tissue infection ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Sporotrichosis ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Staphylococcal bacteraemia ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Streptococcal bacteraemia ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Upper respiratory tract infection ^{†1}	1/324 (0.31%)	1	2/324 (0.62%)	2
Urinary tract infection ^{†1}	5/324 (1.54%)	6	8/324 (2.47%)	11
Urosepsis ^{†1}	2/324 (0.62%)	2	0/324 (0.00%)	0
Wound infection ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1

Injury, poisoning and procedural complications

Clavicle fracture ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Craniocerebral injury ^{†1}	1/324 (0.31%)	2	0/324 (0.00%)	0
Fall ^{†1}	2/324 (0.62%)	2	2/324 (0.62%)	2
Femur fracture ^{†1}	1/324 (0.31%)	1	1/324 (0.31%)	1
Hip fracture ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Limb injury ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Post procedural complication ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Rib fracture ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1

Arm/Group Title	Zanubrutinib		Ibrutinib	
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Road traffic accident ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Scapula fracture ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Spinal fracture ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Subdural haematoma ^{†1}	0/324 (0.00%)	0	2/324 (0.62%)	2
Traumatic liver injury ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Wound dehiscence ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0

Investigations

Alanine aminotransferase increased ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Aspartate aminotransferase increased ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Blood bilirubin increased ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	2
Blood creatinine increased ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
False positive investigation result ^{†1}	1/324 (0.31%)	3	0/324 (0.00%)	0
Platelet count decreased ^{†1}	2/324 (0.62%)	5	1/324 (0.31%)	2
White blood cell count decreased ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	5

Metabolism and nutrition disorders

Decreased appetite ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	2
Hypercalcaemia ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	2
Hyperglycaemia ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Hyponatraemia ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Tumour lysis syndrome ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0

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Water intoxication ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0

Musculoskeletal and connective tissue disorders

Back pain ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Chondrocalcinosis pyrophosphate ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Haemarthrosis ^{†1}	2/324 (0.62%)	2	0/324 (0.00%)	0
Haematoma muscle ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Intervertebral disc compression ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Mobility decreased ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Pain in extremity ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1

Neoplasms benign, malignant and unspecified (incl cysts and polyps)

Adenocarcinoma gastric ^{†1}	0/324 (0.00%)	0	2/324 (0.62%)	2
Adenocarcinoma of colon ^{†1}	1/324 (0.31%)	3	1/324 (0.31%)	2
Basal cell carcinoma ^{†1}	3/324 (0.93%)	4	1/324 (0.31%)	1
Benign lung neoplasm ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Bladder transitional cell carcinoma ^{†1}	2/324 (0.62%)	2	0/324 (0.00%)	0
Brain neoplasm ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Breast cancer ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Choroid melanoma ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Chromophobe renal cell carcinoma ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Clear cell renal cell carcinoma ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Colon cancer ^{†1}	1/324 (0.31%)	1	1/324 (0.31%)	1

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Colon cancer metastatic ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Colorectal adenocarcinoma ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Colorectal cancer ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Endometrial adenocarcinoma ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Gastrointestinal tract adenoma ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Intraductal proliferative breast lesion ^{†1}	2/324 (0.62%)	3	0/324 (0.00%)	0
Invasive ductal breast carcinoma ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Laryngeal cancer recurrent ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Lip squamous cell carcinoma ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	2
Lipoma ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Lung adenocarcinoma ^{†1}	1/324 (0.31%)	1	2/324 (0.62%)	2
Lung neoplasm ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	2
Malignant melanoma ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Mucoepidermoid carcinoma of salivary gland ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Neuroendocrine carcinoma ^{†1}	2/324 (0.62%)	4	0/324 (0.00%)	0
Oral haemangioma ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Prostate cancer ^{†1}	2/324 (0.62%)	2	1/324 (0.31%)	1
Rectal cancer ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Skin squamous cell carcinoma	0/324 (0.00%)	0	1/324 (0.31%)	1

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metastatic ^{†1}				
Small cell lung cancer metastatic ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Squamous cell carcinoma of skin ^{†1}	3/324 (0.93%)	4	3/324 (0.93%)	3
Superficial spreading melanoma stage II ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Thymoma malignant recurrent ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Transitional cell cancer of the renal pelvis and ureter ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Transitional cell carcinoma ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0

Nervous system disorders

Carotid artery occlusion ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Central nervous system haemorrhage ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	2
Cerebral haemorrhage ^{†1}	1/324 (0.31%)	2	0/324 (0.00%)	0
Cerebral infarction ^{†1}	0/324 (0.00%)	0	2/324 (0.62%)	3
Cerebrovascular accident ^{†1}	3/324 (0.93%)	3	1/324 (0.31%)	2
Dysarthria ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	2
Headache ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Ischaemic stroke ^{†1}	1/324 (0.31%)	2	1/324 (0.31%)	1
Post herpetic neuralgia ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Seizure ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Syncope ^{†1}	1/324 (0.31%)	1	2/324 (0.62%)	2
Transient ischaemic attack ^{†1}	2/324 (0.62%)	2	2/324 (0.62%)	2

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Delirium ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	2
Depression ^{†1}	1/324 (0.31%)	1	1/324 (0.31%)	1
Suicidal behaviour ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1

Renal and urinary disorders

Acute kidney injury ^{†1}	1/324 (0.31%)	1	3/324 (0.93%)	5
Chronic kidney disease ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Haematuria ^{†1}	1/324 (0.31%)	1	2/324 (0.62%)	3
Nephrolithiasis ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Renal failure ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	2

Reproductive system and breast disorders

Uterine polyp ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Vulva cyst ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0

Respiratory, thoracic and mediastinal disorders

Acute respiratory failure ^{†1}	1/324 (0.31%)	1	2/324 (0.62%)	2
Chronic obstructive pulmonary disease ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Dyspnoea ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Haemoptysis ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Haemothorax ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Hypoxia ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Pleural effusion ^{†1}	2/324 (0.62%)	2	2/324 (0.62%)	2
Pulmonary embolism ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	2
Pulmonary hypertension ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Pulmonary oedema ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0

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Respiratory failure ^{†1}	1/324 (0.31%)	1	2/324 (0.62%)	3

Skin and subcutaneous tissue disorders

Skin ulcer ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
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Vascular disorders

Aortic aneurysm rupture ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0
Haematoma ^{†1}	0/324 (0.00%)	0	2/324 (0.62%)	2
Hypertension ^{†1}	2/324 (0.62%)	2	1/324 (0.31%)	1
Peripheral arterial occlusive disease ^{†1}	0/324 (0.00%)	0	1/324 (0.31%)	1
Peripheral artery thrombosis ^{†1}	1/324 (0.31%)	1	0/324 (0.00%)	0

[†] Indicates events were collected by systematic assessment

¹ Term from vocabulary, MedDRA 24.0

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	3%			
Arm/Group Title	Zanubrutinib		Ibrutinib	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	304/324 (93.83%)		308/324 (95.06%)	

Blood and lymphatic system disorders

Anaemia ^{†1}	49/324 (15.12%)	69	49/324 (15.12%)	95
Neutropenia ^{†1}	74/324 (22.84%)	171	58/324 (17.90%)	128
Thrombocytopenia ^{†1}	31/324 (9.57%)	74	31/324 (9.57%)	55

Cardiac disorders

Atrial fibrillation ^{†1}	15/324 (4.63%)	16	36/324 (11.11%)	57
Palpitations ^{†1}	9/324 (2.78%)	9	13/324 (4.01%)	14

Ear and labyrinth disorders

Vertigo ^{†1}	10/324 (3.09%)	10	5/324 (1.54%)	5
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Cataract ^{†1}	11/324 (3.40%)	13	8/324 (2.47%)	8
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Gastrointestinal disorders

Abdominal pain ^{†1}	19/324 (5.86%)	30	16/324 (4.94%)	18
Abdominal pain upper ^{†1}	11/324 (3.40%)	14	4/324 (1.23%)	4
Constipation ^{†1}	22/324 (6.79%)	24	23/324 (7.10%)	25
Diarrhoea ^{†1}	52/324 (16.05%)	90	78/324 (24.07%)	140
Dyspepsia ^{†1}	21/324 (6.48%)	22	21/324 (6.48%)	27
Gastroesophageal reflux disease ^{†1}	15/324 (4.63%)	22	14/324 (4.32%)	16
Mouth ulceration ^{†1}	5/324 (1.54%)	6	10/324 (3.09%)	11
Nausea ^{†1}	26/324 (8.02%)	41	31/324 (9.57%)	37
Vomiting ^{†1}	19/324 (5.86%)	20	26/324 (8.02%)	30

General disorders

Asthenia ^{†1}	19/324 (5.86%)	24	9/324 (2.78%)	12
Fatigue ^{†1}	31/324 (9.57%)	34	42/324 (12.96%)	48
Oedema peripheral ^{†1}	20/324 (6.17%)	23	23/324 (7.10%)	28
Peripheral swelling ^{†1}	13/324 (4.01%)	14	23/324 (7.10%)	25
Pyrexia ^{†1}	26/324 (8.02%)	31	32/324 (9.88%)	42

Immune system disorders

Hypogammaglobulinaemia ^{†1}	11/324 (3.40%)	12	7/324 (2.16%)	7
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Infections and infestations

Bronchitis ^{†1}	13/324 (4.01%)	15	19/324 (5.86%)	24
COVID-19 ^{†1}	65/324 (20.06%)	74	51/324 (15.74%)	54
Cellulitis ^{†1}	10/324 (3.09%)	12	12/324 (3.70%)	14
Conjunctivitis ^{†1}	5/324 (1.54%)	8	10/324 (3.09%)	13

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Herpes zoster ^{†1}	11/324 (3.40%)	12	7/324 (2.16%)	10
Nasopharyngitis ^{†1}	11/324 (3.40%)	11	9/324 (2.78%)	12
Oral herpes ^{†1}	4/324 (1.23%)	9	12/324 (3.70%)	15
Paronychia ^{†1}	4/324 (1.23%)	5	10/324 (3.09%)	10
Pharyngitis ^{†1}	6/324 (1.85%)	8	11/324 (3.40%)	17
Pneumonia ^{†1}	21/324 (6.48%)	31	27/324 (8.33%)	40
Sinusitis ^{†1}	14/324 (4.32%)	19	12/324 (3.70%)	13
Skin infection ^{†1}	6/324 (1.85%)	7	11/324 (3.40%)	14
Upper respiratory tract infection ^{†1}	68/324 (20.99%)	107	46/324 (14.20%)	72
Urinary tract infection ^{†1}	30/324 (9.26%)	55	26/324 (8.02%)	47

Injury, poisoning and procedural complications

Contusion ^{†1}	44/324 (13.58%)	55	34/324 (10.49%)	39
Fall ^{†1}	13/324 (4.01%)	15	16/324 (4.94%)	19
Skin laceration ^{†1}	11/324 (3.40%)	11	3/324 (0.93%)	3

Investigations

Alanine aminotransferase increased ^{†1}	9/324 (2.78%)	12	13/324 (4.01%)	19
Aspartate aminotransferase increased ^{†1}	3/324 (0.93%)	4	11/324 (3.40%)	16
Blood creatinine increased ^{†1}	15/324 (4.63%)	23	7/324 (2.16%)	7
Blood pressure increased ^{†1}	7/324 (2.16%)	14	14/324 (4.32%)	24
Neutrophil count decreased ^{†1}	25/324 (7.72%)	66	21/324 (6.48%)	61
Platelet count decreased ^{†1}	12/324 (3.70%)	28	20/324 (6.17%)	39

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Weight decreased ^{†1}	19/324 (5.86%)	24	14/324 (4.32%)	19

Metabolism and nutrition disorders

Decreased appetite ^{†1}	10/324 (3.09%)	10	19/324 (5.86%)	20
Gout ^{†1}	3/324 (0.93%)	8	10/324 (3.09%)	16
Hyperuricaemia ^{†1}	12/324 (3.70%)	28	19/324 (5.86%)	32
Hypokalaemia ^{†1}	18/324 (5.56%)	27	16/324 (4.94%)	24

Musculoskeletal and connective tissue disorders

Arthralgia ^{†1}	47/324 (14.51%)	59	53/324 (16.36%)	68
Back pain ^{†1}	21/324 (6.48%)	22	23/324 (7.10%)	26
Muscle spasms ^{†1}	10/324 (3.09%)	12	41/324 (12.65%)	48
Myalgia ^{†1}	10/324 (3.09%)	12	12/324 (3.70%)	12
Pain in extremity ^{†1}	20/324 (6.17%)	24	23/324 (7.10%)	27

Neoplasms benign, malignant and unspecified (incl cysts and polyps)

Basal cell carcinoma ^{†1}	9/324 (2.78%)	16	11/324 (3.40%)	26
Squamous cell carcinoma of skin ^{†1}	11/324 (3.40%)	16	12/324 (3.70%)	16

Nervous system disorders

Dizziness ^{†1}	27/324 (8.33%)	32	23/324 (7.10%)	25
Headache ^{†1}	28/324 (8.64%)	35	31/324 (9.57%)	40
Paraesthesia ^{†1}	3/324 (0.93%)	3	10/324 (3.09%)	12

Psychiatric disorders

Anxiety ^{†1}	10/324 (3.09%)	10	11/324 (3.40%)	17
Insomnia ^{†1}	16/324 (4.94%)	17	17/324 (5.25%)	18

Renal and urinary disorders

Haematuria ^{†1}	15/324 (4.63%)	17	12/324 (3.70%)	18
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Respiratory, thoracic and mediastinal disorders

Cough ^{†1}	38/324 (11.73%)	45	34/324 (10.49%)	41
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Dyspnoea ^{† 1}	11/324 (3.40%)	14	12/324 (3.70%)	15
Epistaxis ^{† 1}	24/324 (7.41%)	39	22/324 (6.79%)	42
Oropharyngeal pain ^{† 1}	9/324 (2.78%)	10	10/324 (3.09%)	10
Productive cough ^{† 1}	11/324 (3.40%)	12	9/324 (2.78%)	10

Skin and subcutaneous tissue disorders

Petechiae ^{† 1}	29/324 (8.95%)	37	15/324 (4.63%)	15
Pruritus ^{† 1}	21/324 (6.48%)	29	8/324 (2.47%)	9
Rash ^{† 1}	33/324 (10.19%)	61	40/324 (12.35%)	50
Rash maculo-papular ^{† 1}	12/324 (3.70%)	15	7/324 (2.16%)	10

Vascular disorders

Haematoma ^{† 1}	15/324 (4.63%)	20	14/324 (4.32%)	16
Hypertension ^{† 1}	70/324 (21.60%)	137	64/324 (19.75%)	125

[†] Indicates events were collected by systematic assessment

¹ Term from vocabulary, MedDRA 24.0

Limitations and Caveats

[Not Specified]

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor ⓘ

BeiGene

Investigators ⓘ

- Study Director: Study Director, BeiGene

Publications

General

These publications are provided voluntarily by the person who enters information about the study and may be about anything related to the study.

- [Brown JR, Eichhorst B, Hillmen P, Jurczak W, Kazmierczak M, Lamanna N, O'Brien SM, Tam CS, Qiu L, Zhou K, Simkovic M, Mayer J, Gillespie-Twardy A, Ferrajoli A, Ganly PS, Weinkove R, Grosicki S, Mital A, Robak T, Osterborg A, Yimer HA, Salmi T, Wang MD, Fu L, Li J, Wu K, Cohen A, Shadman M. Zanubrutinib or Ibrutinib in Relapsed or Refractory Chronic Lymphocytic Leukemia. N Engl J Med. 2023 Jan 26;388\(4\):319-332. doi: 10.1056/NEJMoa2211582. Epub 2022 Dec 13.](https://pubmed.ncbi.nlm.nih.gov/36511784) (https://pubmed.ncbi.nlm.nih.gov/36511784).
- [Hillmen P, Eichhorst B, Brown JR, Lamanna N, O'Brien SM, Tam CS, Qiu L, Kazmierczak M, Zhou K, Simkovic M, Mayer J, Gillespie-Twardy A, Shadman M, Ferrajoli A, Ganly PS, Weinkove R, Grosicki S, Mital A, Robak T, Osterborg A, Yimer HA, Salmi T, Ji M, Yecies J, Idoine A, Wu K, Huang J, Jurczak W. Zanubrutinib Versus Ibrutinib in Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma: Interim Analysis of a Randomized Phase III Trial. J Clin Oncol. 2023 Feb 10;41\(5\):1035-1045. doi: 10.1200/JCO.22.00510. Epub 2022 Nov 17.](https://pubmed.ncbi.nlm.nih.gov/36395435) (https://pubmed.ncbi.nlm.nih.gov/36395435).

Study Results

These publications are provided voluntarily by the person who enters information about the study and are about the study results.

- [Hillmen P, Brown JR, Eichhorst BF, Lamanna N, O'Brien SM, Qiu L, Salmi T, Hilger J, Wu K, Cohen A, Huang J, Tam CS. ALPINE: zanubrutinib versus ibrutinib in relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma. Future Oncol. 2020 Apr;16\(10\):517-523. doi: 10.2217/fon-2019-0844. Epub 2020 Mar 24.](https://pubmed.ncbi.nlm.nih.gov/32207333) (https://pubmed.ncbi.nlm.nih.gov/32207333).

More Information

Record History

Certain Agreements ⓘ

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed

BeiGene has 18 months from the end of the study at all sites to publish overall study results. After the 1st multi-site publication or the expiration of publication period, Investigators are free to publish/present the results of the study. Investigators must submit all draft publications/presentations to us for review 60 days prior to the planned publication/presentation date. BeiGene may request deletion of its confidential information & may request a further delay to protect its IP rights.



The U.S. government does not review or approve the safety and science of all studies listed on this website.

Read our full [disclaimer](https://clinicaltrials.gov/about-site/disclaimer) (<https://clinicaltrials.gov/about-site/disclaimer>) for details.

COMPLETED ⓘ

A Study of Zanubrutinib (BGB-3111) Versus Ibrutinib in Participants With Relapsed/Refractory Chronic Lymphocytic Leukemia (ALPINE)

ClinicalTrials.gov ID ⓘ NCT03734016

Sponsor ⓘ BeiGene

Information provided by ⓘ BeiGene (Responsible Party)

Last Update Posted ⓘ 2024-04-01

Record History Tab

Study Record Versions

- This table shows all the versions of this study record arranged in order by submitted date.
 - To view one version of the study record, click the submitted date.
 - To compare two versions, select them using the check boxes and click "Compare" at the bottom of the list.

Version		Date submitted (YYYY-MM-DD)	Changes
☐	1	2018-11-06	• None (earliest version on record)
☐	2	2018-11-07	• Study Status • Eligibility • Contacts/Locations
☐	3	2018-12-14	• Study Status • Study Identification
☐	4	2019-04-02	• Study Status • Contacts/Locations
☐	5	2019-04-03	• Study Status • Contacts/Locations
☐	6	2019-04-05	• Study Status • Contacts/Locations
☐	7	2019-06-18	• Study Status • Contacts/Locations
☐	8	2019-06-21	• Study Status • Contacts/Locations
☐	9	2019-06-25	• Study Status
			• Contacts/Locations
☐	11	2019-07-16	• Study Status • Study Identification • Contacts/Locations

Version		Date submitted (YYYY-MM-DD)	Changes
☐	12	2019-07-17	• Study Status • Contacts/Locations
☐	13	2019-07-30	• Study Status • Contacts/Locations
☐	14	2019-08-07	• Study Status • Contacts/Locations
☐	15	2019-09-17	• Study Status • Contacts/Locations
☐	16	2019-09-25	• Study Status • Contacts/Locations
☐	17	2019-10-08	• Study Status • Contacts/Locations
☐	18	2019-10-17	• Study Status • Contacts/Locations
☐	20	2019-11-01	• Study Status
☐	21	2019-12-05	• Recruitment Status • Study Status • Contacts/Locations
☐	22	2020-02-27	• Recruitment Status • Study Status • Contacts/Locations • Study Identification • Study Description • Arms and Interventions • Outcome Measures • Eligibility • IPDSharing • Study Design
☐	23	2020-04-20	• Study Status • Contacts/Locations
☐	24	2020-04-20	• Study Status • Contacts/Locations
☐	25	2020-05-04	• Study Status
☐	26	2020-06-10	• Study Status • Outcome Measures
☐	27	2020-08-11	• Study Status • References
☐	28	2021-04-27	• Recruitment Status • Study Status • Study Design
☐	29	2021-09-10	• Study Status
☐	30	2021-11-08	• Study Status
☐	31	2021-11-11	• Study Status

	Version	Date submitted (YYYY-MM-DD)	Changes
☐	32	2021-11-19	• Study Status
☐	33	2021-12-03	• Study Status
☐	34	2022-12-02	• Study Status
☐	35	2023-02-24	• Study Status
☐	36	2023-07-26	• Study Status • Study Description • Arms and Interventions • Outcome Measures • Eligibility • Contacts/Locations • References • Participant Flow • Baseline Characteristics • Adverse Events • More Information • Document Section
☐	37	2023-08-24	• Study Status • Contacts/Locations
☐	38	2023-11-03	• Study Status
☐	39	2024-03-28	• Recruitment Status • Study Status