

# AN ITALIAN RETROSPECTIVE-PROSPECTIVE OBSERVATIONAL STUDY ON THE USE OF ZANUBRUTINIB IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA (AZALEA)

**First published:** 20/02/2025

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Study

Ongoing

## Administrative details

### **PURI**

<https://redirect.ema.europa.eu/resource/1000000437>

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### **EU PAS number**

EUPAS1000000437

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### **Study ID**

1000000437

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### **DARWIN EU® study**

No

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## Study countries

Italy

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## Study description

This retrospective-prospective observational study is designed to collect information on the population of treatment-naïve (TN) or relapsed or refractory (R/R) chronic lymphocytic leukaemia (CLL) patients treated with zanubrutinib and clinical outcome of patients who received treatment according to the legislative decree on compassionate use (cohort A, retrospective and prospective study) and to collect information on the population of CLL patients treated with zanubrutinib in clinical practice who start treatment with zanubrutinib from the beginning of the study (cohort B, prospective only study).

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## Study status

Ongoing

# Research institutions and networks

## Institutions

**BeiGene**

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**Institution**

OSPEDALE A. PERRINO-BRINDISI

OSPEDALI RIUNITI DELLE MARCHE

ARCISPEDALE SANT'ANNA, FERRARA

AOOR VILLA SOFIA-CERVELLO

AZIENDA OSPEDALIERA NAZIONALE SS.ANTONIO E

BIAGIO E CESARE ARRIGO

ARNAS GARIBALDI, PRESIDIO OSPEDALIERO

NESIMA

AZIENDA OSPEDALIERA DI PADOVA

OSPEDALE DI BUSTO ARSIZIO

FONDAZIONE POLICLINICO UNIVERSITARIO

AGOSTINO GEMELLI

AZIENDA SOCIO SANITARIA TERRITORIALE DEGLI

SPEDALI CIVILI DI BRESCIA

AZIENDA OSPEDALIERO UNIVERSITARIA PISANA

ISTITUTO EUROPEO DI ONCOLOGIA

FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI

TUMORI

ISTITUTO ROMAGNOLO PER LO STUDIO DEI

TUMORI "DINO AMADORI" - IRST

UNIVERSITA DEGLI STUDI DI MODENA-AZIENDA

OSPEDALIERE POLICLINICO

AZIENDA OSPEDALIERA UNIVERSITARIA

POLICLINICO SANT'ORSOLA MALPIGHI

AZIENDA SANITARIA UNIVERSITARIA GIULIANO-

ISONTINA

AZIENDA OSPEDALIERA POLICLINICO DI BARI

AZIENDA OSPEDALIERA S MARIA DI TERNI

ARCISPEDALE S. MARIA NUOVA - AUSL REGGIO

EMILIA - ONCOLOGIA

OSPEDALE SANTA MARIA DELLA MISERICORDIA

AZIENDA OSPEDALIERA CITTÀ DELLA SALUTE E

DELLA SCIENZA DI TORINO

CRO IRCCS AVIANO

AO BROTZU - OSPEDALE ONCOLOGICO ARMANDO

BUSINCO

AOU MAGGIORE DELLA CARITA

AOU CAREGGI, SERVIZIO SANITARIO TOSCANA

AZIENDA OSPEDALIERA UNIVERSITARIA

POLICLINICO UMBERTO I - UNIVERSITÀ DI ROMA LA  
SAPIENZA

AZIENDA SOCIO SANITARIA TERRITORIALE

GRANDE OSPEDALE METROPOLITANO NIGUARDA

FONDAZIONE IRCCS CA GRANDA OSPEDALE

MAGGIORE POLICLINICO

OSPEDALE SAN RAFFAELE

AO CARDINALE G. PANICO

AZIENDA OSPEDALIERA SANT'ANNA E SAN  
SEBASTIANO

A.R.N.A.S. OSPEDALI CIVICO DI CRISTINA  
BENFRATELLI

OSPEDALE SAN GIOVANNI DI DIO E RUGGI  
D'ARAGONA

AZIENDA OSPEDALIERA UNIVERSITARIA  
POLICLINICO TOR VERGATA

Contact details

### **Study institution contact**

Clinical Trials BeiGene

Study contact

[clinicaltrials@beigene.com](mailto:clinicaltrials@beigene.com)

### **Primary lead investigator**

Clinical Trials BeiGene

Primary lead investigator

## Study timelines

### **Date when funding contract was signed**

Planned: 31/01/2024

Actual: 31/01/2024

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### **Study start date**

Planned: 01/03/2025

Actual: 26/02/2025

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### **Date of final study report**

Planned: 30/06/2029

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

BeiGene (Italy) S.r.l.

## Regulatory

**Was the study required by a regulatory body?**

No

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**Is the study required by a Risk Management Plan (RMP)?**

Not applicable

## Other study registration identification numbers and links

BGB-3111-MA-IT-401

## Methodological aspects

### Study type

### Study type list

**Study topic:**

Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Effectiveness study (incl. comparative)

Safety study (incl. comparative)

**Data collection methods:**

Primary data collection

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**Study design:**

The study will be conducted as a retrospective/prospective design.

Cohort A: Retrospective and prospective data collection

Cohort B: Prospective data collection

**Main study objective:**

The purposes of this study are to assess: The persistency of zanubrutinib treatment; the clinical characteristics of patients initiating treatment with zanubrutinib, the clinical outcomes of patients treated with zanubrutinib; and the safety of zanubrutinib when administered to patients with TN or R/R CLL. The primary endpoint is time to permanent discontinuation (TTD) of treatment with zanubrutinib.

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

**Name of medicine**

BRUKINSA

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**Name of medicine, other**

BGB-3111

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**Study drug International non-proprietary name (INN) or common name**

ZANUBRUTINIB

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**Medical condition to be studied**

Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia refractory

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**Additional medical condition(s)**

treatment-naive chronic lymphocytic leukaemia, relapsed or refractory chronic lymphocytic leukaemia

## Population studied

**Short description of the study population**

Cohort A: patients with CLL who were enrolled and treated as part of the BeiGene Compassionate Use Program and legislative decree on compassionate uses (7 September 2017).

Cohort B: patients with a confirmed diagnosis of CLL per the iwCLL criteria, TN or R/R, who were prescribed zanubrutinib in clinical practice, based on the standard of care criteria at the practice. A prescription for zanubrutinib must precede the patient's signature on the informed consent form.

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**Age groups**

Adult and elderly population ( $\geq 18$  years)

Elderly ( $\geq 65$  years)

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## **Estimated number of subjects**

250

## **Study design details**

### **Outcomes**

Primary: Time to permanent discontinuation (TTD) of treatment with zanubrutinib

Secondary:

- Reasons for permanent discontinuations of treatment with zanubrutinib
- Rate of discontinuations of zanubrutinib due to adverse events
- Cumulative incidence of treatment discontinuation according to reasons (i.e. PD, AEs, etc)
- Modality of treatment with zanubrutinib (daily dose and regimen of administration, i.e. QD and BID), dose reduction and rate of permanent dose reduction
- Overall survival (OS) and survival at predetermined time points (months, 6, 12, 18, 24, end of study)
- Progression-free survival (PFS) by Kaplan-Meier method
- Response rate (iwCLL criteria)
- Health resource utilization during the study: number and rates of hospitalizations, emergency room attendance, unscheduled visits
- Adherence to treatment (PROMIS questionnaire) at predetermined time points (months 3, 6, 9, 12, 18, 24, and every six months thereafter until end of treatment - EOT)
- Changes from baseline in patient-reported outcomes measured by the Global health status/QoL (GHS) and physical and role functioning scales of EORTC QLQC30, and symptom burden and fatigue scales of EORTC QLQ-CCL17 at

predetermined time points (months 3, 6, 9, 12, 18, 24, and every six months thereafter until EOT)

- Rate of adverse drug reactions to zanubrutinib
  - Rate of serious and not serious adverse events (related and not related to zanubrutinib)
  - Changes in concomitant medications
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### **Data analysis plan**

Data from all patients who signed the informed consent will be used in the analysis. All statistical analyses will be performed using all data collected in the database up to the data cutoff date.

The patient disposition will be summarized from the evaluable analysis set. The reason for discontinuation will be summarized. Unless otherwise specified, the analysis will be based on the evaluable analysis set. Data will be summarized overall and by cohort (cohort A and cohort B).

Quantitative data will be described by standard descriptive statistics (eg, mean, standard deviation, minimum, and maximum), and qualitative data will be summarized by frequency tables with number and proportion in each category. A missing category will be included as applicable.

For categorical endpoints, number and proportion of patients for each category will be summarized.

Time-to-event endpoints, i.e. time to permanent discontinuation of zanubrutinib, OS and PFS, will be summarized graphically using Kaplan-Meier plots overall and for each cohort.

Two interim analyses are planned for this study. The first interim analysis will

be performed in the retrospective part of cohort A, and the second interim analysis will be performed in the prospective part of cohort A and cohort B, at 6 months after the last prospective patient enrolled.

## Data management

### Data sources

#### **Data sources (types)**

Electronic healthcare records (EHR)

Expanded access program (compassionate use)

Non-interventional study

### Use of a Common Data Model (CDM)

#### **CDM mapping**

No

### Data quality specifications

#### **Check conformance**

Unknown

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#### **Check completeness**

Unknown

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**Check stability**

Unknown

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**Check logical consistency**

Unknown

## Data characterisation

**Data characterisation conducted**

No