

# ROSEWOOD Clinical Trial Fact Sheet

## FOR MEDICAL PRESS ONLY

Disclaimer: Any information on the products of the diseases contained herein is not intended to provide medical advice and/or treatment guidance.

The ROSEWOOD trial is a pivotal study designed to evaluate the efficacy, safety, and tolerability of BRUKINSA® (zanubrutinib) plus obinutuzumab versus obinutuzumab alone in patients with relapsed/refractory (R/R) follicular lymphoma (FL) who have received two or more lines of therapy.<sup>i,ii</sup>

A slow-growing and incurable cancer, FL is the most common non-Hodgkin lymphoma (NHL), accounting for 20%–30% of all NHL cases.<sup>iii,iv</sup>

## THE ROSEWOOD TRIAL (NCT03332017)<sup>i,ii</sup>

### Trial Design



Randomized, open-label, Phase 2 trial comparing the highly selective next-generation Bruton's tyrosine kinase (BTK) inhibitor BRUKINSA combined with obinutuzumab with obinutuzumab monotherapy



Enrolled 217 patients from Asia, Australia, North America, and Europe (France, Spain, Italy, Czechia, United Kingdom, Poland, Bulgaria, Germany, Russia, and Saint Barthélemy)



#### Key Inclusion Criteria

- Histologically confirmed diagnosis of FL
- $\geq 2$  prior systemic treatments for FL
- Prior treatment with an anti-CD20 antibody and an appropriate alkylator-based combination therapy
- Relapsed or refractory disease
- Presence of measurable disease
- Availability of archival tissue confirming diagnosis
- Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2
- Adequate bone marrow, renal, and hepatic functions



#### Key Exclusion Criteria

- Prior exposure to a BTK inhibitor
- Known central nervous system involvement by FL
- Evidence of transformation from FL to other aggressive histology
- Allogeneic hematopoietic stem cell transplantation within 12 months of enrollment
- Prior malignancy within the past two years, except for curatively treated basal or squamous cell skin cancer, superficial bladder cancer, carcinoma in situ of the cervix or breast, or localized Gleason score 6 prostate
- Clinically significant cardiovascular disease
- Major surgery or significant injury  $\leq 4$  weeks prior to start of study treatment
- Active fungal, bacterial, or viral infection requiring systemic treatment
- History of a severe bleeding disorder

### The ROSEWOOD Trial Consisted of Two Arms

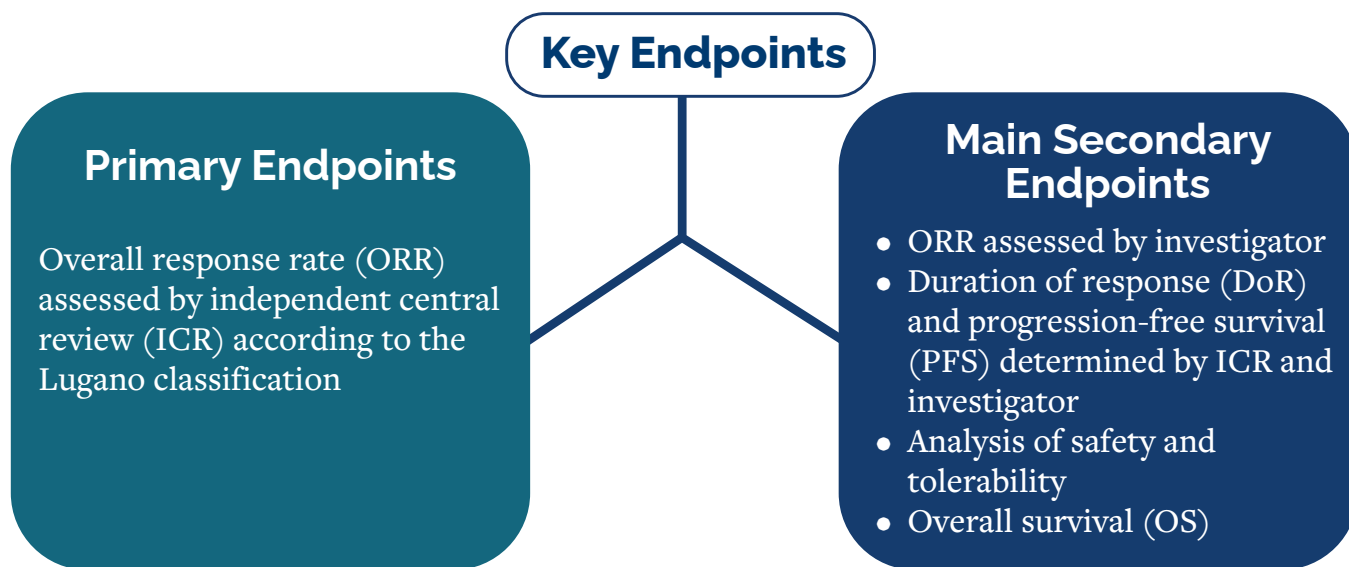


**Enrolled  
145 Patients**



**Enrolled  
72 Patients**

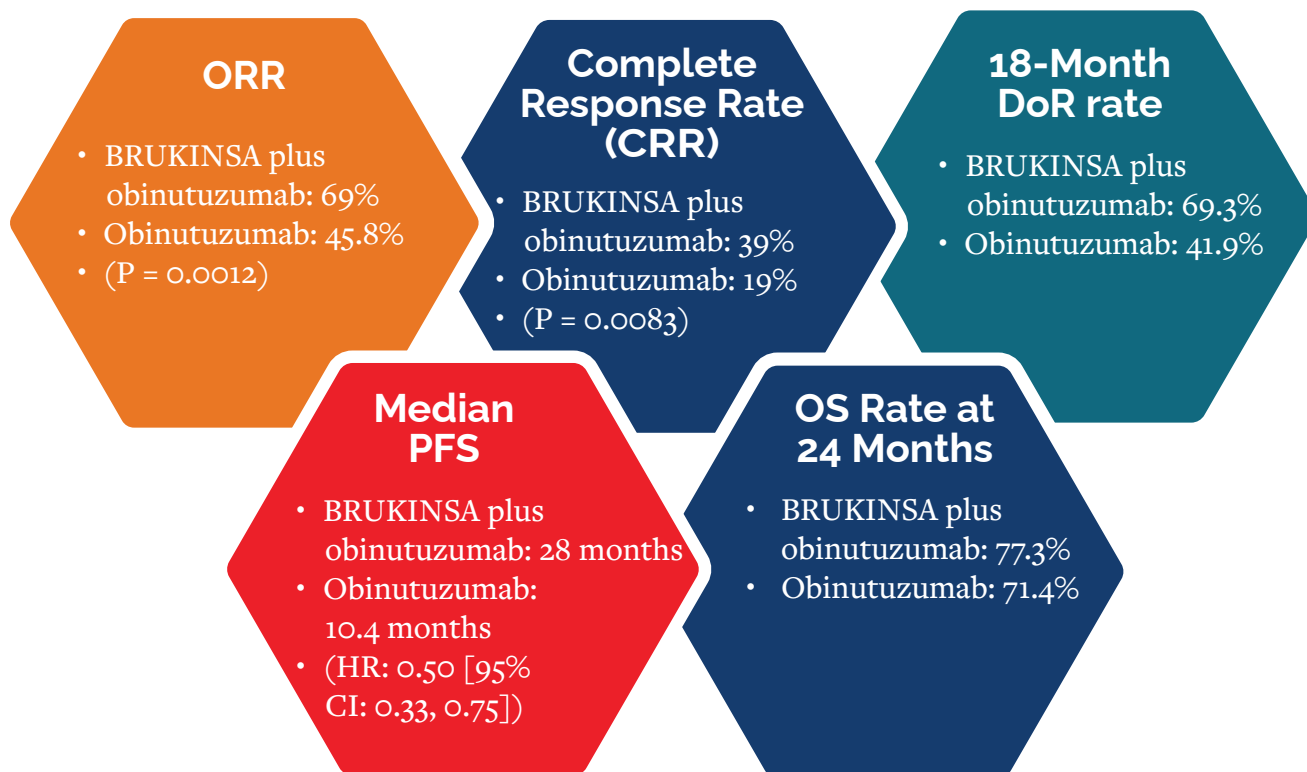
- Arm 1: 160 mg BRUKINSA twice daily plus 1,000 mg obinutuzumab intravenously on days one, eight, and 15 of cycle 1, then 1,000 mg on day 1 of cycles 2 to 6, then optional maintenance with 1,000 mg every eight weeks for up to two years.
- Arm 2: 1,000 mg obinutuzumab intravenously on days one, eight, and 15 of cycle 1, then 1,000 mg on day 1 of cycles 2 to 6, then optional maintenance with 1,000 mg every eight weeks for up to two years.
  - Patients were randomized 2:1 in favor of Arm 1.
- Among patients enrolled:
  - The median age of patients was 64 years (range, 31-88).
  - A total of 53% of patients had a high Follicular Lymphoma International Prognostic Index (FLIPI) score at screening.
  - The median number of prior lines of therapy was three (range, two-11).
  - A total of 53% and 35% of patients were refractory to rituximab or to the most recent line of therapy; 37% of patients had POD24.
  - A total of 99% of patients had received  $\geq 1$  prior immunochemotherapy.



## TRIAL RESULTS

At 20.2 months, the ROSEWOOD trial met its primary endpoint, demonstrating statistically significant higher ORR as assessed by ICR. BRUKINSA plus obinutuzumab was generally well tolerated, with safety results consistent with previous studies of both medicines. BRUKINSA plus obinutuzumab showed consistent benefit over obinutuzumab across prespecified subgroups.

## Key Efficacy Findings<sup>v</sup>



## Key Safety Findings<sup>i,v</sup>



The safety profile of BRUKINSA was consistent with that seen in prior studies and uniform between indications and treatment groups.



Incidences of atrial fibrillation and hypertension were low and similar in both treatment arms.



Infusion-related reactions were more frequent in the obinutuzumab monotherapy arm (9.9%) versus the BRUKINSA plus obinutuzumab arm (2.8%).



In Arm 1, 9% of patients had a BRUKINSA dose reduction due to adverse events (AEs); discontinuation due to treatment emergent adverse events (TEAEs) occurred in 16% of patients; 8% in Arm 1 had  $\geq 1$  TEAE leading to death, with no death related to TEAEs.

## Adverse Events

- The most common any-grade and grade  $\geq 3$  toxicities in the BRUKINSA plus obinutuzumab arm were hematologic toxicities, and other toxicities were similar between the two arms.
- Neutropenia (Arm 1: 14%, Arm 2: 23%)
- Thrombocytopenia (Arm 1: 15%, Arm 2: 7%)
- Incidence of atrial fibrillation (Arm 1: 0.7%)
- Major bleeding (Arm 1: 1.4%)



## About BRUKINSA<sup>®</sup> (zanubrutinib)



BRUKINSA is a small molecule inhibitor of BTK discovered by BeiGene scientists that is currently being evaluated globally in a broad clinical program as a monotherapy and in combination with other therapies to treat various B-cell malignancies. BRUKINSA was designed to deliver complete and sustained inhibition of the BTK protein by optimizing bioavailability, half-life, and selectivity. With differentiated pharmacokinetics compared to other approved BTK inhibitors, BRUKINSA has been demonstrated to inhibit the proliferation of malignant B cells within a number of disease-relevant tissues.

## U.S. Indications and Important Safety Information for BRUKINSA<sup>®</sup> (zanubrutinib)

### INDICATIONS

BRUKINSA is a kinase inhibitor indicated for the treatment of adult patients with:

- Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
- Waldenström's macroglobulinemia (WM)
- Mantle cell lymphoma (MCL) who have received at least one prior therapy.
- Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen.
- Relapsed or refractory follicular lymphoma (FL), in combination with obinutuzumab, after two or more lines of systemic therapy.

The MCL, MZL and FL indications are approved under accelerated approval based on overall response rate and durability of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

## IMPORTANT SAFETY INFORMATION

### Warnings and Precautions

#### Hemorrhage

Fatal and serious hemorrhage has occurred in patients with hematological malignancies treated with BRUKINSA. Grade 3 or higher hemorrhage including intracranial and gastrointestinal hemorrhage, hematuria, and hemothorax was reported in 3.8% of patients treated with BRUKINSA in clinical trials, with fatalities occurring in 0.2% of patients. Bleeding of any grade, excluding purpura and petechiae, occurred in 32% of patients.

Bleeding has occurred in patients with and without concomitant antiplatelet or anticoagulation therapy. Coadministration of BRUKINSA with antiplatelet or anticoagulant medications may further increase the risk of hemorrhage.

Monitor for signs and symptoms of bleeding. Discontinue BRUKINSA if intracranial hemorrhage of any grade occurs. Consider the benefit-risk of withholding BRUKINSA for 3-7 days before and after surgery depending upon the type of surgery and the risk of bleeding.

#### Infections

Fatal and serious infections (including bacterial, viral, or fungal infections) and opportunistic infections have occurred in patients with hematological malignancies treated with BRUKINSA. Grade 3 or higher infections occurred in 26% of patients, most commonly pneumonia (7.9%), with fatal infections occurring in 3.2% of patients. Infections due to hepatitis B virus (HBV) reactivation have occurred.

Consider prophylaxis for herpes simplex virus, *pneumocystis jirovecii* pneumonia, and other infections according to standard of care in patients who are at increased risk for infections. Monitor and evaluate patients for fever or other signs and symptoms of infection and treat appropriately.

#### Cytopenias

Grade 3 or 4 cytopenias, including neutropenia (21%), thrombocytopenia (8%) and anemia (8%) based on laboratory measurements, developed in patients treated with BRUKINSA. Grade 4 neutropenia occurred in 10% of patients, and Grade 4 thrombocytopenia occurred in 2.5% of patients.

Monitor complete blood counts regularly during treatment and interrupt treatment, reduce the dose, or discontinue treatment as warranted. Treat using growth factor or transfusions, as needed.

#### Second Primary Malignancies

Second primary malignancies, including non-skin carcinoma, have occurred in 14% of patients treated with BRUKINSA. The most frequent second primary malignancy was

non-melanoma skin cancers (8%), followed by other solid tumors in 7% of the patients (including melanoma in 1% of patients) and hematologic malignancies (0.7%). Advise patients to use sun protection and monitor patients for the development of second primary malignancies.

#### Cardiac Arrhythmias

Serious cardiac arrhythmias have occurred in patients treated with BRUKINSA. Atrial fibrillation and atrial flutter were reported in 4.4% patients treated with BRUKINSA, including Grade 3 or higher cases in 1.9% of patients. Patients with cardiac risk factors, hypertension, and acute infections may be at increased risk. Grade 3 or higher ventricular arrhythmias were reported in 0.3% of patients.

Monitor for signs and symptoms of cardiac arrhythmias (e.g., palpitations, dizziness, syncope, dyspnea, chest discomfort), manage appropriately, and consider the risks and benefits of continued BRUKINSA treatment.

#### Embryo-Fetal Toxicity

Based on findings in animals, BRUKINSA can cause fetal harm when administered to a pregnant woman. Administration of zanubrutinib to pregnant rats during the period of organogenesis caused embryo-fetal toxicity, including malformations at exposures that were 5 times higher than those reported in patients at the recommended dose of 160 mg twice daily. Advise women to avoid becoming pregnant while taking BRUKINSA and for 1 week after the last dose. Advise men to avoid fathering a child during treatment and for 1 week after the last dose. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

#### Adverse Reactions

The most common adverse reactions ( $\geq 30\%$ ), including laboratory abnormalities, in patients who received BRUKINSA (N=1729) are decreased neutrophil count (51%), decreased platelet count (41%), upper respiratory tract infection (38%), hemorrhage (32%), and musculoskeletal pain (31%).

#### Drug Interactions

**CYP3A Inhibitors:** When BRUKINSA is co-administered with a strong CYP3A inhibitor, reduce BRUKINSA dose to 80 mg once daily. For coadministration with a moderate CYP3A inhibitor, reduce BRUKINSA dose to 80 mg twice daily.

**CYP3A Inducers:** Avoid coadministration with strong or moderate CYP3A inducers. Dose adjustment may be recommended with moderate CYP3A inducers.

#### Specific Populations

**Hepatic Impairment:** The recommended dose of BRUKINSA for patients with severe hepatic impairment is 80 mg orally twice daily.

Please see full [Prescribing Information](#) including [Patient Information](#).

### References:

- i. BeiGene Clinical Data Presentations at 2022 ASCO Annual Meeting Demonstrate Mature and Growing Oncology Portfolio. Accessed July 7, 2023. <https://ir.beigene.com/news-details/?id=a04cfe0f-2879-4539-9c67-89cfd388b60>.
- ii. A Study Comparing Obinutuzumab and BGB-3111 Versus Obinutuzumab Alone in Treating R/R Follicular Lymphoma (ROSEWOOD). ClinicalTrials.gov. Accessed July 7, 2023. <https://classic.clinicaltrials.gov/ct2/show/NCT03332017>.
- iii. Leukemia & Lymphoma Society. Follicular Lymphoma (FL). Accessed July 7, 2023. <https://www.lls.org/research/follicular-lymphoma-fl#:~:text=FL%20has%20an%20annual%20incidence,average%20age%20of%20approximately%2060>.
- iv. Lymphoma Research Foundation. What is Lymphoma? Accessed July 7, 2023. <https://lymphoma.org/understanding-lymphoma/aboutlymphoma/nhl/follicular-lymphoma/>.
- v. Zinsani PL, et al. ROSEWOOD: A Phase II Randomized Study of Zanubrutinib Plus Obinutuzumab Versus Obinutuzumab Monotherapy in Patients With Relapsed or Refractory Follicular Lymphoma. *J Clin Oncol*. 2023;41(33):5107-5117.