Phase 3 Zanubrutinib (BGB-3111) vs Bendamustine Plus Rituximab in Patients With Treatment-Naïve Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

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INTRODUCTION

- Bruton tyrosine kinase (BTK) plays a critical role in B-cell receptor (BCR) signaling, which mediates B-cell proliferation, migration, and adhesion.
- The BCR pathway is an established therapeutic target in chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and the first-generation BTK inhibitor ibritinib has become a standard of care.

STUDY DESIGN

- International, open-label, phase 3, randomized study of zanubrutinib vs BR in patients with treatment-naïve CLL/SLL considered unsuitable for treatment with fludarabine, cyclophosphamide, plus rituximab (FCR) (Figure 3).
- 420 patients without del17p (cohort 1) randomized to receive either zanubrutinib (arm A) or BR (arm B).
- Approximately 47 patients with del17p (cohort 2) assigned to receive zanubrutinib monotherapy (arm C).

DRUG ADMINISTRATION

- Zanubrutinib: administered as two 80-mg capsules taken orally twice per day (160 mg twice per day) with or without food.
- Bendamustine administered intravenously at a dose of 90 mg/m²/day on days 1 and 2 of each 28-day cycle for 6 cycles.
- Rituximab: administered intravenously at a dose of 375 mg/m² on day 0 of cycle 1, and at a dose of 500 mg/m² on day 1 of cycles 2 through 6.

STUDY ENDPOINTS

- PRIMARY
  - To compare efficacy between treatment groups in cohort 1, as measured by progression-free survival (PFS) determined by independent central review.
- SECONDARY
  - To evaluate efficacy in cohort 1, as measured by the following:
    - ORR determined by independent central review and by investigator assessment.
    - Duration of response (DOR) determined by independent central review.
    - Safety in cohort 1.
  - Efficacy in cohort 2 (patients with del17p).
  - Pharmacokinetics of zanubrutinib in patients who received this treatment (arms A and C).

ELIGIBILITY CRITERIA

- Key Inclusion Criteria
- Key Exclusion Criteria

STUDY STATUS

- This study opened to accrual in October 2017 and will be recruiting patients from 165 participating sites throughout the European Union, Asia-Pacific, and North America.

ENROLLMENT

- Enrollment started in November 2017
- Contact information:
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REFERENCES

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DISCLOSURES

- JB: Has served as a consultant/advisor for AbbVie, AstraZeneca, Celgene, Glaxo, Janssen, Pfizer, and Roche; received honoraria and research funding from AbbVie, Janssen, and Pfizer. This study is supported by Beigene. Editorial support was provided by Bio Connections, LLC and funded by Beigene.

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