Trial in Progress: A Phase 2, Multicenter, Single-Arm Study of Zanubrutinib (BGB-3111) in Patients With Previously Treated B-Cell Malignancies Intolerant to Ibrutinib or Acalabrutinib

Background:
- Zanubrutinib (BGB-3111) is a second-generation Bruton tyrosine kinase (BTK) inhibitor approved by the FDA for use in patients with R/R MCL.
- It has been shown in nonclinical studies to be a highly potent, selective, bioavailable, and irreversible BTK inhibitor.
- Complete and sustained BTK occupancy in both peripheral blood mononuclear cells and lymph nodes has been demonstrated.

Key Eligibility Criteria:
- Patients must be intolerant to prior treatment with ibrutinib or acalabrutinib.
- Patients must have previously treated B-cell malignancies.
- Patients must have had disease progression on prior treatment.

Study Design:
- This is a Phase 2, open-label, single-arm study.
- Zanubrutinib will be administered orally once daily (qd) in 28-day cycles.
- The primary endpoint is progression-free survival (PFS) by investigator.

Key Safety Parameters:
- Common and serious adverse events experienced by patients on this study include:
  - Fatigue
  - Diarrhea
  - Dyspnea
  - Anemia
  - Fever

Key Pharmacokinetic Parameters:
- Zanubrutinib has a half-life of approximately 24 hours, allowing once-daily dosing.
- Bioavailability is high, with a Cmax of 160 mg bid.

Conclusion:
- Zanubrutinib shows promise in patients with previously treated B-cell malignancies intolerant to ibrutinib or acalabrutinib.

References:
- Choe H, Ruan J. JCO 2016;34:847-858.
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Statistical Methods:
- All analyses will be done in the safety analysis set, which includes all patients who received at least one dose of zanubrutinib.
- No formal hypothesis testing is planned for this study; all analyses are descriptive in nature.

Secondary Endpoints:
- Overall response rate
- Progression-free survival (PFS)
- Progression-free survival (PFS) by investigator
- Patient-reported outcomes measured by EQ-5D-5L and EORTC QoL-C30 questionnaires

Disclosures:
- This study is supported by Research Grants from the National Cancer Institute (NCI), the National Institutes of Health (NIH), and the National Science Foundation (NSF).
- The sponsors had no role in the design, conduct, or analysis of this study.

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ENROLLMENT:
- Enrollment started in October 2019 and is ongoing.
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REFERENCES:
- Choe H, Ruan J. JCO 2016;34:847-858.