ALPINE: Phase III zanubrutinib (BGB-3111) versus ibrutinib in patients with relapsed/refractory (R/R) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).

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Background:
Inhibition of Bruton tyrosine kinase (BTK) has emerged as a strategy for targeting B-cell malignancies including CLL/SLL. Zanubrutinib, an investigational inhibitor of BTK, was specifically engineered to optimize selectivity, half-life and solubility in an effort to decrease toxicities and better penetrate tumor tissue. Early clinical data suggested that zanubrutinib treatment in patients with treatment-naïve (TN; n = 16) or R/R (n = 50) CLL/SLL induced deep responses: 94% overall response rate (ORR), including 6% and 2% complete response rates in TN and R/R CLL/SLL, respectively (ICML 2017). This study is designed to evaluate whether zanubrutinib monotherapy exhibits non-inferior and potentially superior efficacy based on the ORR vs ibrutinib monotherapy in patients with R/R CLL/SLL.

Methods:
This ongoing phase 3, randomized, open-label, global study (NCT03734016, BGB-3111-305) is comparing the efficacy and safety of zanubrutinib vs ibrutinib in adult patients with R/R CLL/SLL. Approximately 400 patients will be randomized, 1:1 to each arm and stratified by age (< 65 vs ≥ 65 years), refractory status (yes vs no), geographic region, and del(17p)/*TP53* mutation status (present vs absent). Key inclusion criteria include R/R CLL/SLL requiring treatment per iwCLL criteria, ECOG PS 0-2, and adequate hematologic function. The primary endpoint is ORR as determined by an independent review committee according to iwCLL guidelines, with modification for treatment-related lymphocytosis for patients with CLL and per 2014 Lugano Classification for patients with SLL. The study is powered to test the non-inferiority and superiority of the ORR for zanubrutinib vs ibrutinib. Secondary endpoints include progression-free survival, safety, duration of response, and overall survival. Recruitment is ongoing. Clinical trial information: NCT03734016