Title: Randomized phase 2 zanubrutinib (BGB-3111) + obinutuzumab (obi) vs obi monotherapy in patients (pts) with relapsed/refractory follicular lymphoma (R/R FL)

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Background: Bruton tyrosine kinase (BTK) inhibition has emerged as a strategy for targeting B-cell malignancies, including R/R FL. Zanubrutinib, an investigational BTK inhibitor, 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 in pts with R/R FL, zanubrutinib + obi induced deep and sustained responses, was generally well tolerated, and had an overall response rate (ORR) of 76.2% (16 of 21 pts; Tam et al ASH 2017). This study is designed to evaluate the safety and efficacy zanubrutinib + obi vs obi monotherapy in pts with R/R FL.

Methods: This ongoing, phase 2, global, randomized, open-label, active-controlled study (NCT03332017, BGB-3111-212) is examining a total of 210 patients: obi + zanubrutinib vs. obi in pts with R/R FL with $\geq$2 prior lines of therapy. Pts are randomized 2:1 to receive oral zanubrutinib 160 mg twice daily + obi or obi alone until progressive disease (PD), toxicity, or a max of 30 mo of obi. Randomization is stratified by prior therapies (2-3 vs >3) and rituximab-refractory status. Eligible pts must have histologically confirmed grade 1-3a B-cell FL, received prior anti-CD20 antibody and alkylator-based combination therapy, and measurable disease. Disease response is assessed per the 2014 Lugano Classification for NHL. The primary endpoint is ORR by independent review committee (IRC). Key secondary endpoints include ORR by investigator assessment, rate of complete response or complete metabolic response, time to and duration of response, progression-free survival (all IRC and investigator assessments), overall survival, and safety. At the investigator's discretion, pts in the obi arm can crossover to combination arm if they have PD at any time or less than partial response after 12 cycles. Recruitment is ongoing.