ZANUBRUTINIB PLUS OBINUTUZUMAB (ZO) VERSUS OBINUTUZUMAB (O) MONOTHERAPY IN PATIENTS WITH RELAPSED OR REFRACTORY (R/R) FOLLICULAR LYMPHOMA (FL): PRIMARY ANALYSIS OF THE PHASE 2 RANDOMIZED ROSEWOOD TRIAL

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ABSTRACT

FL is the most common type of indolent non-Hodgkin lymphoma but has limited approved treatment options. In a phase 1b trial, ZO was tolerable and associated with an early efficacy signal. ROSEWOOD (BGB-3111-212) is a phase 2 randomized study to assess efficacy and safety of ZO vs O in pts with R/R FL with ≥2 prior therapy lines (ie, anti-CD20 antibody and alkylating agent). Pts were randomized 2:1 to ZO and O arms. O was given on Days 1, 8, and 15 of Cycle 1, Day 1 of Cycles 2-6, then every 8 wks for ≤20 doses. Z (160 mg twice daily) was given until progressive disease (PD) or unacceptable toxicity; O arm pts with confirmed PD could crossover to ZO. The primary endpoint was overall response rate (ORR) by independent central review. Secondary endpoints were complete response rate (CRR), duration of response (DOR), progression-free survival (PFS), overall survival (OS), and safety. ORR by investigator after crossover was an exploratory endpoint. Primary analysis cutoff was 10/8/2021. In all, 217 pts were randomized to ZO (n=145) or O (n=72). Median follow-up was 12.5 mo; median age was 64 y. 53% (ZO) and 51% (O) had high FL International Prognostic Index scores. The median prior lines of therapy was 3; 28% (ZO) and 25% (O) received >3 lines. Proportion of pts refractory to rituximab, refractory to the most recent therapy line, or with PD within 24 mo of first-line immunochemotherapy initiation was 54%, 32% and 28% (ZO) and 50%, 40% and 32% (O), respectively. The primary endpoint was met; ORR was 68.3% (ZO) vs 45.8% (O; *P*=.0017). CRR was 37.2% (ZO) vs 19.4% (O); 18-mo DOR rate was 70.9% (ZO) vs 54.6% (O); median PFS was 27.4 mo (ZO) vs 11.2 mo (O; hazard ratio [HR], 0.51 [95% CI, 0.32–0.81], *P*=0.0040). Median time to new anti-lymphoma therapy or crossover was not evaluable (NE; ZO) vs 12.1 mo (O; HR, 0.37 [95% CI, 0.23–0.60], *P*<0.0001). ORR for ZO crossovers (n=29) was 24.1%. Median OS was NE; 18-mo OS was 85.4% (ZO) vs 72.6% (O). Most common AEs in the ZO arm were thrombocytopenia (34.3%), neutropenia (27.3%), diarrhea (16.1%), and fatigue (14.0%). Grade ≥3 AEs in >5% of pts with ZO were neutropenia (22.4%) and thrombocytopenia (14.0%); incidence of atrial fibrillation was 0.7% and major bleeding was 1.4%. Incidence of fatal treatment-emergent AEs was 5.6% (ZO) and 9.9% (O). In all, ZO demonstrated superior efficacy to O and had a favorable benefit-risk profile in pts with R/R FL, suggesting that ZO may be a potential combination therapy for pts with R/R FL.