High overall response rate with the BTK inhibitor BGB-3111 in patients with chronic lymphocytic leukemia / small lymphocytic lymphoma: an update on safety and activity

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Introduction: BGB-3111 is a potent, highly specific, and irreversible Bruton tyrosine kinase (BTK) inhibitor, with greater selectivity for BTK vs other TEC- and EGFR-family kinases and favorable pharmacokinetic and pharmacodynamic properties. BGB-3111 was shown to achieve complete, continuous BTK occupancy in peripheral blood mononuclear cells and lymph nodes and was associated with durable clinical responses in patients (pts) with CLL/SLL and Waldenström macroglobulinemia. Here, updated preliminary safety and activity data in relapsed/refractory (R/R) and treatment-naïve (TN) pts with CLL/ SLL are reported. Methods: This is an open-label, multicenter, phase 1b study of BGB-3111 in pts with B-cell malignancies. Pts with R/R CLL/SLL were included in dose escalation, and both TN and R/R CLL/SLL pts were included in expansion cohorts at the recommended phase 2 dose (320 mg/d, given once daily [QD] or split as a twice-daily [BID] dose). Adverse events (AEs) are reported per Common Terminology Criteria for AEs version 4.03, and response per the modified iwCLL criteria (Hallek 2008, Cheson 2012 clarification for novel therapies). Results: As of 15 Dec 2016, 68 pts with CLL/SLL (50 R/R and 18 TN) were enrolled: 4 pts in dose escalation and 64 in cohort expansion at doses of 160 mg QD (n = 3), 160 mg BID (n = 25), and 320 mg QD (n = 40). Patient characteristics are shown in Table 1. Safety: Median follow-up was 7.2 (range, 0-23.3) months. The most frequent AEs of any cause were bruising (35%) and petechiae (11%), upper respiratory tract infection (28%), fatigue (25%), cough (22%), and diarrhea (21%). Four serious AEs related to BGB-3111 were seen in 3 pts: grade (Gr) 2 cardiac failure, Gr 2 pleural effusion, Gr 3 purpura, and Gr 3 pneumonia. The case of Gr 3 purpura (subcutaneous hemorrhage) was the only major bleeding event reported. Atrial fibrillation (Gr 3) occurred in 1 pt. One pt discontinued BGB-3111 for an AE (pleural effusion). Activity: of the 54 pts evaluable for response (>12 weeks follow-up or discontinuation before 12 weeks), the objective response rate was 96% (52/54), with partial response in 67% (36/54), partial response with lymphocytosis in 30% (16/54), stable disease in 1 R/R pt, and no assessment for 1 R/R pt because of AE. No instances of disease progression or Richter transformation were reported. Conclusions: BGB-3111 is well tolerated and highly active in R/R and TN CLL/SLL. With only 7.2 months of median follow-up, only 1 toxicity-related discontinuation, and no progressive disease seen thus far on study. (Table Presented).