Preliminary Safety and Efficacy Of BGB-11417, a Potent and Selective B-Cell Lymphoma 2 (BCL2) Inhibitor, in Patients (Pts) with Acute Myeloid Leukemia (AML)

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ABSTRACT

Background: BCL2, a key apoptosis regulator, is aberrantly expressed in many hematologic malignancies. The highly selective BCL2 inhibitor, BGB-11417, demonstrated more potent antitumor activity than venetoclax in preclinical studies. Here, preliminary results for BGB-11417 + azacitidine (aza) in AML are presented.

Methods: BGB-11417-103 (NCT04771130) is an ongoing, phase 1b/2, global, dose-escalation/expansion study. Eligible pts have treatment (tx)-naïve (TN) AML (unfit for intensive induction chemotherapy) or relapsed/refractory (R/R) AML (no prior aza or BCL2 inhibitors). Pts received 40mg (Cohort 1), 80mg (Cohort 2), or 160mg (Cohort 3) BGB-11417 for 10 d + aza (75 mg/m^2 x 7 d). Cycle 1 had a 4-d BGB-11417 ramp-up. Dose-limiting toxicity (DLT) through Day 28 (nonhematologic) and Day 42 (hematologic), tx-emergent AEs, and responses (2017 European LeukemiaNet criteria) were assessed.

Results: As of 10 Jan2022, 27 pts were treated (Cohort 1 n=6; Cohort 2 n=15; Cohort 3 n=6). Median age was 80 y (TN n=18) and 70 y (R/R n=9); 44% had adverse karyotype. At a median follow-up of 2.1 mo and median tx duration of 1.8 mo (range 0.3-7.6), 2/23 evaluable pts had DLTs: Grade [Gr]4 neutropenia and Gr4 thrombocytopenia (Cohort 2) which did not meet safety stopping criteria. 1 pt (Cohort 3) with chronic kidney disease had asymptomatic laboratory tumor lysis syndrome. The most common nonhematologic AEs were constipation (37%) and aza injection-site reaction (33%). The most common Gr≥3 hematologic AEs were neutropenia (44%), thrombocytopenia (41%), and anemia (37%). No pts had BGB-11417 dose reductions. 10 pts discontinued tx: AEs (n=3), proceeding to transplant (n=3), withdrawal (n=2), or disease progression (n=2). CR/CRh rates were 56% (TN) and 44% (R/R). 7/9 CRs occurred by the end of Cycle 1.

Discussion: Preliminary data suggest that 10-d BGB-11417 + aza was well-tolerated with promising activity in AML. Most AEs were low-grade in severity. 2 DLTs were seen across the 3 dose levels tested.

Conclusions: BGB-11417 + aza resulted in a majority of CR by the end of Cycle 1 and was well-tolerated in AML.