Preliminary safety and efficacy of BGB-11417, a potent and selective B-cell lymphoma 2 (BCL2) inhibitor, in patients with acute myeloid leukaemia (AML)

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ABSTRACT

Aim: 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 in AML are presented.

Method: BGB-11417-103 (NCT04771130) is an ongoing, phase 1b/2, global, dose-escalation/expansion study. Eligible patients have treatment-naïve (TN) AML (unfit for intensive induction chemotherapy) or relapsed/refractory (R/R) AML (no prior azacitidine or BCL2 inhibitors). Patients received 40mg (Cohort 1), 80mg (Cohort 2), or 160mg (Cohort 3) BGB-11417 for 10 days + azacitidine (75mg/m^2x7 days). Cycle 1 had a 4-day BGB-11417 ramp-up. Dose-limiting toxicity (DLT) through Day-28 (nonhematologic) and Day-42 (hematologic), treatment-emergent AEs, and responses (2017 European LeukemiaNet criteria) were assessed.

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

Conclusion: Preliminary data suggest that 10-day BGB-11417+azacitidine treatment was well-tolerated with promising activity in AML. Most AEs were low-grade in severity. 2 DLTs occurred across 3 dose levels tested. BGB-11417+azacitidine resulted in a majority of CR by the end of Cycle 1 and was well-tolerated in AML.