PRELIMINARY SAFETY AND EFFICACY OF BGB-11417, A POTENT AND SELECTIVE B-CELL LYMPHOMA 2 (BCL2) INHIBITOR, IN PATIENTS WITH ACUTE MYELOID LEUKEMIA (AML)

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ABSTRACT

Introduction: 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.

Methods: BGB-11417-103 (NCT04771130) is an ongoing, phase 1b/2, global, dose-escalation/expansion study. Eligible patients are those with treatment-naïve (TN) AML who are unfit for intensive induction chemotherapy or with relapsed/refractory (R/R) AML and have not had prior treatment with azacitidine or BCL2 inhibitors. Patients received 40mg (cohort 1), 80mg (cohort 2), or 160mg (cohort 3) BGB-11417 for 10 days + azacitidine (75mg/m^2) for 7 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 adverse events (AEs), and responses per 2017 European LeukemiaNet criteria were assessed.

Results: As of 10Jan2022, 27 patients were enrolled (cohort 1: n=6; cohort 2: n=15; cohort 3: n=6). After the 10Jan2022 data cut, 5 patients have been enrolled across 2 currently active sites in Spain. For all patients, the median age was 80 years (TN: n=18) and 70 years (R/R: n=9) and 44% had adverse karyotype. At a median follow-up of 2.1 months and median treatment duration of 1.8 months (range 0.3-7.6), 2 of 23 evaluable patients had DLTs (Grade 4 neutropenia and Grade 4 thrombocytopenia, both in cohort 2) which did not meet safety stopping criteria. One patient in cohort 3 with chronic kidney disease had asymptomatic laboratory tumor lysis syndrome which resolved within 4 days. The most common nonhematologic AEs were constipation (37%) and azacitidine injection-site reaction (33%). The most common Grade ≥3 hematologic AEs were neutropenia (44%), thrombocytopenia (41%), and anemia (37%). No patients had BGB-11417 dose-reductions. Ten patients discontinued treatment due to AEs (n=3), to proceed to transplant (n=3), due to withdrawal (n=2), or because of disease progression (n=2). CR/CRh rates were 56% (TN) and 44% (R/R). Median time to CR was 1.31 and 3.75 months for TN and R/R AML, respectively. Seven of 9 CRs occurred by the end of Cycle 1.

Conclusions: 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. Two DLTs occurred across 3 dose levels tested. BGB-11417 +

azacitidine resulted in a majority of CRs by the end of Cycle 1 and was well-tolerated in AML.