A Phase 1 Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Preliminary Antitumor Activity of Bcl-2 Inhibitor BGB-11417 in Adult Patients With Mature B-Cell Malignancies

INTRODUCTION

• B-cell lymphoma 2 (Bcl-2), a key regulatory protein of the intrinsic apoptotic pathway, is abnormally expressed in many hematologic malignancies and promotes tumor cell resistance to apoptosis.
• The Bcl-2 inhibitor venetoclax, a selective Bcl-2 inhibitor, has demonstrated antitumor activity and is being developed as a single agent or in combination therapies.

METHODS

• BGB-11417 (SGT483) is an ongoing phase I-2 study to evaluate the tolerability, antitumor activity of BGB-11417 in adult with B-cell malignancies (Figure 1).
• Daily (non-Hodgkin lymphoma [NHL]) or weekly (CLL/SLL) BGB-11417 dose ramp-up schedules were used to lessen the risk of tumor lysis syndrome (TLS).

RESULTS

• As of February 4, 2023, 17 patients (R/R NHL, n=5; R/R CLL/SLL, n=12) had received BGB-11417 doses of up to 640 mg (Figure 2).
• Of these 17 patients, 32% (n=11) of CLL/SLL patients received discontinuation study treatment.

CONCLUSIONS

• These initial results from BGB-11417-102 indicated that BGB-11417 monotherapy, at all tested doses up to 640 mg, was well tolerated without dose-dependent increases in toxicity.
• The risk of TLS was low and manageable in this study, with no clinical TLS observed.
• Initial antitumor activity of BGB-11417 monotherapy was promising, with responses observed in patients with R/R CLL/SLL at lower dose levels.
• Preliminary antitumor activity was observed in patients with NHL with BGB-11417 monotherapy; further expansion data are being generated.

REFERENCES

1. Caixia Li, Jia Wei, Keshu Zhou, Peng Liu, He Huang, Fei Li, Qiongqiong Cai, Juyun Dong, Shenmiao Yang, Hui Zhou, Lu Zhang, Zaixing Shi, Zhiyu Liang, Binghao Wu, and Depei Wu. Presenting at the European Hematology Association Annual Meeting, June 8-11, 2023, Frankfurt, Germany

DISCLOSURES

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