Sonrotoclax in combination with dexamethasone and daratumumab for t(11;14) relapsed/refractory multiple myeloma: Preliminary safety and efficacy results from the phase 1b/2 BGB-11417-105 study

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Introduction: Multiple myeloma (MM) with t(11;14) is dependent on BCL2-mediated survival signaling; however, there are no approved BCL2 therapies for MM. Sonrotoclax is a next-generation BCL2 inhibitor designed to have high target selectivity, enhanced pharmacologic potency, and an optimized pharmacokinetic profile characterized by a shorter half-life and

minimal drug accumulation. These properties may enable deeper target inhibition while mitigating toxicity. BGB-11417-105 (NCT04973605) is an ongoing phase 1b/2 study evaluating sonrotoclax combinations in t(11;14) relapsed/refractory (RR) MM. Here, we report preliminary results from the sonrotoclax + daratumumab + dexamethasone (SDd) cohort.

Methods: Eligible patients had RRMM with centrally confirmed t(11;14). Part 1 enrolled patients with ≥3 prior lines of therapy (PLoT), including a proteasome inhibitor (PI), immunomodulatory drug (IMiD), and anti-CD38 antibody (Ab). Part 2 enrolled patients with 1-3 PLoT, including a PI and IMiD; prior anti-CD38 Ab was allowed; however, patients refractory to their most recent anti-CD38 Ab, patients with early relapse or intolerance to anti-CD38 Ab, and patients exposed to anti-CD38 Ab within 6 months were excluded. Oral sonrotoclax (160/320/640 mg once daily) was given with oral/intravenous dexamethasone (40 mg once weekly) and subcutaneous daratumumab (1800 mg per standard schedule) in 28-day cycles. Dose-limiting toxicities (DLTs) were assessed up to day 28 of the first cycle. Treatment-emergent adverse events (TEAEs) were classified per MedDRA v29.0 and graded per CTCAE v5.0. The primary endpoint was safety and tolerability. Efficacy was assessed by investigators per International Myeloma Working Group criteria.

Results: As of May 20, 2026, 72 patients with t(11;14) RRMM received SDd at sonrotoclax doses of 160 mg (n=5), 320 mg (n=33), or 640 mg (n=34). Overall, median age was 65 years (range, 36-91); 51% were male; 49% were White, and 19% had high-risk cytogenetics. Median PLoT was 3 (range, 1-10); 25% had ≥4 PLoT. The R-ISS stage at initial diagnosis was I in 22%, II in 42%, and III in 17% of patients. Prior anti-CD38 Ab was used in 58% of patients, including 33% with anti-CD38-refractory disease; 56% were triple-class exposed, including 22% triple-class refractory. At data cutoff, median follow-up was 7.2 months (range, 3.3-19.1), and 56 patients (78%) remained on treatment. Among 16 patients who discontinued treatment, the most common reason was progressive disease (PD; n=11), followed by patient withdrawal (n=2), investigator decision (n=2), and AE (n=1). The most common (≥20%) all-grade TEAEs

were upper respiratory tract infection (36%), fatigue (31%), neutrophil count decreased (26%), diarrhea (26%), insomnia (25%), and nausea (24%). Grade 3/4 TEAEs occurred in 64% of patients; grade 3/4 hematologic TEAEs occurred in 33%, most commonly neutropenia (28%). Grade 3/4 infections and infestations occurred in 21%; no grade 5 infectious events were reported. Serious AEs occurred in 29%, most commonly pneumonia (8%). Two patients had DLTs: grade 4 neutropenia (320 mg) and grade 4 thrombocytopenia (640 mg); the maximum tolerated dose was not reached. No investigator-assessed sonrotoclax-related TEAEs led to sonrotoclax discontinuations; one patient required sonrotoclax dose reduction due to neutrophil count decreased. No grade 5 TEAEs were reported. Two patients died during the study (PD and respiratory/circulatory failure), both deemed unrelated to study treatment and occurring >30 days after the last dose. Among 70 efficacy-evaluable patients, the overall response rate (ORR), very good partial response or better (≥VGPR), and complete response or better (≥CR) were 87% (95% CI, 77-94), 59% (95% CI, 46-70), and 23% (95% CI, 14-34), respectively. For the 320-mg cohort, the ORR, ≥VGPR, and ≥CR were 88%, 63%, and 22%, respectively. For the 640-mg cohort, the ORR, ≥VGPR, and ≥CR were 91%, 61%, and 24%, respectively. Median time to response was 1.0 month (range, 0.9-4.0). Median duration of response (DOR) and progression-free survival (PFS) were not reached; 12-month DOR and PFS were 77% (95% CI, 52-91) and 69% (95% CI, 46-84), respectively.

Conclusion: SDd was well tolerated and had promising antimyeloma activity in heavily pretreated patients with t(11;14) RRMM, including those previously treated with an anti-CD38 Ab. These findings further support the broad clinical activity of sonrotoclax across hematologic malignancies.