Updated results of sonrotoclax + dexamethasone in patients with t(11;14)-positive relapsed/refractory multiple myeloma: An all-oral treatment

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ABSTRACT

Objective: Despite the clinical efficacy of BCL2 inhibition in t(11;14)-positive multiple myeloma (MM), no BCL2-targeted treatments are approved. Sonrotoclax (BGB-11417), a next-generation BCL2 inhibitor, is a more selective and pharmacologically potent inhibitor of BCL2 than venetoclax, with a shorter half-life and no drug accumulation. BGB-11417-105 (NCT04973605) is an ongoing phase 1b/2 study evaluating safety and efficacy of sonrotoclax as mono- or combination therapy in patients with t(11;14)-positive relapsed/refractory (R/R) MM. Here, we report updated safety and efficacy results in patients treated with sonrotoclax 320 or 640 mg + dexamethasone (dex).

Methods: Eligible patients had R/R MM with centrally confirmed t(11;14) and received oral daily sonrotoclax (320 mg or 640 mg) and weekly dex (40 mg) until end of treatment. Adverse events (AEs) were graded by CTCAE v5.0, and efficacy was assessed by the investigator per International Myeloma Working Group criteria.

Results: As of January 20, 2025, 14 and 36 evaluable patients had been enrolled in the sonrotoclax 320-mg and 640-mg cohorts, respectively; median (range) follow-up was 6.2 months (2.6-34.5) and 12.1 months (0.1-28.9), respectively. In the 320-mg vs 640-mg cohorts, respectively, median age (range) was 69.5 years (44-86) vs 69.0 years (48-80); 42.9% vs 52.8% were male; and 57.1% vs 75.0% were White. The median (range) prior lines of treatment were 3 (1-7) in the 320-mg cohort and 3 (1-12) in the 640-mg cohort; 78.6% and 66.7% of patients were refractory to 3 treatment classes, respectively. At data cutoff, 7 patients (50.0%) in the 320-mg cohort and 14 (38.9%) in the 640-mg cohort remained on study treatment; progression was the most common reason for discontinuation (35.7% and 41.7%, respectively). The ORR (95% CI) was 64.3% (35.1-87.2) in the 320-mg cohort and 80.6% (64.0-91.8) in the 640-mg cohort, with VGPR or better rates (95% CI) of 35.7% (12.8-64.9) and 55.6% (38.1-72.1), respectively. The median time to response was 0.7 months in both cohorts. Median (95% CI) duration of response was 5.9 months (1.8-not estimable [NE]) in the 320-mg cohort and 12.2 months (8.3-18.9) in the 640-mg cohort. Median (95% CI) progression-free survival was 6.6 months (2.9-NE) in the 320-mg cohort and 13.3 months (9.0-19.6) in the 640-mg cohort.
The safety profile was tolerable and manageable for both cohorts. The most common TEAEs were fatigue (n=5 [35.7%]) in the 320-mg cohort, and insomnia (38.9%) and diarrhea (38.9%, all grade 1 or 2) in the 640-mg cohort. Grade ≥3 TEAEs occurred in 5 patients (35.7%) in the 320-mg cohort and 17

patients (47.2%) in the 640-mg cohort; serious TEAEs occurred in 3 (21.4%) and 10 (27.8%), respectively. Grade ≥3 hematologic TEAEs occurred in 1 (7.1%) and 9 (25.0%) and grade ≥3 infections in 3 (21.4%) and 4 (11.1%) patients, respectively. Two patients (14.3%) in the 320-mg cohort and 2 (5.6%) in the 640-mg cohort died during the treatment-emergent portion of the study for reasons unrelated to sonrotoclax or dex (320-mg cohort, pneumonia RSV and COVID-19; 640-mg cohort, hypoventilation [related to pulmonary involvement of progressive disease] and metastatic pancreatic cancer). Four additional deaths occurred >30 days after the last 640-mg dose.

Conclusion: The all-oral combination of sonrotoclax + dex continued to show a tolerable safety profile, with low rates of infection and hematologic toxicity, and promising efficacy, with an ORR of 81% in the 640-mg cohort, in this t(11;14)-positive R/R MM population. The study is ongoing; additional treatment combinations with sonrotoclax are being investigated.