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

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ABSTRACT

Introduction: Despite the clinical efficacy of BCL2 inhibition in t(11;14)-positive MM, no BCL2-targeted treatments (tx) are approved. Sonrotoclax (sonro; 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 of sonro as mono- or combination tx in patients (pts) with t(11;14)-positive R/R MM. Updated results in pts treated with sonro + dexamethasone (dex) are presented.

Methods: Eligible pts had R/R MM with centrally confirmed t(11;14) and received oral sonro (320 or 640 mg QD) + dex (40 mg QW). Tx-emergent adverse events (TEAEs) were graded by CTCAE v5.0 and efficacy was assessed by the investigator per IMWG criteria.

Results: As of Jan 20, 2025, 14 and 36 evaluable pts were enrolled in the sonro 320-mg and 640-mg cohorts, respectively; median (range) follow-up was 6.2 mo (2.6-34.5) and 12.1 mo (0.1-28.9), respectively. The median (range) prior lines of tx were 3 (1-7) in the 320-mg cohort and 3 (1-12) in the 640-mg cohort; 78.6% and 66.7% of pts were refractory to 3 tx classes, respectively. At data cutoff, 7 pts (50.0%) in the 320-mg cohort and 14 (38.9%) in the 640-mg cohort remained on tx; 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 mo in both cohorts. Median (95% CI) duration of response was 5.9 mo (1.8-not estimable [NE]) in the 320-mg cohort and 12.2 mo (8.3-18.9) in the 640-mg cohort. Median (95% CI) PFS was 6.6 mo (2.9-NE) in the 320-mg cohort and 13.3 mo (9.0-19.6) in the 640-mg cohort.

The most common TEAEs were fatigue (35.7%) in the 320-mg cohort, and insomnia (38.9%) and diarrhea (38.9%, all grade 1/2) in the 640-mg cohort. Grade ≥3 TEAEs occurred in 5 pts (35.7%) in the 320-mg cohort and 17 pts (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%) pts, respectively. Two pts (14.3%) in the 320-mg cohort and 2 (5.6%) in the 640-mg cohort died during the tx-emergent part for reasons unrelated to tx (320 mg, pneumonia RSV and COVID-19; 640 mg, hypoventilation [related to pulmonary involvement with PD] and metastatic pancreatic cancer). Four more deaths occurred >30 d after the last 640-mg dose.

Conclusion: This ongoing study showed that the all-oral combination of sonro + dex is tolerable, 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. Additional tx combinations with sonro are being investigated.