Sonrotoclax (sonro; BGB-11417) + dexamethasone (dex) is tolerable and demonstrates antimyeloma activity in patients with relapsed/refractory (R/R) multiple myeloma (MM) harboring t(11;14)

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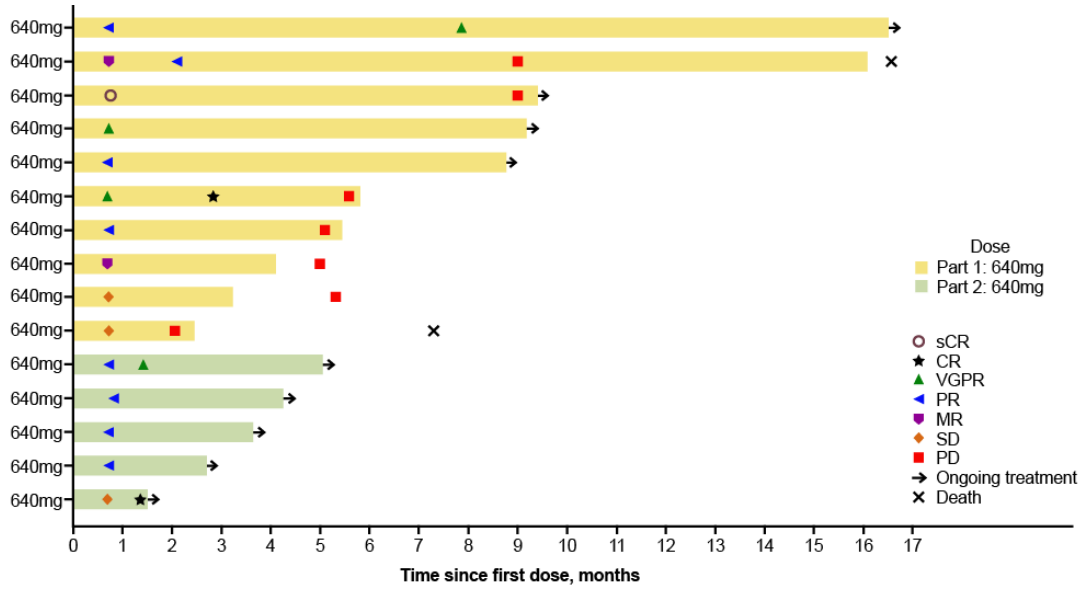
ABSTRACT

Introduction: Sonro (BGB-11417) is a more selective and pharmacologically potent BCL2 inhibitor than venetoclax in biochemical assays. BGB-11417-105 (NCT04973605) is an ongoing phase 1b/2 trial of sonro monotherapy or combination treatment (tx) for R/R MM harboring t(11;14); presented here are updated data from the sonro (640mg) + dex cohort.

Methods: Eligible pts had centrally confirmed t(11;14) and ≥3 (escalation cohorts) or ≥1 (expansion cohorts) prior tx lines. Pts received sonro 640mg orally once daily + dex 40mg weekly until progression or intolerance. AEs were graded per CTCAE v5.0, and response was investigator assessed per IMWG criteria.

Results: As of Jan 8, 2024, 20 pts were enrolled in the 640-mg escalation (n=10) and expansion (n=10) cohorts (median follow-up, 6.2 mo; range, 0.3-16.6). Pts had a median of 4 prior tx lines (range, 1-12); 70% and 80% were refractory to anti-CD38 and IMiDs, respectively. At the data cutoff, 13 pts (65%) were still on tx (discontinuations: progression, n=3; AE, n=2 [hematuria, pancreatic cancer]; withdrawal, n=1; physician decision, n=1). Insomnia (30%) and diarrhea, fatigue, and nausea (each 25%) were the most common TEAEs. Hematologic TEAEs occurred in 3 pts (thrombocytopenia, n=2 [grades 1 and 3]; neutropenia, n=1 [grade 1]). Serious TEAEs occurred in 3 pts (15%), and grade ≥3 AEs occurred in 4 pts (20%); none were considered related to sonro (2 pts had both serious TEAEs and grade ≥3 TEAEs). No DLTs were seen. Two pts died on study; neither death was tx related (1 TEAE [metastatic pancreatic cancer]; 1 non-TEAE [liver failure from hepatocellular carcinoma]). Infections in >1 pt were COVID-19 (10%) and upper respiratory tract infection (10%). In 15 efficacy-evaluable pts, the ORR was 80% (95% CI, 51.9-95.7), with 40% VGPR or better. Median time to response was 0.7 mo; median DOR was 8.3 mo (95% CI, 4.4-not reached), with a maximum DOR of 15.4 mo (ongoing) (**Figure**).

Conclusions: With longer follow-up, sonro + dex has a manageable safety profile, with low rates of hematologic toxicities and infections, and deep and durable responses were seen. In this ongoing study, other sonro combination tx are being investigated.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