Sonrotoclax plus dexamethasone was tolerable and demonstrated antimyeloma activity in patients with relapsed/refractory multiple myeloma harboring t(11;14)

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Introduction/Background: Although BCL2 inhibitors have shown clinical activity in patients with multiple myeloma (MM), no BCL2-targeted therapies are currently approved for MM. Sonrotoclax (BGB-11417) is more selective and a more pharmacologically potent inhibitor of BCL2 than venetoclax in biochemical assays. BGB-11417-105 (NCT04973605), an ongoing phase 1b/2 trial, evaluated sonrotoclax as monotherapy or combination therapy in patients with relapsed/refractory (R/R) MM harboring t(11;14). Updated data for sonrotoclax 640 mg plus dexamethasone are presented.

Methods: Eligible patients had R/R MM, centrally confirmed t(11;14), and ≥3 (dose finding) or ≥1 (dose expansion) prior therapy. Patients received sonrotoclax 640 mg orally once daily and dexamethasone 40 mg weekly. Adverse events (AEs) were graded per CTCAE v5.0 and disease responses were assessed per International Myeloma Working Group response criteria.

Results: As of January 8, 2024, 20 patients (median prior therapies, 4; range, 1-12) were enrolled (640-mg dose escalation, n=10; dose expansion, n=10). Median follow-up was 6.2 months (range, 0.3-16.6); 70% and 80% of patients were refractory to anti-CD38 and immunomodulatory drugs, respectively. Thirteen patients (65%) remained on treatment (discontinuations: disease progression, n=3; AE, n=2 [hematuria, pancreatic cancer]; patient withdrawal, n=1; physician decision, n=1). The most common treatment-emergent AEs (TEAEs) were insomnia (30%) and diarrhea, fatigue, and nausea (each 25%). Three patients had hematologic TEAEs (thrombocytopenia, n=2 [grades 1 and 3]; neutropenia, n=1 [grade 1]).

Three patients (15%) had serious TEAEs and 4 (20%) had grade ≥3 AEs; none were sonrotoclax related. No dose-limiting toxicities occurred. Two patients died on study (TEAE, n=1 [metastatic pancreatic cancer]; non-TEAE, n=1 [hepatocellular carcinoma–associated liver failure]; neither was considered treatment related). Infections in >1 patient were COVID-19 and upper respiratory tract infection (n=2 each [10%]). In efficacy-evaluable patients, objective response rate was 80% (12/15; 95% CI, 51.9%-95.7%); very good partial response or better rate was 40% (6/15). Median time to response was 0.7 months. Median duration of response (DOR) was 8.3 months (95% CI, 4.4-NR) and maximum DOR was 15.4 months (ongoing).

Conclusion: With longer follow-up, sonrotoclax plus dexamethasone demonstrated a manageable safety profile, with low hematologic toxicity and infection rates. The combination provided deep and durable responses in this R/R population.