Combination treatment (tx) with novel BCL2 inhibitor sonrotoclax (sonro; BGB-11417) and zanubrutinib (zanu) induces high rate of complete remission in patients (pts) with relapsed/refractory (R/R) mantle cell lymphoma (MCL)

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ABSTRACT

Introduction: Sonro (BGB-11417), a next-generation BCL2 inhibitor, is a more selective and pharmacologically potent inhibitor of BCL2 than venetoclax. Zanu, a next-generation BTK inhibitor (BTKi), has shown improved PFS and OS vs ibrutinib and is approved for R/R MCL. Safety and efficacy of sonro+zanu in pts with R/R MCL in the ongoing BGB-11417-101 (NCT04277637) study are presented.

Methods: Pts with R/R MCL (≥1 prior tx) received zanu (320 mg QD or 160 mg BID) 8-12 wk before sonro dose-escalation (80, 160, 320, or 640 mg QD) ramp-up to mitigate TLS risk. Sonro expansions at 160 and 320 mg followed. The primary endpoint was safety per CTCAE v5.0. A secondary endpoint was ORR per Lugano 2014 criteria. TLS was assessed per Howard 2011 criteria.

Results: As of Oct 31, 2023, 35 pts with R/R MCL were enrolled (80 mg, n=6; 160 mg, n=12; 320 mg, n=14; 640 mg, n=3). Pts had a median of 1 (range, 1-3) prior tx; 11 (31%) had a prior autologous stem cell transplant, and 3 had a prior BTKi. Dose escalation occurred per protocol at all defined doses. No DLTs occurred. MTD was not reached with doses up to 640 mg. Sonro dose levels of 160 and 320 mg were chosen for expansion cohorts. Three pts were still in zanu lead-in and 29 had started sonro. Of 9 pts who discontinued tx, 6 discontinued both drugs (progressive disease [PD], n=3; AE, n=2 [MDS and diarrhea]; withdrawal, n=1) and 3 did not complete zanu lead-in due to early PD. Five patients died due to PD (3 during zanu lead-in). TEAEs occurring in ≥20% of pts were neutropenia (31%), contusion (29%), thrombocytopenia (23%), and diarrhea (23%). Neutropenia was the most common grade ≥3 TEAE (20%). No TLS or atrial or ventricular fibrillation occurred. In 27 response-evaluable pts, the ORR was 85% (CR, n=18 [67%]). In the dose-expansion cohorts, ORRs were 91% (320 mg, 10/11; 10 CR) and 88% (160 mg, 8/9; 4 CR [44%]) (**Figure**). Median time to CR was 6.4 mo. In 2 response-evaluable pts with progression on a prior BTKi, 1 CR and 1 PD were observed.

Conclusions: Sonro+zanu is generally well tolerated and showed promising efficacy in R/R MCL, including deep and durable responses. Further expansion of the 320-mg cohort is ongoing.