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

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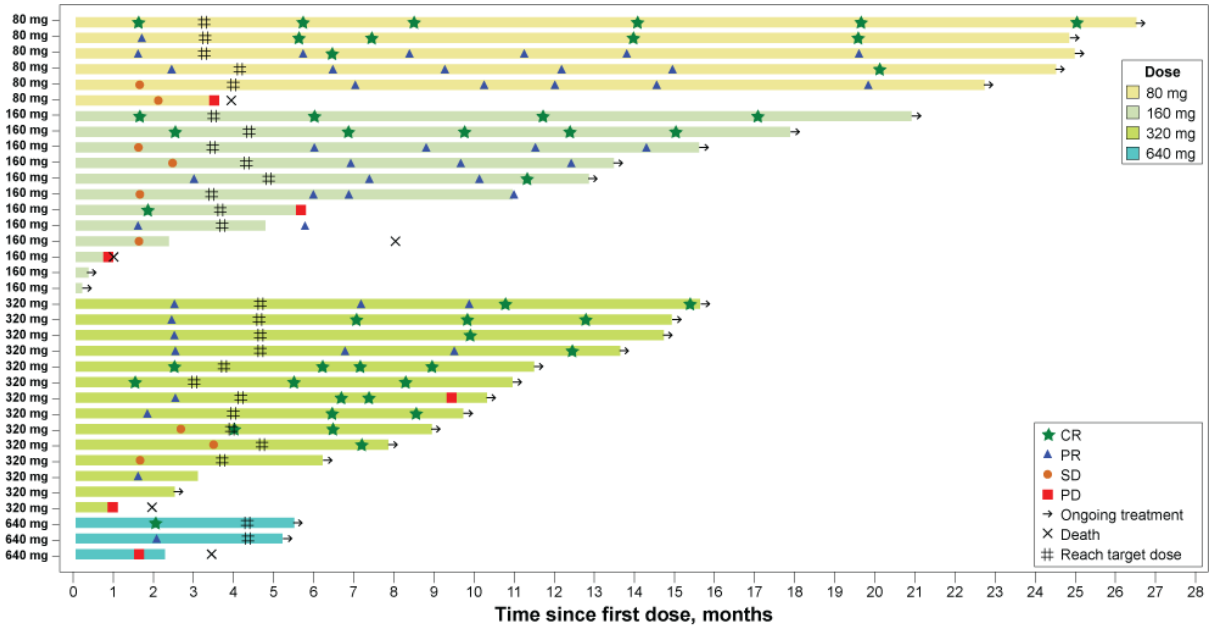
ABSTRACT

Aim: Sonrotoclax is a more selective and pharmacologically potent BCL2 inhibitor than venetoclax in biochemical assays. Zanubrutinib, a next-generation BTK inhibitor (BTKi), is approved for R/R MCL and improved PFS and OS vs ibrutinib. Data for sonrotoclax + zanubrutinib in R/R MCL from the ongoing BGB-11417-101 (NCT04277637) study are presented.

Method: Patients with ≥1 prior treatment received zanubrutinib (320mg QD/160mg BID) 8-12 weeks before sonrotoclax ramp-up (80/160/320/640mg QD); expansion cohorts followed. Endpoints included safety (CTCAE v5.0) and ORR (Lugano 2014 criteria). TLS was assessed per Howard 2011 criteria.

Results: As of 31Oct2023, 35 patients were enrolled (80mg, n=6; 160mg, n=12; 320mg, n=14; 640mg, n=3). Three patients were in zanubrutinib lead-in; 29 had started sonrotoclax. Overall, patients had a median of 1 prior treatment; 11 had prior autologous stem cell transplant and 3 had prior BTKi. Dose escalation occurred per protocol at all defined doses. No DLTs occurred; MTD was not reached up to 640mg. Sonrotoclax 160 and 320mg were chosen for expansion. Of 9 patients who discontinued treatment, 6 discontinued both drugs and 3 did not complete zanubrutinib lead-in due to early PD. Five patients died from PD (3 during zanubrutinib lead-in). TEAEs in ≥20% were neutropenia (31%), contusion (29%), thrombocytopenia (23%), and diarrhea (23%). Neutropenia was the most common grade ≥3 TEAE (20%). No TLS or atrial/ventricular fibrillation occurred. In 27 response-evaluable patients, ORR was 85% (18 CR; [67%]). In the dose-expansion, ORRs were 91% (320mg: 10/11; 10 CR) and 88% (160mg: 8/9; 4 CR [44%]) (Figure). Median time to CR was 6.4 months. In 2 patients with progression on prior BTKi, 1 CR and 1 PD were observed.

Conclusion: Sonrotoclax + zanubrutinib was well tolerated and showed promising efficacy in R/R MCL, including deep and durable responses. Expansion of the 320mg cohort is ongoing.


80 mg
160 mg
320 mg
640 mg
Dose
CR
PR
SD
PD
Ongoing treatment
Death
Reach target dose
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
Time since first dose, months