Monotherapy with second-generation BCL2 inhibitor sonrotoclax (BGB-11417) is well tolerated with high response rates in relapsed/refractory (R/R) marginal zone lymphoma (MZL): data from an ongoing phase 1 study

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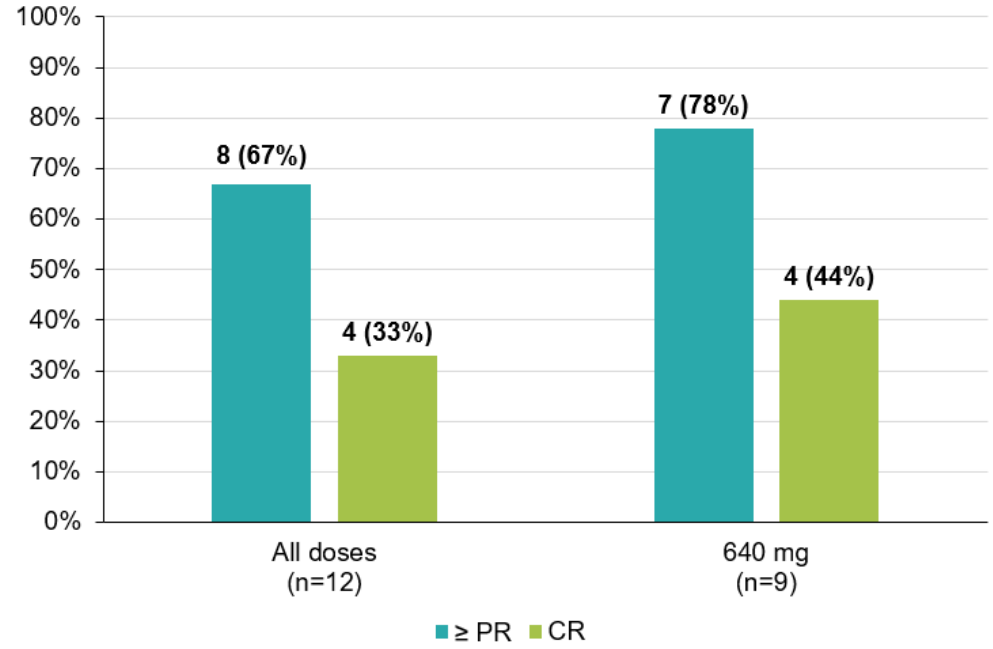
ABSTRACT

Aim: Sonrotoclax is a more selective and potent BCL2 inhibitor than venetoclax in biochemical assays. BGB-11417-101 (NCT04277637) is an ongoing, first-in-human, dose-escalation/expansion study in patients with B-cell malignancies. Presented here are data for R/R MZL.

Method: Patients received sonrotoclax with a 3-day dose ramp-up during dose-escalation (40mg/80mg/160mg/320mg/640mg QD) and expansion (640mg/320mg). DLTs were evaluated from ramp-up through day 21 at the intended dose. The primary endpoint was safety (CTCAE v5.0); objective response rate (ORR; Lugano 2014 criteria) was a secondary endpoint. Tumor lysis syndrome (TLS) was assessed per Howard 2011 criteria.

Results: As of 24April2023, 13 patients received sonrotoclax (40mg, n=1; 160mg, n=2; 640mg, n=10). Four patients progressed on BTK inhibitors (BTKi); three had BTKi as their last therapy. Dose escalation occurred per protocol at all defined doses. MTD was not reached up to 640mg. One DLT occurred (160mg; febrile neutropenia). Median follow-up was 7.8 months (range, 2.6-36.6). TEAEs in ≥20% of patients were nausea (39%) and pyrexia, diarrhea, and constipation (31% each). The most common grade ≥3 TEAEs were neutropenia, febrile neutropenia/neutropenic sepsis, and TLS (15% each). Five patients discontinued treatment (disease progression, n=3; AE [infection], n=1; withdrawal, n=1). No TEAEs led to death. Two patients (640mg) had laboratory TLS after initial ramp-up doses. TLS resolved within 24 hrs without sequela or dose change. Of 12 response-evaluable patients across dose levels, ORR was 67% (CR 33%). Of 9 response-evaluable patients at 640mg, ORR was 78% (CR 44%; Figure). All 4 patients with prior progression on BTKi responded to treatment.

Conclusion: Sonrotoclax was tolerable and had antitumor activity across tested doses in MZL. Two patients had laboratory TLS following initial doses that resolved. No clinical TLS was observed. An exploratory 320mg cohort is enrolling.



CR, complete response; MZL, marginal zone lymphoma; PR, partial response; R/R, relapsed/refractory.