# Combination Treatment With Novel BCL2 Inhibitor Sonrotoclax (BGB-11417) and Zanubrutinib in Patients With Relapsed/Refractory Mantle Cell Lymphoma (R/R MCL): Results From a Phase 1/1b Study

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**Background:** MCL is characterized by recurrent relapse after short remission periods. Venetoclax + ibrutinib demonstrated efficacy in R/R MCL but treatments (tx) with improved tolerability and efficacy are needed. Sonrotoclax (sonro), a next-generation BCL2 inhibitor, is a more selective and pharmacologically potent BCL2 inhibitor vs venetoclax, with a shorter half-life and no drug accumulation. Zanubrutinib (zanu) is a next-generation covalent BTK inhibitor with fewer off-target adverse events vs other BTK inhibitors and is FDA approved for R/R MCL.

**Aims:** To report safety and efficacy of sonro + zanu (SZ) combination therapy in patients (pts) with R/R MCL with median follow-up of ~2 y.

**Methods:** BGB-11417-101 (NCT04277637) is an ongoing open-label, phase 1/1b dose escalation and expansion study. Eligible adults have R/R MCL and received ≥1 prior therapy. Tx started with zanu lead-in (320mg once daily [QD] or 160mg twice daily) for 8-12 wk; then sonro was added. Ramp-up to sonro target dose (80, 160, 320, or 640mg QD) was used to mitigate risk of tumor lysis syndrome (TLS). Combination therapy continued until progressive disease (PD), unacceptable toxicity, or elective

discontinuation after 96 wk. The primary endpoint was safety (eg, TLS; Howard criteria); secondary endpoints included overall response rate (ORR; partial response [PR] or better; Lugano 2014 criteria).

**Results:** As of Dec 6, 2025, 51 pts were enrolled in sonro dose cohorts: 80mg (n=6), 160mg (n=13), 320mg (n=27), and 640mg (n=5). Forty-six pts (90.2%) initiated SZ; as of data cutoff, 25 (49.0%) remained on tx. Median age was 68 y and 70.6% of pts were male. Pts had a median of 1 prior tx (range, 1-4; median duration of last tx, 6.0 mo [range, 0.1-65.6]); prior tx included stem cell transplant (n=15; 1 allogeneic, 14 autologous), CAR-T (n=1), and BTK inhibitor (n=4). Maximum tolerated dose was not reached; RP2D was 320mg QD.

Twenty-one pts (41.2%) discontinued SZ and 6 (11.8%) discontinued zanu only. TEAEs led to discontinuation of SZ in 4 pts (7.8%) and zanu only in 2 (3.9%; diarrhea and cryptococcal meningoencephalitis); none led to discontinuation of sonro only. TEAEs led to death in 2 pts (3.9%; pneumonia; abdominal sepsis). The most common any-grade TEAEs were diarrhea (37.3%), neutropenia (33.3%), and COVID-19 (33.3%). Grade ≥3 TEAEs occurred in 66.7% of pts; neutropenia (21.6%) was the most common. Serious TEAEs occurred in 41.2% of all pts; pneumonia (15.7%) was the most common. In sonro 320mg + zanu pts, the most common any-grade TEAE was diarrhea (51.9%; most grade 1-2) and grade ≥3 TEAE was neutropenia (22.2%). No laboratory or clinical TLS occurred.

In 51 pts across doses, ORR was 80.4%; complete response (CR) rate was 60.8%. Median time to CR was 6.4 mo (range, 1.5-32.5). With a median study follow-up of 25.5 mo (range, 0.7-51.6), 80.6% of pts who achieved CR (25/31) remain in CR. In sonro 320mg + zanu pts (median follow-up, 21.3 mo), ORR was 81.5% (22/27); CR rate was 59.3% (16/27). Median duration of response (DOR) was not reached; 30-mo DOR rate was 77.7% (95% CI, 50.2%-91.2%). Of 4 pts with prior BTK inhibitor therapy, 2 achieved PR. All 6 pts who elected to discontinue tx achieved CR and remain in complete remission (median time off tx, 9.6 mo; range, 2.9-12.1).

**Summary/Conclusion:** SZ is well tolerated with promising antitumor activity. A phase 3 registrational trial assessing sonro 320mg + zanu is ongoing (NCT06742996).