

## Results from the phase 1 study of the novel BCL2 inhibitor sonroclax (sonro; BGB-11417) in combination with zanubrutinib (zanu) for relapsed/refractory (R/R) CLL/SLL show deep and durable responses

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### ABSTRACT

**Background:** Sonro (BGB-11417), a next-generation BCL2 inhibitor, is a more selective and potent inhibitor of BCL2 than venetoclax in biochemical assays. Zanu, a next-generation BTK inhibitor (BTKi), has shown improved PFS and tolerability, including fewer cardiac AEs, vs ibrutinib in pts with R/R CLL/SLL. Updated safety and efficacy data for sonro + zanu in pts with R/R CLL/SLL in the ongoing BGB-11417-101 (NCT04277637) study are presented.

**Methods:** Pts received zanu (320 mg QD or 160 mg BID) 8 to 12 wk before starting sonro with ramp-up to target dose (40, 80, 160, 320, or 640 mg QD). Pts were treated until progression or unacceptable toxicity. The primary endpoint was safety (CTCAE v5.0); ORR (iwCLL 2008 criteria) and minimal residual disease in blood by ERIC flow every 24 wk (uMRD4) were secondary and exploratory endpoints, respectively.

**Results:** As of October 31, 2023, 45 pts with R/R CLL/SLL were enrolled (40 mg, n=4; 80 mg, n=9; 160 mg, n=6; 320 mg, n=20; 640 mg, n=6). Four pts were still in zanu lead-in and 41 had started sonro. Of tested pts, 28% (11/40) had del(17p) and 72% (13/18) had unmutated IGHV. The median number of prior tx was 1 (range, 1-3); 7 pts had BTKi as their last therapy. The median follow-up was 17 mo (range, 0.5-32.6). No DLTs occurred; MTD was not reached up to 640 mg. Dose expansion was completed with a recommended phase 2 dose of 320 mg. Any-grade TEAEs in ≥20% of pts were COVID-19 (27%), contusion (27%), neutropenia (27%), diarrhea (24%), nausea (24%), and fatigue (24%). Neutropenia was the most common grade ≥3 TEAE (20%). No cases of TLS or atrial fibrillation occurred. No TEAEs led to death, discontinuation, or dose reduction. Sonro dose holds occurred in 14 pts (median duration, 7 days). For 32 response-evaluable pts, ORR was 97% (31/32; 1 SD at 40 mg). CR rate was 50% (40 mg, 25%; 80 mg, 50%; 160 mg, 67%; 320 mg, 56%; 640 mg, 40%); median time to CR was 9.8 mo (range, 5.5-18.2). Of 4 response-evaluable pts with prior BTKi, 3 had PR (n=2) or CR (n=1). All pts treated with sonro + zanu (160, 320, or 640 mg) who reached wk 48 achieved uMRD4 (Figure). Tx is ongoing for all but 1 pt in the 40-mg cohort who discontinued due to progression.

**Conclusions:** Efficacy of sonro + zanu combination tx is encouraging, with a 97% ORR and deep responses, including uMRD, in pts with R/R CLL/SLL. This combination has demonstrated a tolerable safety profile across all dose levels tested.

**Figure. Best MRD by Weeks 24 and 48**

