

## **Primary analysis of a multicenter, open-label, phase 2 study of sonrotoclax (BGB-11417) monotherapy in patients with relapsed/refractory (R/R) chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL)**

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**Introduction:** B-cell lymphoma 2 (BCL2) inhibition is an established treatment strategy in CLL/SLL with the potential to induce deep responses. CLL/SLL treatment guidance in China is similar to that in Western countries; however, novel treatments have limited availability in China. Sonrotoclax (BGB-11417), a next-generation BCL2 inhibitor, is a more selective and pharmacologically potent inhibitor of BCL2 than venetoclax, with a shorter half-life and no drug accumulation. In a phase 1 study (NCT04883957), sonrotoclax monotherapy was well tolerated and induced deep responses in Chinese patients (pts) with R/R CLL/SLL, with a 72.4% overall response rate (ORR) and a 41.4% best undetectable measurable residual disease ( $10^{-4}$  sensitivity; uMRD4) rate in blood. Presented here are primary efficacy and safety data for BGB-11417-202 (NCT05479994), an open-label, phase 2 study of sonrotoclax in Chinese pts with R/R CLL/SLL.

**Methods:** Eligible pts had Bruton tyrosine kinase (BTK) inhibitor + chemoimmunotherapy (CIT) intolerance/failure (CIT not mandatory if pts ineligible for CIT) and no prior BCL2 inhibitor. Pts received sonrotoclax 320 mg once daily, with

ramp-up to the target dose, until progressive disease (PD) or unacceptable toxicity. The primary endpoint was independent review committee (IRC)-assessed ORR per iwCLL 2018 guidelines (CLL) or 2014 Lugano criteria (SLL). Secondary endpoints included IRC- and investigator (INV)-assessed duration of response (DOR), progression-free survival (PFS), time to response (TTR), overall survival (OS), and incidence/severity of treatment-emergent adverse events (TEAEs) and treatment-emergent serious AEs (TESAEs) per NCI-CTCAE v5.0 and the Grading Scale for Hematologic Toxicity in CLL Studies. Tumor lysis syndrome (TLS) was assessed per Howard 2011 criteria. Exploratory endpoints included blood uMRD4 rate evaluated by flow cytometry with ERIC recommended markers. IGHV, *TP53*, and *BTK* mutation status were assessed by next-generation sequencing and del(17p) status by fluorescence in situ hybridization.

**Results:** As of February 7, 2025, 100 pts with R/R CLL/SLL were enrolled and received sonrotoclax 320 mg. Median study follow-up was 14.4 months (range, 0.2-27.5 months). At the data cutoff, 65 pts (65.0%) remained on treatment; the most common reason for treatment discontinuation was PD (20.0%). For all pts, median age was 64.5 years and 61.0% were male. Pts had a median of 2 prior lines of therapy (range, 1-6); 27.0% had  $\geq 3$  prior lines, and 46.0% had previously received both a BTK inhibitor and anti-CD20 therapy. At baseline, 62.8% (54/86) of pts with available data had unmutated IGHV, 38.1% (37/97) had del(17p) and/or *TP53* mutation, and 25.5% (25/98) had a *BTK* mutation.

In 100 pts, IRC-assessed ORR was 76.0% and complete response rate was 19.0%. Median TTR per IRC was 3.7 months (range, 1.3-11.1 months). Responses per IRC were observed in pts with unmutated IGHV (74.1%; 40/54), del(17p) and/or *TP53* mutation (70.3%; 26/37), and *BTK* mutation (72.0%; 18/25). The best blood uMRD4 rate was 49.0% (49/100). Median time to blood uMRD4 was 5.8 months (range, 3-12 months). Median DOR, PFS and OS were not reached.

TEAEs in  $\geq 30\%$  of pts were neutrophil count decreased (54.0%), platelet count decreased (41.0%), anemia (33.0%), hyperuricemia (33.0%), and white blood cell count decreased (30.0%). Grade  $\geq 3$  TEAEs occurred in 61.0% of pts and all-grade TESAEs in 38.0%. Grade  $\geq 3$  TEAEs in  $\geq 10\%$  of pts were neutrophil count decreased (33.0%), pneumonia (17.0%), platelet count decreased (11.0%), and white blood cell count decreased (10.0%). No clinical TLS occurred; laboratory TLS occurred in 4.0% of pts (all grade 3 and resolved in a median of 3.5 days [range, 2-8 days]); none led to treatment discontinuation or death. TEAEs led to dose reduction in 5.0% of pts and treatment discontinuation in 6.0% of pts. Five pts (5.0%) died due to TEAEs, all considered unrelated to treatment.

**Conclusions:** Sonrotoclax monotherapy demonstrated promising efficacy in heavily pretreated Chinese pts with R/R CLL/SLL, with an IRC-assessed ORR of 76%, and deep, rapid responses regardless of risk status, including subgroups with unmutated IGHV, del(17p) and/or *TP53* mutations, and *BTK* mutations. Sonrotoclax monotherapy was well tolerated, and toxicities were manageable with low rates of dose reduction and treatment discontinuation. These data support the potential of sonrotoclax as a promising therapeutic option for pts with R/R CLL/SLL.