Sonrotoclax and zanubrutinib as frontline treatment for CLL demonstrates high MRD clearance rates with good tolerability: data from an ongoing phase 1/1b study BGB-11417-101

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ABSTRACT

Background/Aim: BGB-11417-101 (NCT04277637) is an ongoing, first-in-human, phase 1/1b dose-escalation/expansion study in patients (pts) with B-cell malignancies. Updated safety and efficacy of sonrotoclax (sonro; BGB-11417)+zanubrutinib (zanu) in treatment (tx)-naive (TN) CLL/SLL are presented.

Methods: Pts received zanu (320mg once daily [QD] or 160mg twice daily) for 8-12 wk, then added sonro via ramp-up (160mg or 320mg QD). Endpoints included safety, ORR (iwCLL), and blood minimal residual disease per modified ERIC flow panel (uMRD4).

Results: As of 10May2024, 112 pts were enrolled (high TLS risk, 34%; unmutated IGHV, 51%; *TP53* mutation, 20%; del(17p), 9%). Median follow-up was 18.3 mo (range, 4.4-29.9). The most common TEAEs were neutropenia (41%), contusion (38%), COVID-19 (30%), and diarrhea (29%). Neutropenia was the most common grade ≥3 TEAE (26%); 2 pts had dose reduction/hold, and none discontinued tx. Two pts (160mg) had grade 3 febrile neutropenia. No TLS or deaths occurred. Five pts (160mg) discontinued combination tx: TEAE, PD, pt withdrawal (n=1 each), elective discontinuation after 96 tx wk (n=2); 1 pt (320mg) discontinued zanu only due to intermittent grade 1 diarrhea. In 108 evaluable pts, ORR was 100% (CR: 160mg, 41%; 320mg, 42%). Median time to response was 2.6 mo (range, 1.5-10.8); median time to CR was 8.4 mo (range, 3.9-17.1). Wk 24/48 best blood uMRD4 rates were 61%/79% (sonro 160mg) and 77%/90% (sonro 320mg). Median time to uMRD was 9.7 mo (range, 3.9-20.6) with 160mg and 8.5 mo (range, 5.4-19.9) with 320mg. No progression was seen with sonro 320mg.

Conclusions: Sonro+zanu was well tolerated in pts with TN CLL/SLL. Substantial efficacy was observed, with 100% ORR in assessed pts and 90% best uMRD rate in the 320mg cohort pts with 48 wk of therapy. High blood uMRD4 rates occurred early and were sustained. A registrational phase 3 study (CELESTIAL-TNCLL; BGB-11417-301) sonro 320mg+zanu is recruiting.