Sonrotoclax + zanubrutinib has high uMRD rates and good tolerability in ongoing phase 1/1b study in treatment-naive CLL

Authors: Minoru Kanaya,[1] Jacob D. Soumerai,[2] Chan Y. Cheah,[3,4,5] Mary Ann Anderson,[6,7] Masa Lasica,[8] Emma Verner,[9,10] Stephen S. Opat,[11] Shuo Ma,[12] Robert Weinkove,[13,14] Raul Cordoba,[15] Paolo Ghia,[16,17] Sophie Leitch,[18] David Westerman,[19,20] Sheel Patel,[21] Yiqian Fang,[22] Wei Ding,[21] Constantine S. Tam[23]

Affiliations: [1]Blood Disorders Center, Aiiku Hospital, Sapporo, Hokkaido, Japan; [2]Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA, USA; [3]Sir Charles Gairdner Hospital, Nedlands, WA, Australia; [4]Medical School, University of Western Australia, Crawley, WA, Australia; [5]Linear Clinical Research, Nedlands, WA, Australia; [6]Royal Melbourne Hospital and Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [7]The Walter and Eliza Hall Institute, Melbourne, VIC, Australia; [8]St Vincent's Hospital Melbourne, Fitzroy, VIC, Australia; [9]Concord Repatriation General Hospital, Concord, NSW, Australia; [10]University of Sydney, Sydney, NSW, Australia; [11]Lymphoma Research Group, School of Clinical Sciences at Monash Health, Monash University, Clayton, VIC, Australia; [12]Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [13]Te Rerenga Ora Blood and Cancer Centre, Te Whatu Ora Health New Zealand Capital Coast & Hutt Valley, Wellington, New Zealand; [14]Cancer Immunotherapy Programme, Malaghan Institute of Medical Research, Wellington, New Zealand; [15]Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain; [16]Università Vita-Salute San Raffaele, Milano, Italy; [17]IRCCS Ospedale San Raffaele, Milano, Italy; [18]Te Whatu Ora, Health New Zealand, Waitemata, Auckland, New Zealand; [19]Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [20]University of Melbourne, Melbourne, VIC, Australia; [21]BeiGene USA, Inc, San Mateo, CA, USA; [22]BeiGene (Shanghai) Co, Ltd, Shanghai, China; [23]Alfred Hospital and Monash University, Melbourne, VIC, Australia

ABSTRACT

Background: 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 (160 or 320mg QD). Endpoints included safety, ORR (iwCLL), and minimal residual disease in blood 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 a 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 wk of tx (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 in the sonro 320mg cohort.

Conclusion: 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 who reached 48 wk of therapy. High blood uMRD4 rates occurred early and were sustained. A registrational phase 3 study (CELESTIAL-TNCLL; BGB-11417-301) assessing this combination with sonro 320mg is recruiting.