Initial phase 1b/2 study results with sonrotoclax (BGB-11417) in combination with carfilzomib and dexamethasone in patients with t(11;14)-positive relapsed/refractory multiple myeloma

Authors: Hang Quach,[1] Rakesh Popat,[2] Wenming Chen,[3] Mary Kwok,[4] Andrew Yee,[5] Zhongxing Jiang,[6] Flávia Xavier,[7] Natalie S. Callander,[8] Man Yuk Ho,[9] Susan Bal,[10] Michael Low,[11] Douglas Sborov,[12] Gabriel Man,[13] Huan Cheng,[13] Adam Idoine,[13] Xin Wang,[13] Amit Agarwal,[13] Binod Dhakal[14]

Affiliations: [1]St Vincent's Health Australia, University of Melbourne, Melbourne, VIC, Australia; [2]NIHR UCLH Clinical Research Facility, University College London Hospitals, London, UK; [3]Beijing Chaoyang Hospital, Beijing, China; [4]University of Washington, Seattle, WA, USA; [5]Massachusetts General Hospital, Boston, MA, USA; [6]The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; [7]Hospital DF Star, Oncologia D'Or, Instituto D'Or de Pesquisa e Ensino, Brasília, DF, Brazil; [8]UW Health University Hospital, Madison, WI, USA; [9]Nepean Hospital, Kingswood, NSW, Australia; [10]University of Alabama at Birmingham, Birmingham, AL, USA; [11]Monash Health, Melbourne, VIC, Australia; [12]Huntsman Cancer Institute at the University of Utah, Salt Lake City, UT, USA; [13]BeOne Medicines Ltd, San Carlos, CA, USA; [14]Medical College of Wisconsin, Milwaukee, WI, USA

Introduction: Multiple myeloma (MM) with t(11;14), present in approximately 16-24% of patients with MM, represents a unique disease subset with distinct features. BCL2 inhibition has shown efficacy in this subgroup; however, no BCL2-targeted therapies are currently approved for MM. 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. BGB-11417-105 (NCT04973605) is an ongoing phase 1b/2 study to evaluate the safety and efficacy of sonrotoclax as monotherapy or in combination therapy in patients with t(11;14)-positive relapsed/refractory (R/R) MM. Initial data from BGB-11417-105 showed that sonrotoclax + dexamethasone (dex) was well tolerated and induced deep and durable responses in heavily pretreated patients. Presented here are preliminary results in the sonrotoclax + carfilzomib (K) + dex dose-escalation cohorts of BGB-11417-105.

Methods: Eligible patients have R/R MM with centrally confirmed t(11;14) and have received ≥3 prior lines of therapy, including a proteasome inhibitor, immunomodulatory drug, and anti-CD38 antibody (patients in certain regions did not require prior anti-CD38). Patients receive oral sonrotoclax (320 or 640 mg) once daily + oral or intravenous dex (40 mg) once weekly + intravenous K (56 mg/m^2 [K56] or 70 mg/m^2 [K70]) on days 1, 8, and 15 of each 28-day cycle until disease progression or unacceptable toxicity. Study endpoints include safety per NCI-CTCAE v5.0 and investigator-assessed overall response rate (ORR) per International Myeloma Working Group guidelines.

Results: As of May 16, 2025, a total of 20 patients were enrolled and had been treated in 1 of 3 cohorts: sonrotoclax 320 mg + K56 + dex (n=11), sonrotoclax 320 mg + K70 + dex (n=7), or sonrotoclax 640 mg + K56 + dex (n=2; enrollment ongoing). The median follow-up in all patients was 7.3 months (range, 1.7-22.2 months). Across cohorts, the median age was 65 years (range, 51-77 years), 75% were male, and 50% were White. Patients had a median of 4 prior lines of therapy (range, 2-8); 65% of patients had ≥4 prior lines, 85% were triple-class exposed, and 20% were triple-class refractory. At data cutoff, 13 patients (65%) remained on study treatment; 6 patients discontinued due to disease progression, and 1 withdrew consent. The most common all-grade treatment-emergent adverse events (TEAEs) were insomnia (40%), fatigue (35%), nausea (30%), anemia (30%), and back pain (30%). Grade ≥3 TEAEs occurred in 12 patients (60%), grade ≥3 hematologic TEAEs occurred in 7 (35%), and grade ≥3 infections occurred in 5 (25%). Cardiac disorders occurred in 3 patients (15%; grade 2 arrhythmia, n=1; grade 2 atrial flutter, n=1; grade 1 tachycardia, n=1), and hypertension in 4 patients (20%; grade 1/2, n=2; grade 3, n=2). Eight patients (40%) experienced a serious TEAE; the most common serious TEAE was pneumonia (15%). Dose-limiting toxicities were reported in 2 patients (transient grade 3 thrombocytopenia and acute kidney injury). No TEAEs led to death, sonrotoclax discontinuation, or sonrotoclax dose reduction. Four patients died during the study, all for reasons unrelated to study treatment. In 19 response-evaluable patients across dose groups, the ORR was 84% (95% CI, 60%-97%), which included 32% (95% CI, 13%-57%) of patients with a complete response (CR)/stringent complete response (sCR). The median time to response was 1.0 months (range, 0.9-6.1 months). Median duration of response and median progression-free survival were not reached.

Conclusions: Sonrotoclax + K + dex combination therapy demonstrated a tolerable safety profile and encouraging antimyeloma activity, with an 84% ORR and a 32% CR/sCR rate in heavily pretreated patients with t(11;14)-positive R/R MM. Enrollment in BGB-11417-105 is ongoing, and additional treatment combinations with sonrotoclax are being investigated.