A PHASE 1 STUDY WITH THE NOVEL B-CELL LYMPHOMA 2 (BCL2) INHIBITOR BGB-11417 AS MONOTHERAPY OR IN COMBINATION WITH ZANUBRUTINIB (ZANU) IN PATIENTS (PTS) WITH B-CELL MALIGNANCIES: PRELIMINARY DATA

Authors: Stephan Stilgenbauer,[1] Stephen Opat,[2,3] Chan Y. Cheah,[4,5,6] Masa Lasica,[7] Emma Verner,[8,9] Peter J. Browett,[10] Henry Chan,[11] Jacob D. Soumerai,[12] Eva González Barca,[13] James Hilger,[14] Yiqian Fang,[14] David Simpson,[14] Constantine S. Tam[15,16,17]

Affiliations: [1]University of Ulm, Ulm, Germany; [2]Monash Health, Clayton, Victoria, Australia; [3]Monash University, Clayton, Victoria, Australia; [4]Sir Charles Gairdner Hospital and Pathwest Laboratory Medicine, Nedlands, Western Australia, Australia; [5]Medical School, University of Western Australia, Crawley, Western Australia, Australia; [6]Linear Clinical Research, Nedlands, Western Australia, Australia; [7]St Vincent's Hospital Melbourne, Fitzroy, Victoria, Australia; [8]Concord Repatriation General Hospital, Concord, New South Wales, Australia; [9]University of Sydney, Sydney, New South Wales, Australia; [10]Auckland City Hospital, Auckland, New Zealand; [11]North Shore Hospital Auckland, New Zealand; [12]Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA; [13]Institut Català d'Oncologia-Hospitalet, IDIBELL, Universitat de-Barcelona, Barcelona, Spain; [14]BeiGene (Beijing) Co., Ltd., Beijing, China and BeiGene USA, Inc., San Mateo, CA, USA; [14]Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [16]University of Melbourne, Parkville, Victoria, Australia; [16]Royal Melbourne Hospital, Parkville, Victoria, Australia

ABSTRACT

Introduction: BCL2 is aberrantly expressed in many hematologic malignancies and promotes tumorigenesis. BGB-11417 was developed as a potent and highly selective inhibitor of BCL2.

Methods: BGB-11417-101 (NCT04277637) is an ongoing first-in-human phase 1/1b dose-escalation/expansion study to evaluate safety, tolerability, maximum tolerated dose (MTD), and recommended phase 2 dose of oral BGB-11417 alone or combined with BTK inhibitor zanu, in pts with relapsed/refractory (R/R) B-cell malignancies. Pts in separate monotherapy and combination therapy cohorts received escalating BGB-11417 doses (40, 80, 160, 320, or 640 mg once daily [QD]) with weekly or daily ramp-up to the target dose; combination cohorts received zanu (320 mg QD or 160 mg twice daily) 8-12 wks before BGB-11417. Dose-limiting toxicity for each dose cohort was evaluated by a Bayesian logistic regression model. Adverse events (AEs) were reported per CTCAE v5.0.

Results: As of 17Dec2021, 58 pts received BGB-11417 (32 monotherapy; 26 combination). Of pts receiving BGB-11417 monotherapy, 26 with non-Hodgkin lymphoma (NHL) received doses ≤640 mg and 6 with CLL/SLL received ≤160 mg. Of pts receiving combination treatment, 19 with R/R CLL/SLL received BGB-11417 ≤160 mg and 7 with R/R MCL received ≤80 mg. MTD has not yet been reached. Median follow-up was 3.9 mo (range, 0.1-20.4). Only 2 grade ≥3 AEs (1 neutropenia, 1 autoimmune hemolytic anemia) were reported in combination cohorts. 20 pts discontinued treatment (17 disease progression; 1 AE; 2 other reasons). One high-risk pt with CLL on monotherapy had laboratory tumor lysis syndrome (TLS) that resolved with no intervention (laboratory TLS <2%). Early efficacy data show that most pts had reduction in sum of product of perpendicular diameters; 2 pts with NHL (monotherapy) had responses (1 complete response). Pts with CLL/SLL had notable reductions in absolute lymphocyte count at doses as low as 1 mg; 2 responses (≥partial response) were seen with monotherapy and 12 responses with combination (≥partial response with lymphocytosis).

Conclusions: These preliminary findings suggest that BGB-11417 has promising efficacy and is tolerable at doses ≤640 mg as monotherapy and ≤160 mg in combination with zanu. Dose escalation continues as an MTD has not yet been reached. Enrollment is ongoing, data for Waldenström macroglobulinemia and treatment-naïve CLL/SLL cohorts are forthcoming.