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Updated efficacy and safety results of the Bruton tyrosine kinase degrader BGB-16673 in patients with relapsed/refractory indolent non-Hodgkin lymphoma from the ongoing phase 1 CaDAnCe-101 study

Authors: Romain Guièze,[1] Anna Maria Frustaci,[2] Chan Y. Cheah,[3-5] John F. Seymour,[6] Dok Hyun Yoon,[7] Irina Mocanu,[8] Eric Mou,[9] Pier Luigi Zinzani,[10,11] Amitkumar Mehta,[12] Constantine S. Tam,[13] Judith Trotman,[14] Yanan Zhang,[15] Linlin Xu,[15] Kunthel By,[15] Amber Lussier,[15] Shannon Fabre,[15] Daniel Persky,[15] Ranjana Advani[16]

Affiliations: [1]Estaing University Hospital, Clermont-Ferrand, France; [2]ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy; [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]Peter MacCallum Cancer Centre, Royal Melbourne Hospital, and University of Melbourne, Melbourne, VIC, Australia; [7]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; [8]Institute of Oncology, ARENSIA Exploratory Medicine, Düsseldorf, Germany; [9]University of Iowa Hospitals and Clinics, Iowa City, IA, USA; [10]IRCCS Azienda Ospedaliero-Universitaria di Bologna Istituto di Ematologia “Seràgnoli”, Bologna, Italy; [11]Dipartimento di Scienze Mediche e Chirurgiche, Università di Bologna, Bologna, Italy; [12]The University of Alabama at Birmingham, Birmingham, AL, USA; [13]Alfred Hospital and Monash University, Melbourne, VIC, Australia; [14]Concord Repatriation General Hospital, University of Sydney, Concord, NSW, Australia; [15]BeOne Medicines Ltd, San Carlos, CA, USA; [16]Stanford Cancer Institute, Stanford, CA, USA

Introduction: BGB-16673 is an orally available protein degrader that blocks BTK signaling by tagging BTK for degradation through the cell's proteasome pathway, leading to tumor regression. CaDAnCe-101 (BGB-16673-101, NCT05006716) is an ongoing phase 1/2 study of BGB-16673 monotherapy in patients with various B-cell malignancies. Here, updated phase 1 results in the follicular lymphoma (FL) and marginal zone lymphoma (MZL) cohorts are presented.

Methods: Eligible patients have had ≥2 prior therapies for NHL, including an anti-CD20 antibody for patients with FL and an anti-CD20 antibody (EU and US patients) and covalent BTK inhibitor (US patients only) for patients with MZL; additional eligibility criteria include an ECOG performance status of 0-2 (0-1 in the EU) and adequate end organ function. BGB-16673 was dosed once daily (QD) orally in 28-day cycles, with 6 planned dose levels ranging from 50 to 600 mg QD. The primary study objectives were to assess safety and tolerability according to NCI-CTCAE v5.0 guidelines and to establish the maximum tolerated dose and recommended dose for expansion. The secondary objective was to evaluate the overall response rate (ORR) per 2014 Lugano criteria, with the first assessment occurring after 12 weeks of treatment.

Results: As of May 23, 2025, 60 patients with FL (n=24) or MZL (n=36) were enrolled and treated. The median number of prior lines of therapy was 3 for both FL (range, 2-9) and MZL (range, 2-15) and included covalent BTK inhibitors (FL, n=3 [12.5%]; MZL, n=30 [83.3%]), noncovalent BTK inhibitors (FL, n=1 [4.2%]; MZL, n=4 [11.1%]), and BCL2 inhibitors (MZL, n=6 [16.7%]). Median follow-up was 3.5 months (range, 1.0-32.6) for FL and 5.5 months (range, 0.3-27.8) for MZL.
Overall, any-grade treatment-emergent adverse events (TEAEs) occurred in 87.5% and 97.2% of patients with FL and MZL, respectively. TEAEs occurring in ≥20% of patients in either cohort were fatigue (FL, 20.8%; MZL, 30.6%) and neutropenia (MZL, 22.2%). Grade ≥3 TEAEs occurred in 25.0% of patients with FL and 50.0% with MZL. In the MZL cohort, 3 patients (8.3%) experienced major hemorrhage: 1 patient had a grade 3 gastrointestinal hemorrhage (post rectal surgery), 1 patient had a grade 5 intracranial hemorrhage, and 1 had a grade 2 hemothorax (post pleural effusion drainage). In the MZL cohort, 1 patient (2.8%) had grade 1 atrial fibrillation and 1 (2.8%) had grade 3 febrile neutropenia. TEAEs led to 1 treatment discontinuation in the FL cohort (4.2%) and 5 in the MZL cohort (13.9%). Additionally, 1 death due to a TEAE occurred in the MZL cohort (intracranial hemorrhage, 2.8%).
Twelve patients on treatment have not yet reached the first response assessment time point. In 48 response-evaluable patients, the ORR was 41.2% (7/17) for FL, including 3 patients with responses lasting ≥6 months, 3 censored cases and 1 event occurring before 6 months. For MZL, the ORR was 54.8% (17/31), including 5 patients with responses lasting ≥6 months, 9 censored cases and 3 events occurring prior to 6 months. Seven patients (FL, 11.8% [n=2]; MZL, 16.1% [n=5]) achieved complete response. Responses were also seen in 13 of 26 patients with MZL who were previously treated with a covalent BTK inhibitor. Median time to first response was 2.7 months (range, 2.6-3.3) for FL and 2.8 months (range, 2.6-9.9) for MZL. As of the data cutoff, 33 patients (FL, n=11; MZL, n=22) remained on treatment; in both cohorts, progressive disease was the most common reason for treatment discontinuation (FL, 45.8%; MZL, 22.2%).

Conclusions: These data demonstrate that the novel BTK degrader BGB-16673 is tolerable and shows clinically beneficial responses in heavily pretreated patients with FL and, particularly, MZL, including those who received a prior BTK inhibitor. CaDAnCe-101 enrollment continues for patients with FL and MZL.