Real-world zanubrutinib treatment patterns in CLL/SLL among US community oncology patients with prior acalabrutinib therapy

Jing-Zhou Hou,[1] Rushir Choksi,[1] Gregory A. Maglinte,[2] Xiaoliang Wang,[2] Anna Rui,[3] Manasi Suryavanshi,[2] Beverly Chigarira,[3] Lindsay Aton,[3] Melissa Hagan,[2] Lisa Morere,[3] Rhys Williams,[2] Daniel A. Ermann[4]

[1]University of Pittsburgh Medical Center, Pittsburgh, PA, USA; [2]BeOne Medicines Ltd, San Carlos, CA, USA; [3]IntegraConnect PrecisionQ, West Palm Beach, FL, USA; [4]University of Utah Huntsman Cancer Institute, Salt Lake City, UT, USA

Background Bruton tyrosine kinase inhibitors (BTKis) have demonstrated clinical efficacy in treating chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). Zanubrutinib (zanu) is a highly specific and potent next-generation BTKi designed to maximize BTK occupancy and limit off-target kinase binding. Recent clinical data suggest that patients with CLL who were intolerant of ibrutinib (ibru) or acalabrutinib (acala) and switched to zanu experienced continued or improved clinical benefit (Shadman *Blood Adv.* 2025). Additionally, most of the ibru and acala intolerance adverse events did not recur during zanu treatment. There is limited real-world evidence describing the patient characteristics and treatment journey for patients with CLL/SLL who initiate acala and subsequently receive zanu (Krackeler *Cancer Medicine* 2025; Warner *Blood* [supplement] 2025).

Aims This study describes the characteristics, treatment patterns, and reasons for discontinuation among patients who had previously discontinued acala and changed to zanu in a real-world setting.

Methods The IntegraConnect PrecisionQ database, which contains electronic health records from >3 million de-identified cancer patients across >500 care sites, was used to create a retrospective cohort of CLL/SLL patients who initiated and discontinued acala and then initiated zanu between 11/21/2019 and 11/30/2024. Patients were followed through 2/28/2025. A medical record review was conducted to identify dates of treatment initiation and discontinuation and reasons for acala and zanu discontinuation.

Results A total of 806 patients initiated acala and subsequently received another therapy; of these, 121 patients subsequently received zanu; 102 (84.3%) changed directly from acala to zanu, and 19 (15.7%) changed from acala to another therapy before initiating zanu. The majority of patients received prior acala monotherapy (n=111, 91.7%). Of the 102 patients who changed directly from acala to zanu, 74 (72.6%) received acala in the first line of therapy after the start date and 28 (27.5%) received acala in the second line or later. The median duration of acala therapy prior to zanu treatment was 5.6 months (interquartile range [IQR]: 2.1, 16.5). The median duration of zanu therapy after having received acala was 10.7 months (IQR: 4.1, 18.8), and 59 (57.8%) patients remained on zanu at the end of the follow-up period. Overall, 53 (52.0%) patients discontinued acala within 6 months and 68 (66.7%) discontinued within 1 year. The reasons for acala discontinuation were toxicity (68.6%), other (11.8%), or disease progression (6.9%). A total of 43 (42.2%) patients who changed from acala to zanu discontinued zanu at the time of data cutoff. The reasons for zanu discontinuation were toxicity (58.1%), other (7.0%), or disease progression (2.3%).

Summary/Conclusion In this real-world US community oncology setting, most zanu-treated patients with prior acala therapy had discontinued acala within 1 year. The primary reason for acala discontinuation was toxicity. Consistent with previous research, real-world data from across the US have demonstrated that zanu was well tolerated and maintained effectiveness in patients with CLL who had received a prior BTKi.