Risk of Hypertension in Patients Newly Diagnosed with Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) and Treated with Covalent Bruton Tyrosine Kinase Inhibitors (cBTKi): A Real-World Study

Ayad K. Ali,[1] Lili Zhou,[1] Jamie Colasurdo,[1] Wassim Aldairy,[1] Qianhong Fu,[1] Nicole Lamanna[2]

[1]BeiGene USA, Inc, San Mateo, CA; [2]Columbia University, New York, NY

Background:

Covalent Bruton tyrosine kinase inhibitors (cBTKi) are a mainstay of first-line (1L) therapy in CLL/SLL. However, there are concerns about a potential association between cBTKi and cardiovascular events including hypertension (HTN). Using the Symphony Health Solutions database, this real-world study aimed to describe and compare new-onset or worsening HTN events among CLL/SLL patients treated with 1L zanubrutinib or 1L acalabrutinib compared to those treated with 1L ibrutinib.

Methods:

Patients who were newly diagnosed with CLL/SLL and started 1L cBTKi treatment between Jan 2019 – July 2023 were included in the study. The index date was that of 1L therapy initiation during the study period for the 3 cBTKi cohorts. Proportions of new-onset or worsening HTN were evaluated during a 12-month follow-up period. New-onset HTN was defined as the presence of dispensed new prescriptions of antihypertensive medications during follow-up in patients without baseline HTN. Worsening HTN in patients with preexisting HTN was defined by either an ≥2-fold augmentation of antihypertensive dose relative to baseline dose or addition of an anti-HTN medication. Inverse probability of treatment weighting (IPTW) was used to balance baseline confounders (e.g., age, sex, cardiovascular risk factors, race/ethnicity, region, and comorbidities) between cohorts and Cox Proportional Hazards model was used to calculate and compare hazard ratios (HRs).

Results:

A total of 837 patients received 1L zanubrutinib; 5,071 received 1L acalabrutinib; and 9,409 received 1L ibrutinib. At baseline, the prevalence of preexisting HTN was 51.7% (zanubrutinib), 51.2% (acalabrutinib), and 50.2% (ibrutinib). During the 12-month follow-up, the proportions of patients with new-onset HTN were 13.9% (zanubrutinib), 12.4% (acalabrutinib), and 18.0% (ibrutinib). Compared to ibrutinib, zanubrutinib and acalabrutinib were associated with a lower risk of developing new-onset HTN (zanubrutinib, HR=0.76, 95%CI: 0.57-1.01; acalabrutinib, HR=0.70, 95%CI: 0.61-0.80). Similar trends were observed across study cohorts for worsening HTN.

Conclusions: This real-world study shows that patients newly diagnosed with CLL/SLL treated with 1L zanubrutinib or acalabrutinib had lower rates of developing new-onset HTN compared to patients treated with 1L ibrutinib.

New and worsening HTN during 12-month follow-up period			
New HTN	**Zanubrutinib (n=404)**	**Acalabrutinib (n=2475)**	**Ibrutinib (n=4685)**
n (%)	56 (13.9)	306 (12.4)	844 (18.0)
IPTW weighted HR (95% CI)	0.76 (0.57-1.01)	0.70 (0.61-0.80)	Reference
Worsening HTN	**Zanubrutinib (n=433)**	**Acalabrutinib (n=2596)**	**Ibrutinib (n=4724)**
n (%)	61 (14.1)	265 (10.2)	862 (18.2)
IPTW weighted HR (95% CI)	0.72 (0.55-0.94)	0.55 (0.48-0.63)	Reference