Risk of new-onset hypertension in newly diagnosed chronic lymphocytic leukemia patients treated with Bruton tyrosine kinase inhibitors: a real-world study using the Symphony Health Solutions database

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Background: Bruton tyrosine kinase inhibitors (BTKis) provide an important therapeutic option for patients diagnosed with chronic lymphocytic leukemia (CLL). Concerns have arisen about a potential association with the risk of cardiovascular events with BTKis.

Aims: Using the Symphony Health Solutions database, this study aims to describe the risk of new-onset hypertension in CLL patients treated with and without BTKis.

Methods: Newly diagnosed CLL patients who started ibrutinib or acalabrutinib and those not treated with an approved BTKi between 2019 and 2022 were included in the analysis. The prevalence of hypertension prior to and risk of new-onset hypertension after treatment initiation were defined by use of antihypertensive medication. Patient demographics and comorbidities were described. Multivariate regression and inverse probability treatment weight based on propensity score were used to account for bias due to differences in patient characteristics between groups. Risk of hypertension up to 1 year after index date was estimated. Hazard ratio and multivariate Cox-regression models were used to describe the risk between groups.

Results: In CLL patients treated with (n=7,114) and without BTKis (n=34,571), demographics and clinical characteristics included age at the index date (mean: 70.2 years, BTKi; 69.0 years, without BTKi), sex (male: 59.8%, BTKi; 55.7%, without BTKi), and Charlson comorbidity scores (mean: 3.3, BTKi; 3.1, without BTKi). At baseline, the prevalence of hypertension defined by the use of antihypertensive medication was 67.8% with BTKi and 67.6% without BTKi. Among patients without any antihypertensive medication use at baseline, the rate of new-onset hypertension within 1 year after treatment initiation was greater in patients with BTKis than without BTKis (Table).

Summary/Conclusion: In this real-world analysis, CLL patients treated with BTKis had a higher burden of comorbidities, and use of antihypertensive medication was common. The risk of new-onset hypertension was higher in patients initiated on BTKis than those on non-BTKi treatments. These data suggest that development of hypertension is an important consideration in the long-term management of CLL patients undergoing BTKi treatment.

In Patients Without Prior Medical Encounter or Medication Use for Hypertension	**BTKi (n=2,172)**	**Non-BTKi (n=10,626)**	**Hazard Ratio (95% CI)**
Hypertension defined by any antihypertensive medication use New onset of hypertension, n (%) Event rate of hypertension (per 100 patient-months) (95% CI)	 375 (17.2) 1.60 (1.40-1.80)	 1,322 (12.4) 1.12 (1.06-1.18)	**Unadjusted** 1.45 (1.30-1.63)
Absolute risk difference	**0.048 or 4.8%**	Reference	
Number needed to treat	**21**		
Post hoc power calculation			>80%
Multivariate regression models, adjusted hazard ratio (95% CI)			
Model 1: Age and sex			1.40 (1.25-1.57)
Model 2: Age and sex, Charlson comorbidity score grouping (0, 1, 2, 3, 4+), index year			1.37 (1.22-1.54)
Model 3: Age and sex, individual Charlson comorbidity category, year of treatment initiation or diagnosis			1.39 (1.24-1.56)
Inverse probability treatment weight based on propensity score, hazard ratio (95% CI)			1.44 (1.29-1.61)