Risk of New-Onset or Worsening Hypertension in Patients With Newly Diagnosed Chronic Lymphocytic Leukemia Treated With BTK Inhibitors: A Real-World Study Using the Symphony Health Solutions Database

P1847

Tzuyung Douglas Kou,[1] Lili Zhou,[1] Jinzhi Zhou,[1] Aileen Cohen,[1] Wassim Aldairy,[1] William B. White[2]

[1]BeiGene USA, Inc, San Mateo, CA, USA; [2]Cardiology Center, University of Connecticut Health Center, Canton, CT, USA

INTRODUCTION

- Bruton tyrosine kinase (BTK) inhibitors are an important therapeutic option for CLL[1]
- Concerns have arisen about the potential association between BTK inhibitors and the risk of cardiovascular AEs[2]
- Hypertension has been associated with increased major cardiovascular AEs, including arrhythmia, myocardial infarction, stroke, heart failure, and cardiovascular death[3]
- This study aims to describe the risk of new-onset and worsening hypertension in patients with CLL treated with and without BTK inhibitors

METHODS

Data Source

- This retrospective cohort study used the Symphony Health Solutions Database, which contains deidentified and tokenized information that allows linkage of patient-level data from varied sources, such as hospital claims, physician offices, and prescription data, with record dates as recent as one month prior
- Patients with newly diagnosed CLL who initiated BTK inhibitor treatment (BTK inhibitor cohort) or were first diagnosed (non–BTK inhibitor cohort) between January 1, 2019, and December 31, 2022, were included

Study Assessments

- The primary analysis assessed the event rate of new-onset or worsening hypertension within 1 year after the index date in BTK inhibitor and non–BTK inhibitor cohorts
- New-onset hypertension was defined by antihypertensive medication use in the year following the index date in patients without pre-existing hypertension
- Worsening hypertension was defined by an increase in the number of concomitant antihypertensive medications in the year following the index date, or a ≥2 fold increase in antihypertensive drug dose with ≥2 prescriptions compared with baseline daily dose in patients with pre-existing hypertension
- Cox regression was used to compare the risk of developing new-onset or worsening hypertension between cohorts
- Multivariable regression models, 1:1 propensity score matching, and inverse probability treatment weighting (IPTW) were used to account for differences in patient characteristics between groups

RESULTS

- A total of 30,559 patients with CLL were included in the analysis (BTK inhibitor cohort, n=2,392; non–BTK inhibitor cohort, n=28,167) (**Table 1**)
- Baseline prevalence of hypertension, defined as use of antihypertensive medication or a medical encounter for hypertension, was 73% in the BTK inhibitor cohort and 72% in the non–BTK inhibitor cohort
- Approximately 64% of patients in both cohorts had received ≥1 antihypertensive medication at baseline

Table 1. Demographic and Baseline Characteristics at Treatment Initiation

	BTK Inhibitor Cohort (n=2,392)	Non–BTK Inhibitor Cohort (n=28,167)
Age, median, years	72.5	72.0
Male sex, n (%)	1,457 (61)	14,812 (53)
CCI, mean (SD) [median]	3.0 (2.5) [3]	2.7 (2.5) [2]
Baseline hypertension, n (%)[a]	1,748 (73)	20,166 (72)

[a] Determined based on use of antihypertensive medication or medical encounter for hypertension in the 3 years prior to treatment.
CCI, Charlson Comorbidity Index; SD, standard deviation.

- Within 1 year after the index date, more patients in the BTK inhibitor cohort (19.5%-24.8%) increased their number of antihypertensive drug classes vs patients in the non–BTK inhibitor cohort (14.2%-17.5%) (**Table 2**)

Table 2. Antihypertensive Medication Use Patterns

BTK inhibitor cohort, n (%)		Drug classes at baseline[a] 0 (n=872)	1 (n=520)	2 (n=550)
Drug classes after index date[b]	0	686 (79)	71 (14)	43 (8)
	1	**124 (14)**	320 (62)	80 (15)
	2	**43 (5)**	**102 (20)**	320 (58)
	≥3	**19 (2)**	**27 (5)**	**107 (20)**

Non–BTK inhibitor cohort, n (%)		Drug classes at baseline[a] 0 (n=10,253)	1 (n=6,626)	2 (n=6,133)
Drug classes after index date[b]	0	8,550 (83)	890 (13)	305 (5)
	1	**1,187 (12)**	4,576 (69)	733 (12)
	2	**372 (4)**	**888 (13)**	4,223 (69)
	≥3	**144 (1)**	**272 (4)**	**872 (14)**

[a] Drug classes used 1 year prior to index date. [b] Drug classes used within 1 year after index date.

- Patients in the BTK inhibitor cohort had a higher rate of new-onset or worsening hypertension within 1 year of treatment initiation vs the non–BTK inhibitor cohort (**Table 3**) (IPTW HR, 1.28; 95% CI, 1.23-1.33)
- Among patients without baseline hypertension, the rate of new-onset hypertension was greater in the BTK inhibitor cohort vs the non–BTK inhibitor cohort (IPTW HR, 1.50; 95% CI, 1.39-1.62)
- The rate of worsening hypertension in patients with baseline hypertension was greater in the BTK inhibitor cohort than in the non–BTK inhibitor cohort (IPTW HR, 1.16; 95% CI, 1.11-1.23)

CONCLUSIONS

- In this real-world analysis, patients with CLL had a high comorbidity burden, and use of antihypertensive medication was common
- The risk of new-onset or worsening hypertension was higher in patients who initiated BTK inhibitors during the index period than in those on non–BTK inhibitor treatments
- These data suggest that development of hypertension is an important consideration in the long-term management of patients with CLL undergoing treatment with BTK inhibitors

Table 3. New-Onset or Worsening Hypertension Within 1 Year After Index Date

	Patients Without Baseline Hypertension		Patients With Baseline Hypertension		Overall Patients	
	BTK Inhibitor (n=644)	Non–BTK Inhibitor (n=8,001)	BTK Inhibitor (n=1,748)	Non–BTK Inhibitor (n=20,166)	BTK Inhibitor (n=2,392)	Non–BTK Inhibitor (n=28,167)
Patients, n (%)[a]	111 (17)	979 (12)	259 (15)	2537 (13)	370 (15)	3516 (12)
Event rate per 100 person-months (95% CI), %	1.58 (1.31-1.90)	1.10 (1.03-1.17)	1.36 (1.21-1.54)	1.14 (1.10-1.19)	1.42 (1.29-1.58)	1.13 (1.09-1.17)
Cox proportional hazards regressions, HR (95% CI)						
Unadjusted	1.44 (1.18-1.75)	Ref	1.19 (1.05-1.35)	Ref	1.25 (1.13-1.40)	Ref
Multivariable regression						
Model 1: age, sex, race/ethnicity	1.38 (1.14-1.69)	Ref	1.20 (1.05-1.36)	Ref	1.25 (1.12-1.39)	Ref
Model 2: age, sex, race/ethnicity, CCI grouping, index yr	1.37 (1.12-1.67)	Ref	1.17 (1.03-1.33)	Ref	1.23 (1.1-1.37)	Ref
IPTW based on propensity score	1.50 (1.39-1.62)	Ref	1.16 (1.11-1.23)	Ref	1.28 (1.23-1.33)	Ref

[a] New cases of hypertension in patients without existing hypertension, and cases of worsening hypertension in patients with existing hypertension.
CCI, Charlson Comorbidity Index; IPTW, inverse probability treatment weighting; Ref, reference group.

REFERENCES

1. Mato AR, et al. *Clin Cancer Res.* 2022;28(4):603.
2. Quartermaine C, et al. *JACC CardioOncol.* 2023;5(5):570.
3. Estupiñán HY, et al. *Front Cell Dev Biol.* 2021;9:630942.

DISCLOSURES

TDK, LZ, JZ, WA: Employment and may hold stock: BeiGene. **AC:** Consultant: BeiGene; Equity holder: BeiGene. **WBW:** Consultant: BeiGene.

ACKNOWLEDGMENTS

The authors thank the patients and their families, investigators, co-investigators, and the study teams at each of the participating centers. This study was supported by BeiGene Ltd. Medical writing support was provided by Shanen Perumal, PhD, of Nucleus Global, an Inizio company, and supported by BeiGene.

Presented at the EHA2024 Hybrid Congress; June 13-16, 2024; Madrid, Spain