Electronic Patient-Reported Cardiovascular-Related and Clinically Relevant Symptoms in Patients Diagnosed With Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma and Treated With a Second-Generation Bruton Tyrosine Kinase Inhibitor

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CONCLUSIONS

- Use of ePRO-based RTM provides real-world, real-time insights into the experience of patients undergoing treatment with targeted therapy, such as a second-generation BTKis
- In this study, patients diagnosed with CLL/SLL and newly treated with zanubrutinib generally reported fewer cardiovascular-related and other clinically relevant symptoms in the first 6 months of treatment compared to patients newly treated with acalabrutinib
- Understanding the patient experience in real-time can enable timely and targeted management of patient symptoms, may optimize outcomes, and improve patient quality of life

INTRODUCTION

- Bruton tyrosine kinase inhibitors (BTKis) have revolutionized the treatment of hematological cancers, including chronic lymphocytic leukemia and small lymphocytic lymphoma (CLL/SLL)[1-2]
- These therapies, taken orally in the outpatient setting, may come with challenges associated with monitoring and the management of adverse events[3-4]
- Previous studies have demonstrated the effectiveness of electronic patient-reported outcomes (ePRO) for monitoring symptoms and patient health-related quality of life[5]
- The Canopy Remote Therapeutic Monitoring (RTM) platform captures symptoms and medication adherence through electronic patient-reported outcomes (ePROs) and integrates those insights via an EHR-interface
- The platform assists clinicians to quickly understand the patient's experience, prioritize concerning reports, and proactively intervene[6]

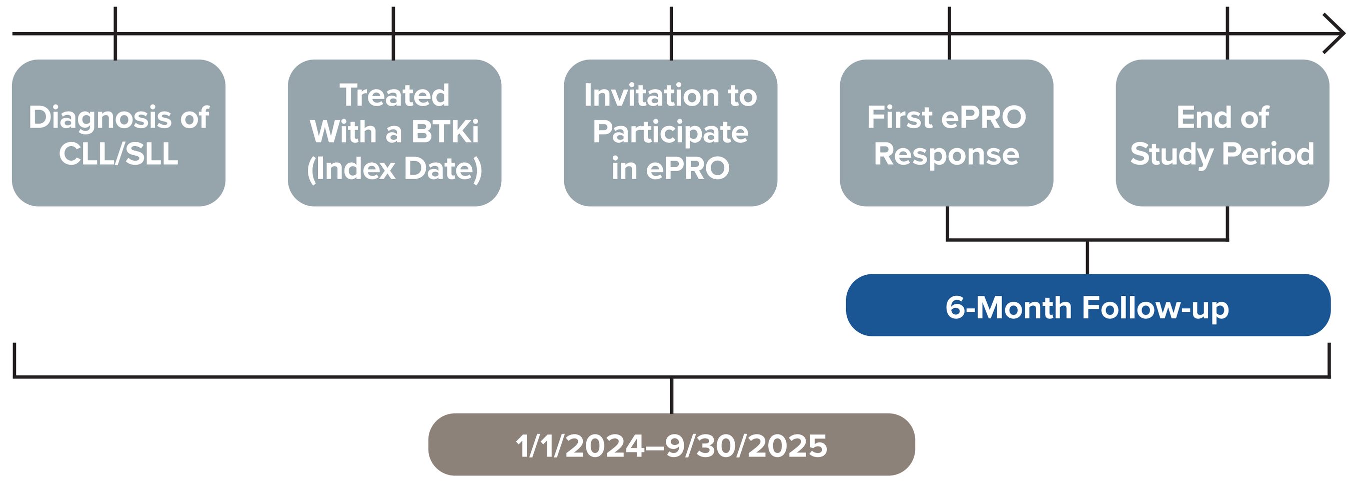
OBJECTIVE

- Using the ePRO-based Canopy RTM platform, to characterize cardiovascular-related and other clinically relevant symptoms reported by patients diagnosed with CLL/SLL and treated with a second-generation BTKi (zanubrutinib or acalabrutinib) during the first 6 months of BTKi treatment

METHODS

- This was a retrospective study of adult patients diagnosed with CLL/SLL, who were BTKi-treatment-naïve and treated with a second-generation BTKi from January 1, 2024, to September 30, 2025, in a US community oncology setting (**Figure 1**)
- Patients were identified from electronic health records, and the index date was the date of BTKi treatment initiation
- Once identified as eligible, patients were invited to participate in the Canopy RTM program
- Once enrolled, patients received a weekly reminder to submit an ePRO report. Reports could be submitted even if the patient was not experiencing symptoms
- Patients were included in the analysis if they submitted at least one ePRO symptom report in the first 6 months of BTKi treatment
- Patients were stratified into cohorts by BTKi (zanubrutinib or acalabrutinib)
- Symptoms of interest included chest pain, heart palpitations, difficulty breathing, weakness/fatigue, lightheadedness/dizziness, nausea/vomiting, headache, pain, and edema

Figure 1. Study Design



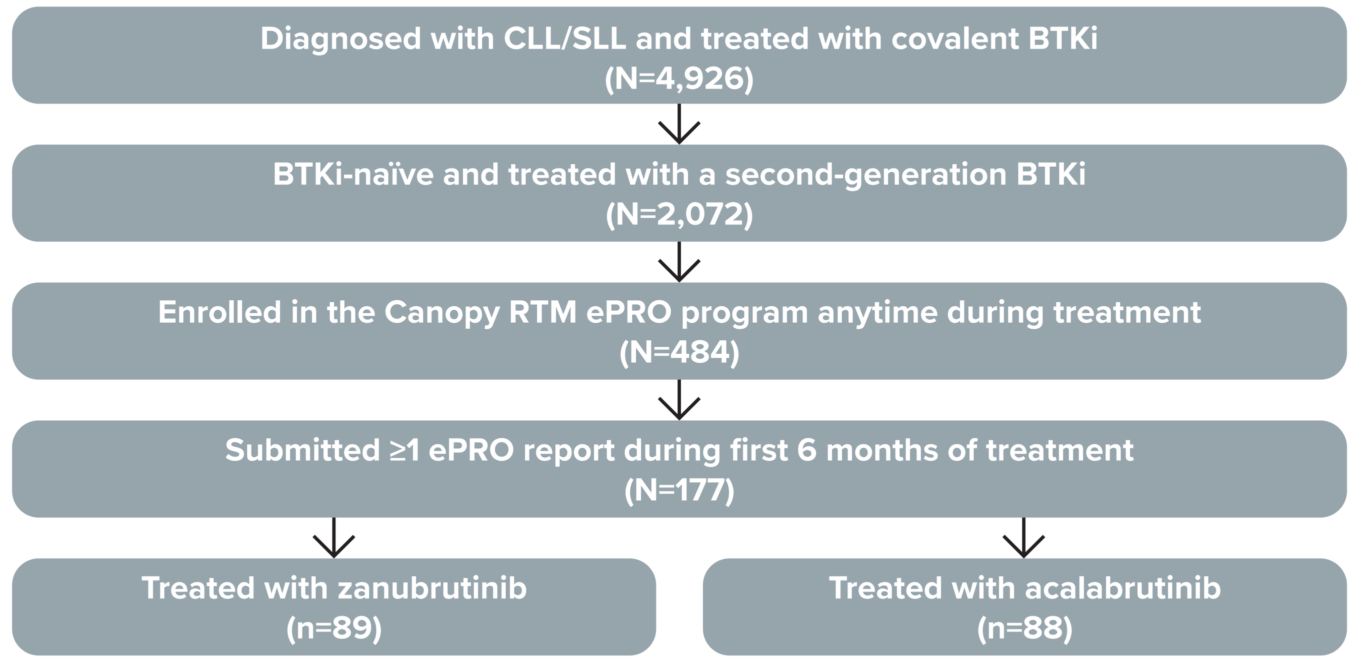
BTKi, Bruton tyrosine kinase inhibitor; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; ePRO, electronic patient-reported outcomes.

RESULTS

Demographic and Clinical Characteristics

- A total of 177 patients submitted at least one ePRO report in the first 6 months of treatment (**Figure 2**)

Figure 2. Attrition



BTKi, Bruton tyrosine kinase inhibitor; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; ePRO, electronic patient-reported outcomes.

- Of these, 89 (50.3%) were treated with zanubrutinib and 88 (49.7%) with acalabrutinib
- Patient demographics and clinical characteristics for the overall sample and by cohort are presented in **Table 1**
- The mean age was 73 years, 66.1% of patients were male, and of those for whom race was known (N=108), 79.8% identified as White
- The median Charlson Comorbidity Index (CCI) at the time of BTKi treatment was 3.0
- Common comorbidities prior to BTKi treatment included blood disorders (22.0%), metabolic disorders (16.4%), and anemia (11.9%)
- Time from CLL/SLL diagnosis to BTKi treatment initiation was a median of 26 months for the zanubrutinib cohort and 17 months for the acalabrutinib cohort
- Patients treated with zanubrutinib vs acalabrutinib had equivalent median CCI (3.0 vs 3.0, respectively) at the time of treatment
- A greater proportion of patients treated with zanubrutinib vs acalabrutinib had cardiovascular disease (9.0% vs 3.4%) and other cardiac diagnoses (10.1% vs 5.7%)

Table 1. Demographic and Clinical Characteristics

Characteristic	Overall (N=177)	Zanubrutinib (N=89)	Acalabrutinib (N=88)
Age at Index, Mean (Range)	73 (65, 81)	74 (66, 81)	73 (65, 80)
Gender, N (%)			
Male	117 (66.1%)	54 (60.7%)	63 (71.6%)
Female	60 (33.9%)	35 (39.3%)	25 (28.4%)
Race/Ethnicity, N (%)			
White	83 (46.9%)	50 (56.2%)	33 (37.5%)
Black	12 (6.8%)	6 (6.7%)	6 (6.8%)
Hispanic	4 (2.3%)	3 (3.4%)	1 (1.1%)
Other	5 (2.8%)	3 (3.4%)	2 (2.3%)
Unknown/Missing	73 (41.2%)	27 (30.3%)	46 (52.3%)
CLL/SLL Dx to Tx start in Months, Mean (Range)	21 (2, 51)	26 (4, 49)	17 (1, 52)
CCI at Index (Median, IQR)	3.0 (2.0, 4.0)	3.0 (3.0, 4.0)	3.0 (2.0, 3.0)
CCI at Index N (%)			
0	5 (2.8%)	1 (1.1%)	4 (4.5%)
1	11 (6.2%)	5 (5.6%)	6 (6.8%)
2	35 (19.8%)	16 (18.0%)	19 (21.6%)
3-4	104 (58.8%)	52 (58.4%)	52 (59.1%)
>4	22 (12.4%)	15 (16.9%)	7 (8.0%)
Common Comorbidities at Pre-Index, N (%)			
Disorders of Blood And Blood-forming Organs	39 (22.0%)	23 (25.8%)	16 (18.2%)
Metabolic Disorders	29 (16.4%)	18 (20.2%)	11 (12.5%)
Anemias and Other Bone Marrow Failure Syndromes	21 (11.9%)	13 (14.6%)	8 (9.1%)
Coagulopathy	16 (9.0%)	12 (13.5%)	4 (4.5%)
Any Cardiac Dx[a]	14 (7.9%)	9 (10.1%)	5 (5.7%)
Diabetes without Chronic Complication	14 (7.9%)	8 (9.0%)	6 (6.8%)
Diabetes, uncomplicated	14 (7.9%)	8 (9.0%)	6 (6.8%)
GI Disease	13 (7.3%)	7 (7.9%)	6 (6.8%)
Cardiovascular Disease[a]	11 (6.2%)	8 (9.0%)	3 (3.4%)
Renal Disease	11 (6.2%)	8 (9.0%)	3 (3.4%)
Renal Failure	11 (6.2%)	8 (9.0%)	3 (3.4%)

[a]Cardiovascular disease includes cardiovascular and cerebrovascular diagnoses. Cardiac diagnoses are heart-specific diagnoses including hypertensive, rheumatic, and ischemic heart diseases. The categories are not mutually exclusive.

CCI, Charlson Comorbidity Index; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; Dx, diagnosis; GI, gastrointestinal; IQR, interquartile range; Tx, treatment.

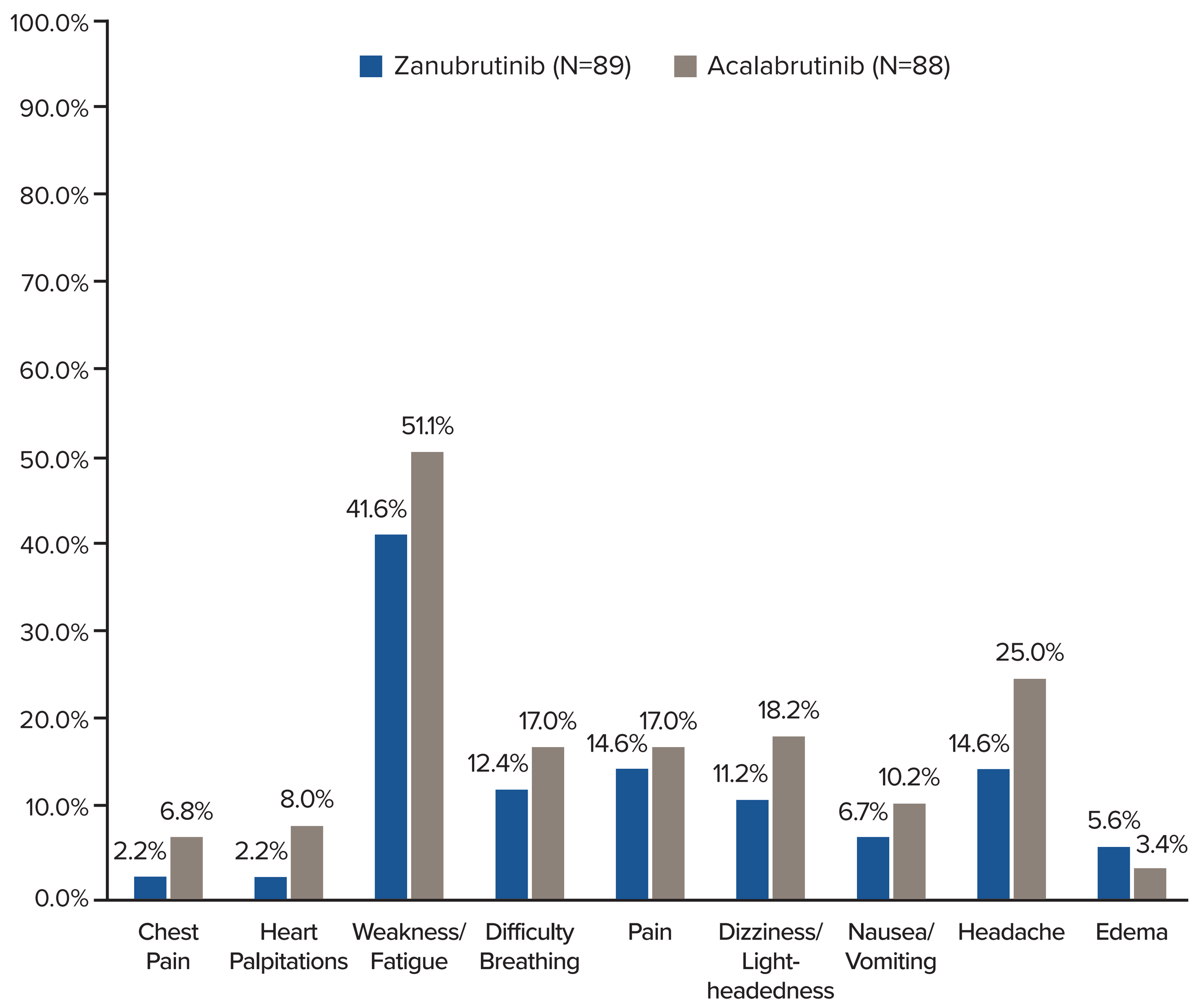
Self-Reported Symptoms

- Among all patients, the most common patient-reported symptoms included weakness/fatigue, headache, pain, sleep issues, bruising, anxiety, dizziness/lightheadedness, difficulty breathing, cough, and appetite issues (**Table 2**)
- With regard to cardiovascular-related and other clinically relevant symptoms, patients treated with zanubrutinib vs acalabrutinib generally reported less chest pain (2.2% vs 6.8%, respectively), heart palpitations (2.2% vs 8.0%), weakness/fatigue (41.6% vs 51.1%), difficulty breathing (12.4% vs 17.0%), pain (14.6% vs 17.0%), dizziness/lightheadedness (11.2% vs 18.2%), nausea/vomiting (6.7% vs 10.2%), and headache (14.6% vs 25.0%), but more edema (5.6% vs 3.4%) (**Figure 3**)

Table 2. Top 10 Commonly Reported Symptoms

Symptom	Overall (N=177)	Zanubrutinib (N=89)	Acalabrutinib (N=88)
Weakness/Fatigue	46.3%	41.6%	51.1%
Headache	19.8%	14.6%	25.0%
Pain	15.8%	14.6%	17.0%
Sleep Issues	15.8%	13.5%	18.2%
Bruising	15.3%	14.6%	15.9%
Anxiety	15.3%	18.0%	12.5%
Dizziness/Lightheadedness	14.7%	11.2%	18.2%
Difficulty Breathing	14.7%	12.4%	17.0%
Cough	14.1%	15.7%	12.5%
Eating/Appetite Issues	14.1%	7.9%	20.5%

Figure 3. Cardiovascular-Related and Clinically Relevant Symptoms by Cohort



DISCUSSION

- Patients with CLL/SLL newly treated with zanubrutinib generally reported fewer cardiovascular-related and other clinically relevant symptoms in the first 6 months of treatment compared to patients newly treated with acalabrutinib
- Additional research is needed to verify these findings and gain insight into the impact of these symptoms on real-world BTKi treatment utilization patterns
- Limitations of the study include the retrospective nature of the study design, different times from CLL/SLL diagnosis to zanubrutinib or acalabrutinib initiation, enrollment and ePRO participation occurring at different time intervals during treatment, the analysis only including those who submitted at least one ePRO response, and that no statistical analysis was completed

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DISCLOSURES

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