Characterizing Self-Reported Missed Medication Doses and Cardiovascular-Related Clinically Relevant Symptoms in Patients Diagnosed With CLL/SLL and Treated With a Second-Generation BTKi Using an Electronic Patient-Reported Outcomes (ePRO) Platform

CLL - 180

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CONCLUSIONS

- Patients treated with zanubrutinib reported fewer missed BTKi doses and lower rates of cardiovascular-related and other clinically relevant symptoms compared with patients treated with acalabrutinib
- The smaller differences in symptom reporting between missed-dose and non-missed-dose reports with zanubrutinib suggest a more favorable patient-reported treatment experience

BACKGROUND

- The covalent Bruton tyrosine kinase inhibitors (BTKis) zanubrutinib and acalabrutinib have revolutionized the treatment of hematological cancers, including chronic lymphocytic leukemia and small lymphocytic lymphoma (CLL/SLL)[1,2]
- These oral therapies, designed for outpatient care, require ongoing attention to support adherence and management of potential adverse events[3]
- The Canopy Remote Therapeutic Monitoring (RTM) platform captures medication adherence (measured in missed medication doses) and symptoms through electronic patient-reported outcomes (ePROs), and integrates those insights via an electronic health record (EHR) interface[4,5]
- The platform assists clinicians in quickly understanding the patient experience, prioritizing concerning reports, and proactively intervening[6]

OBJECTIVE

- To examine self-reported missed BTKi doses, cardiovascular-related/clinically relevant symptoms, and their concurrence among adult patients diagnosed with CLL/SLL and treated with zanubrutinib or acalabrutinib in a community oncology setting

METHODS

- This was a retrospective study of patients diagnosed with CLL/SLL and treated with a second-generation BTKi (zanubrutinib or acalabrutinib) from January 1, 2024, to December 31, 2025
- Patients were identified using structured EHR data and were invited to enroll in the Canopy ePRO-based RTM program; ePRO monitoring included weekly reminders
- Patients who submitted at least one ePRO report following enrollment were included in the analysis
- ePRO responses of interest included self-reported missed BTKi doses and self-reported cardiovascular-related/clinically relevant symptoms (defined as previously described)[7,8]
- Patient-level propensity score weighting was conducted using an inverse probability of treatment weighting (IPTW) strategy to control baseline demographic and clinical differences between treatment groups
  - Control variables included age, sex, Charlson Comorbidity Index (CCI), cardiac diagnoses, previous lines of therapy, months from CLL diagnosis to BTKi initiation, and months from treatment initiation to enrollment
- Missed BTKi doses and cardiovascular-related/clinically relevant symptoms were analyzed using ePRO responses "since the last report", as these measures can vary over the course of treatment
- Differences in missed BTKi doses by BTKi treatment were calculated using a zero-inflated incidence rate ratio (IRR)
- The weighted prevalence of cardiovascular-related/clinically relevant symptoms by treatment was summarized and symptoms were examined overall and among ePRO reports that indicated a missed BTKi dose or no missed dose

RESULTS

Patient Population

- Of the 410 eligible patients enrolled in the Canopy ePRO-based RTM program, 320 (78.0%) patients submitted at least one ePRO report and were included in the analysis
  - Of these, 155 (48.4%) were treated with zanubrutinib and 165 (51.6%) were treated with acalabrutinib (**Table 1**)
  - Following propensity score weighting, the resulting population (N=305) consisted of 147 (48.4%) patients treated with zanubrutinib and 157 (51.6%) patients treated with acalabrutinib (rounded weighted counts; precise counts: overall N = 304.6, zanubrutinib n = 147.3, acalabrutinib n = 157.3) (**Table 2**)

Table 1. Unweighted Patient Demographics and Clinical Characteristics

Characteristic	Overall (N=320)	Zanubrutinib (n=155)	Acalabrutinib (n=165)
Median age (Q1, Q3) at BTKi initiation (years)	72 (64, 79)	73 (65, 80)	71 (62, 78)
Sex			
Male	204 (63.8%)	93 (60.0%)	111 (67.3%)
Female	116 (36.3%)	62 (40.0%)	54 (32.7%)
Race/ethnicity			
White	216 (67.5%)	108 (69.7%)	108 (65.5%)
Black	17 (5.3%)	5 (3.2%)	12 (7.3%)
Hispanic/Latino	7 (2.2%)	5 (3.2%)	2 (1.2%)
Other	33 (10.3%)	13 (8.4%)	20 (12.1%)
Unknown/Missing	47 (14.7%)	24 (15.5%)	23 (13.9%)
CCI			
CCI composite	3.00 (2.00, 4.00)	3.00 (2.00, 4.00)	3.00 (2.00, 3.00)
Prior lines of therapy			
0	258 (80.6%)	116 (74.8%)	142 (86.1%)
1	23 (7.2%)	12 (7.7%)	11 (6.7%)
2	15 (4.7%)	10 (6.5%)	5 (3.0%)
≥3	24 (7.6%)	17 (10.9%)	7 (4.2%)

Abbreviations: BTKi, Bruton tyrosine kinase inhibitor; CCI, Charlson Comorbidity Index; Q1, first quartile; Q3, third quartile.

Table 2. Weighted Patient ePRO Enrollment and Reporting

Characteristic	Overall[a] (N=305)	Zanubrutinib (n=147)	Acalabrutinib (n=157)
Mean months from diagnosis to BTKi initiation (SD)	31.7 (39.3)	33.3 (45.8)	30.3 (32.1)
Months from BTKi initiation to enrollment	5.0 (1.0, 14.0)	4.0 (1.0, 14.0)	5.0 (1.0, 14.0)
Days enrolled during treatment	92.1 (27.8, 161.2)	88.1 (27.5, 189.1)	92.1 (27.8, 146.1)
Active days during treatment	28.0 (9.0, 105.0)	28.0 (8.0, 105.0)	34.0 (12.0, 109.0)
ePRO reports submitted (weighted)	2529	1303	1226
Median ePRO reports submitted during treatment per patient	6.0 (3.0, 19.0)	6.0 (2.0, 16.0)	7.0 (3.0, 21.0)
Median days between ePRO reports	7.0 (7.0, 9.0)	7.0 (7.0, 8.0)	7.0 (7.0, 9.0)

[a]Counts represent weighted observations generated through IPTW adjustment. Overall total is 305 due to rounding.

Abbreviations: BTKi, Bruton tyrosine kinase inhibitor; ePRO, electronic patient-reported outcome; IPTW, inverse probability of treatment weighting; Q1, first quartile; Q3, third quartile; SD, standard deviation.

Patient-Reported Missed BTKi Doses

- Among all ePRO reports submitted, 9.5% showed a missed BTKi dose, with fewer reports for zanubrutinib vs acalabrutinib (IRR=0.49, 95% confidence interval: 0.36, 0.66, P<0.001) (**Table 3**)
- Most missed dose reports showed 1–2 missed doses

Table 3. Weighted Patient-Reported Missed BTKi Doses at the Report

Medication ePRO Reports	Overall (N=2529)	Zanubrutinib (n=1303)	Acalabrutinib (n=1226)
Have you missed any doses?			
Yes	240 (9.5%)	100 (7.7%)	140 (11%)
No	1820 (72.0%)	988 (75.8%)	831 (67.8%)
I don't know	27 (1.1%)	14 (1.1%)	12 (1.0%)
Not asked[a]	442 (17.5%)	200 (15.3%)	242 (19.7%)
Number of missed doses (among those who missed a dose)			
1–2	171 (71.3%)	66 (66.0%)	105 (75.0%)
3–4	27 (11.3%)	12 (12.0%)	15 (10.7%)
>4	42 (17.5%)	22 (22.0%)	20 (14.3%)

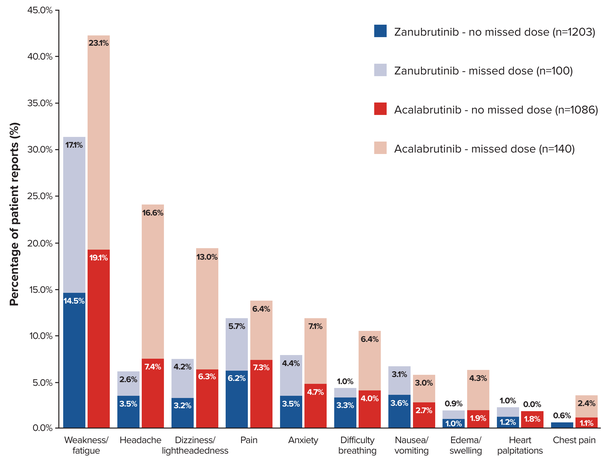
[a]Canopy's adherence reporting is designed to prioritize clinical relevance: missed-dose questions are asked only when a patient confirms the medication is current for them. If a patient does not confirm that they are actively on treatment, the adherence questions are not asked. This helps ensure adherence data reflect active therapy rather than timing differences between EHR-based enrollment and real-world medication use.

Abbreviations: BTKi, Bruton tyrosine kinase inhibitor; EHR, electronic health record; ePRO, electronic patient-reported outcome.

Patient-Reported Missed BTKi Doses and Cardiovascular-Related/Clinically Relevant Symptoms

- Among all patients, compared with zanubrutinib, acalabrutinib was associated with higher rates of weakness/fatigue, headache, and dizziness/lightheadedness (**Figure 1**)
  - Among patients who missed a BTKi dose, fewer reports submitted by patients with zanubrutinib vs acalabrutinib indicated cardiovascular-related/clinically relevant symptoms

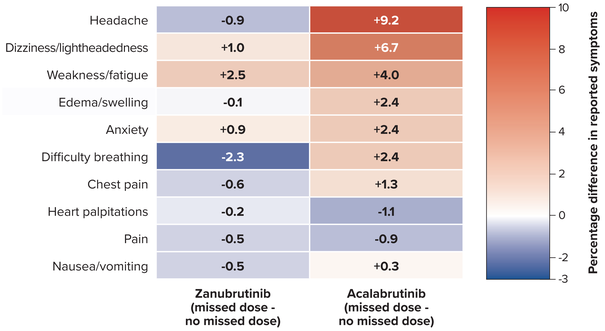
Figure 1. Weighted Patient-Reported Missed BTKi Doses and Cardiovascular-Related/Clinically Relevant Symptoms on Reports of Missed vs No Missed Doses at the Report Level



Abbreviations: BTKi, Bruton tyrosine kinase inhibitor.

- The largest difference in cardiovascular-related/clinically relevant symptoms on reports of missed vs no missed doses was observed for acalabrutinib, most notably for headache, dizziness/lightheadedness, and weakness/fatigue, while differences for zanubrutinib were small, near zero, or in the opposite direction (**Figure 2**)

Figure 2. Weighted Difference in Cardiovascular-Related/Clinically Relevant Symptoms Between Reports With Missed Doses and Reports With No Missed Doses[a]



[a]Darker red shading indicates greater differences in symptom reporting by missed vs no missed dose.

LIMITATIONS

- Results are predominantly descriptive in nature, with limited statistical comparisons
- Analysis was limited to ePRO reports from patients treated for CLL/SLL at community oncology practices
- Medication adherence was operationalized as missed medication doses and no pill counts/pharmacy fills were examined
- The study did not differentiate between symptoms associated with CLL/SLL, other comorbidities, or the BTKi

DISCUSSION

- In this real-world cohort of patients with CLL/SLL monitored through the Canopy ePRO-based RTM platform, zanubrutinib was associated with fewer self-reported missed BTKi doses and lower rates of cardiovascular-related/clinically relevant symptoms compared with acalabrutinib
- Missed doses were associated with greater symptom reporting, particularly among acalabrutinib-treated patients, highlighting the value of ePRO-based remote monitoring for identifying adherence and symptom burden in routine clinical practice

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DISCLOSURES

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