Real-World Bruton Tyrosine Kinase Inhibitor Treatment Patterns and Outcomes Among Patients With Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma in US Community Oncology Practices

Jing-Zhou Hou,[1] Simon Blanc,[2] Gregory A. Maglinte,[3] Anupama Vasudevan,[2] Anna Rui,[2] Mike Gart,[2] Hoa Pham,[3] Lindsay Aton,[2] Brandon Wang,[2] Rushir Choksi[1]

[1]UPMC, Pittsburgh, Pennsylvania, USA; [2]Integra Connect, West Palm Beach, Florida, USA; [3]BeiGene USA, Inc, San Mateo, CA, USA

INTRODUCTION

- Bruton tyrosine kinase inhibitors (BTKis) are now standard-of-care therapies for both first-line and second-line (1L/2L) relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL) and small lymphocytic leukemia (SLL)
- National Comprehensive Cancer Network (NCCN) Guidelines list second-generation BTKis zanubrutinib and acalabrutinib as preferred agents over first-generation BTKi ibrutinib based on the toxicity profile[1]
- Among high-risk patients with R/R CLL in the phase 3 ELEVATE-RR trial, progression-free survival (PFS) with acalabrutinib was noninferior to that of ibrutinib[2]
- The phase 3 ALPINE study in R/R CLL/SLL demonstrated superior PFS for zanubrutinib compared with ibrutinib, and zanubrutinib was associated with fewer adverse events (AEs) leading to discontinuation, including fewer cardiac AEs and a lower rate of atrial fibrillation[3]

OBJECTIVE

- To investigate the clinical characteristics, treatment patterns, and AEs among BTKi-treated patients with CLL/SLL in the real-world setting

METHODS

Data Source

- IntegraConnect-PrecisionQ de-identified database of electronic health records, practice management, and claims data from 55 practices and more than 1600 providers from the community oncology setting across the United States

Patient Population

- Adults with CLL/SLL who initiated BTKi treatment between January 1, 2020 – January 31, 2023 with follow-up through October 31, 2023
- Patients had ≥5 CLL/SLL visits or more CLL/SLL visits than non-CLL/SLL visits; all patients had ≥2 evaluation and management visits

Data Analysis

- Descriptive analyses of structured electronic data
- Kaplan-Meier analyses were performed for time-to-event outcomes

Outcomes

- Cardiovascular AEs
- Time-to-next-treatment (TTNT): time from line of therapy (LOT) initiation to initiation of next LOT or death
- Time-to-treatment discontinuation (TTD) or death: time between treatment initiation and treatment discontinuation or death

RESULTS

Figure 1. Disposition of Patients with CLL/SLL Initiated on Treatment Identified During the Study

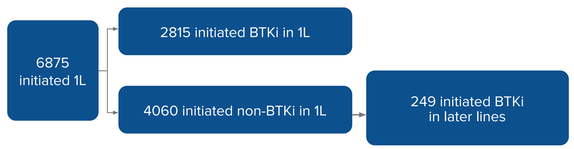
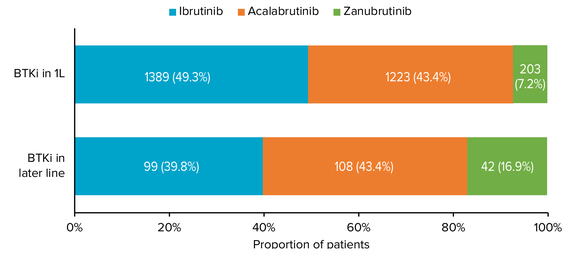


Figure 2. BTKi Utilization



RESULTS

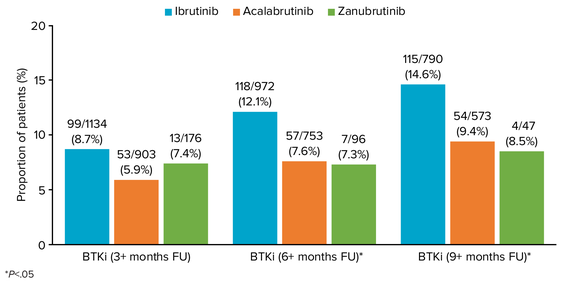
Table 1. Demographics and Baseline Characteristics for 1L BTKi Patients

	Ibrutinib (n=1389)	Acalabrutinib (n=1223)	Zanubrutinib (n=203)
Median age (range), years	71 (35, 90)	72 (36, 90)	72 (33, 90)
Sex, n (%)			
Female	503 (36.2)	450 (36.8)	79 (38.9)
Male	883 (63.6)	770 (63)	123 (60.6)
Not documented/unknown/other	3 (0.2)	3 (0.2)	1 (0.5)
Race, n (%)			
White	842 (60.6)	775 (63.4)	127 (62.6)
African American	98 (7.1)	60 (4.9)	9 (4.4)
Asian	10 (0.7)	6 (0.5)	0 (0.0)
Not documented/unknown/other	439 (31.6)	382 (31.2)	67 (33)
ECOG status at index, n (%)			
ECOG 0-1	861 (62.0)	750 (61.3)	134 (66.0)
ECOG 2+	93 (6.7)	91 (7.4)	19 (9.4)
N/A	435 (31.3)	382 (31.2)	50 (24.6)
Comorbidities, n (%)			
Chronic pulmonary disease	34 (2.4)	40 (3.3)	6 (3.0)
Diabetes without chronic complications	65 (4.7)	48 (3.9)	5 (2.5)
Diabetes with chronic complications	27 (1.9)	13 (1.1)	0 (0.0)
Gastroesophageal reflux disease	61 (4.4)	46 (3.8)	5 (2.5)
Gastrointestinal disease	105 (7.6)	99 (8.1)	10 (4.9)
Iron-deficient anemia	66 (4.8)	69 (5.6)	6 (3.0)
Renal disease	57 (4.1)	58 (4.7)	3 (1.5)
Cardiac comorbidities, n (%)			
All cardiac comorbidities	230 (16.6)	192 (15.7)	21 (10.3)
Acute ischemic heart disease	2 (0.1)	1 (0.1)	0 (0.0)
Angina pectoris	2 (0.1)	2 (0.2)	0 (0.0)
Atrial fibrillation	44 (3.2)	38 (3.1)	4 (2.0)
Atrial flutter	2 (0.1)	0 (0.0)	0 (0.0)
Cardiac arrest	0 (0.0)	1 (0.1)	0 (0.0)
Cardiac arrhythmia	10 (0.7)	2 (0.2)	0 (0.0)
Cardiomyopathy	7 (0.5)	7 (0.6)	0 (0.0)
Cardiotoxicity	0 (0.0)	0 (0.0)	0 (0.0)
Congestive heart failure	4 (0.3)	8 (0.7)	2 (1.0)
Hypertension	207 (14.9)	172 (14.1)	18 (8.9)
Ischemic stroke (cerebral infarction)	3 (0.2)	6 (0.5)	0 (0.0)
Left ventricular dysfunction	1 (0.1)	1 (0.1)	0 (0.0)
Myocardial infarction	7 (0.5)	10 (0.8)	0 (0.0)
Pulmonary arterial hypertension	0 (0.0)	1 (0.1)	0 (0.0)
Stroke	6 (0.4)	6 (0.5)	0 (0.0)
Ventricular tachycardia	4 (0.3)	0 (0.0)	0 (0.0)

ECOG PS, Eastern Cooperative Oncology Group; N/A, not available.

- The proportion of patients using zanubrutinib was greater in >1L of therapy than in 1L of therapy (**Figure 2**)

Figure 3. Cardiovascular AEs in the 1L Setting



*P<.05
FU, follow-up.

- Of patients within the first 3 months of follow-up post-BTKi initiation, the rate of cardiac AEs was highest in patients who initiated ibrutinib (8.7%), followed by zanubrutinib (7.4%), and acalabrutinib (5.9%)
- Significantly more patients experienced cardiovascular AEs among those who received 1L ibrutinib vs acalabrutinib or zanubrutinib at month 6 (12.1%, 7.6%, and 7.3%, respectively; P<.05) and at month 9 (14.6%, 9.4%, and 8.5%, respectively; P<.05)

Figure 4. Time to Discontinuation

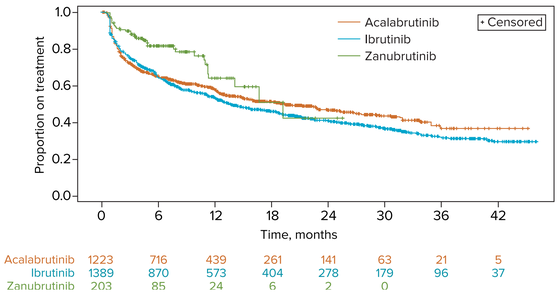
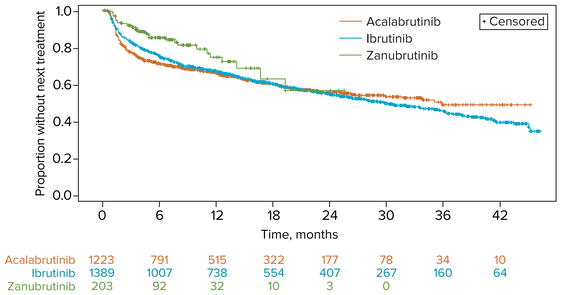


Table 2. Time to Treatment Discontinuation or Death in 1L BTKi

	Overall (n=2815)	Ibrutinib (n=1389)	Acalabrutinib (n=1223)	Zanubrutinib (n=203)
Median duration of follow-up from BTKi initiation, mo	-	20.5 (0.4, 46.0)	14.2 (0.1, 46.0)	6 (1.1, 26.6)
Discontinued/ death, n (%)	1376 (48.9)	775 (55.8)	556 (45.5)	45 (22.2)
Censored, n (%)	1439 (51.1)	614 (44.2)	667 (54.5)	158 (77.8)
Median TTD (95% CI), mo	16.2 (14.4, 19.1)	13.7 (12.2, 16.0)	19.2 (15.1, 25.3)	19.3 (14.1, NR)
Probability of Continuing Same Treatment (95% CI), %				
6 mo	65.9 (64.1, 67.7)	64.8 (62.2, 67.3)	64.8 (62.0, 67.4)	81.6 (75.1, 86.6)
12 mo	56.1 (54.1, 58)	53.3 (50.5, 56.0)	57.7 (54.7, 60.6)	64.1 (51.0, 74.6)
18 mo	49.1 (47, 51.2)	46.2 (43.3, 49.0)	51.2 (48.0, 54.4)	51 (30.5, 68.4)
24 mo	44 (41.7, 46.2)	40.9 (37.9, 43.8)	46.9 (43.3, 50.4)	42.5 (20.6, 62.9)
30 mo	39.8 (37.4, 42.3)	36.5 (33.5, 39.6)	43.9 (39.9, 47.8)	-
36 mo	34.6 (31.6, 37.6)	32.0 (28.6, 35.4)	37.0 (30.6, 43.3)	-
42 mo	32.6 (29.2, 36)	29.8 (26, 33.6)	37.0 (30.6, 43.3)	-

CI, confidence interval; NR, not reached.

Figure 5. Kaplan-Meier Curves for Time to Next Treatment or Death in 1L BTKi



CONCLUSIONS

- This study demonstrated better real-world CLL/SLL safety and effectiveness outcomes for acalabrutinib and zanubrutinib vs ibrutinib
- More patients experienced cardiovascular AEs when treated with ibrutinib than acalabrutinib or zanubrutinib
- The proportions of patients continuing treatment and the median TTNT was longer for patients who received zanubrutinib
- Additional research is needed to explain and validate observed differences favoring zanubrutinib over acalabrutinib

Table 3. Time to Next Treatment or Death in 1L BTKi

	Overall (n=2815)	Ibrutinib (n=1389)	Acalabrutinib (n=1223)	Zanubrutinib (n=203)
Next treatment/ death, n (%)	1111 (39.5)	617 (44.4)	457 (37.4)	37 (18.2)
Median TTNT (95% CI), mo	32.3 (29.1, 36.0)	30.2 (26.2, 35.5)	35.8 (29.8, NR)	NR (16.7, NR)
Probability of No Next Treatment (95% CI), %				
6 mo	74.3 (72.6, 75.9)	75.4 (73, 77.6)	71.3 (68.7, 73.8)	85.3 (79.2, 89.8)
12 mo	67.4 (65.6, 69.2)	67.3 (64.6, 69.7)	66.3 (63.4, 69.0)	75 (64.3, 82.9)
18 mo	60.9 (58.8, 62.8)	60.5 (57.7, 63.2)	60.3 (57.1, 63.3)	63.3 (46.1, 76.3)
24 mo	55.6 (53.4, 57.8)	54.9 (51.9, 57.7)	56.1 (52.6, 59.4)	57 (37.2, 72.6)
30 mo	51.4 (49, 53.8)	50.0 (46.9, 53.1)	53.9 (49.9, 57.6)	-
36 mo	47.1 (44.2, 49.9)	45.8 (42.3, 49.2)	49.2 (43.5, 54.7)	-
42 mo	42 (38.3, 45.5)	39.9 (35.7, 44)	49.2 (43.5, 54.7)	-

1L, first-line; BTKi, Bruton tyrosine kinase inhibitor; CI, confidence interval; NR, not reached; TTNT, time-to-next treatment.

- Of patients treated with 1L ibrutinib, 12.7% discontinued ibrutinib and switched to a second-generation BTKi
- The median TTD in 1L was shorter for ibrutinib than acalabrutinib or zanubrutinib
  - The median TTD (95% CI) in the 1L setting was 13.7 (12.2, 16.0) months for ibrutinib, 19.2 (15.1, 25.3) months for acalabrutinib, and 19.3 (14.1, NR) months for zanubrutinib
- The associated probability of continuing treatment and not having new treatment were higher with zanubrutinib vs ibrutinib or acalabrutinib at month 6
- The median TTNT (95% CI) was not reached (16.7, NR) for those who received zanubrutinib in the 1L setting, while it was 35.8 (29.8, NR) months for acalabrutinib and 30.2 (26.2, 35.5) months for ibrutinib

LIMITATIONS

- Zanubrutinib had a relatively smaller sample size and shorter follow-up
- Analyses were based only on structured data

REFERENCES

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DISCLOSURES

J-ZH, RC: Consultant: BeiGene and Integra Connect. **SB, AV, AR, MG, LA, BW:** Employment: Integra Connect. **GAM, HP**: Employment and may hold stock: BeiGene.

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