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

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Background: Bruton tyrosine kinase inhibitor (BTKi) therapies are standard of care for chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL), with acalabrutinib (acala) and zanubrutinib (zanu) having improved safety profiles vs ibrutinib (ibru).

Aims: This study assessed real-world clinical characteristics, treatment patterns, and adverse events (AEs) among BTKi-treated patients with CLL/SLL.

Methods: This is a retrospective observational study, updated with 5 months of additional data from a previous analysis. Adults in the US community oncology setting initiated BTKi treatment between January 1, 2020, and July 31, 2023, and were followed to October 31, 2023. De-identified structured electronic health records were analyzed from the Integra Connect-PrecisionQ real-world database. Cardiovascular (CV) AEs (based on ICD codes), time to treatment discontinuation (TTD), and time to next treatment (TTNT) were reported.

Results: A total of 3064 patients initiated BTKi therapies during the index period (1L n=2815; 2L+ n=249). Median age (range) was 72 years (33-90) in 1L and 72 years (42-89) in 2L+. There were 63.1% and 65.5% males in 1L and 2L+, respectively. In 1L, 49.3% of patients were treated with ibru, 43.4% with acala, and 7.2% with zanu. Similar trends were observed for 2L+. More patients experienced CV AEs among those who received 1L ibru vs acala or zanu; 12.1%, 7.6%, and 7.3% at month 6 (P<0.05) and 14.6%, 9.4%, and 8.5% at month 9 (P<0.05). Of patients treated with 1L ibru, 12.7% discontinued ibru and switched to acala or zanu. Median TTD in 1L was shorter for ibru than acala or zanu (**Table**). The associated probability of remaining on treatment was higher with zanu vs ibru or acala at months 6 and 12 (Table). Median TTNT was not reached for zanu, while it was 30.2 months for ibru and 35.8 months for acala.

Summary/Conclusion: While zanu had relatively smaller sample size and shorter follow-up, this study demonstrated better real-world safety and efficacy outcomes for acala and zanu vs ibru. Additional research is needed to explain and validate observed differences favoring zanu over acala.

Table: TTD and TTNT in patients initiating BTKi therapies during index period

1L		**Ibru (N=1389)**	**Acala (N=1223)**	**Zanu (N=203)**
	Median follow-up (range, mos)	20.5 (0.4, 46.0)	14.2 (0.1, 46.0)	6 (1.1, 26.6)
TTD	Discont / Death (n, %)	775 (55.8)	556 (45.5)	45 (22.2)
	Median TTD (95% CI, mos)	13.7 (12.2, 16.0)	19.2 (15.1, 25.3)	19.3 (14.1, NR)
	Prob of continuing same Tx at 6 mos (%, 95% CI)	64.8 (62.2, 67.3)	64.8 (62, 67.4)	81.6 (75.1, 86.6)

	Prob of continuing same Tx at 12 mos (%, 95% CI)	53.3 (50.5, 56)	57.7 (54.7, 60.6)	64.1 (51, 74.6)
TTNT	NT / Death (n, %)	617 (44.4)	457 (37.4)	37 (18.2)
	Median TTNT (95% CI, mos)	30.2 (26.2, 35.5)	35.8 (29.8, NR)	NR (16.7, NR)
	Prob of continuing 1L Tx at 6 mos (%, 95% CI)	75.4 (73, 77.6)	71.3 (68.7, 73.8)	85.3 (79.2, 89.8)
	Prob of continuing 1L Tx at 12 mos (%, 95% CI)	67.3 (64.6, 69.7)	66.3 (63.4, 69)	75 (64.3, 82.9)

1L, first line; acala, acalabrutinib; BTKi, Bruton tyrosine kinase inhibitor; CI, confidence interval; discont, discontinued; ibru, ibrutinib; mos, months; NR, not reached; NT, next treatment; prob, probability; TTD, time to treatment discontinuation; TTNT, time to next treatment; Tx, treatment; zanu, zanubrutinib.