Real-world comparative effectiveness of first-line Bruton tyrosine kinase inhibitors in patients with chronic lymphocytic leukemia

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ABSTRACT

Objectives: Next-generation Bruton tyrosine kinase inhibitor (BTKi) monotherapy is a preferred first-line (1L) treatment (tx) option, as categorized by the National Comprehensive Cancer Network (NCCN) guidelines, for patients (pts) with chronic lymphocytic leukemia (CLL). In phase 3 randomized trials among pts with relapsed or refractory CLL, zanubrutinib (zanu) demonstrated superior efficacy vs ibrutinib (ibr), while acalabrutinib (acala) only showed noninferiority to ibr. In the absence of head-to-head trial comparison, we evaluated real-world (rw) clinical outcomes in 1L BTKi monotherapy in pts with CLL in a large US population.

Methods: This is a retrospective observational study utilizing the US nationwide Flatiron Health electronic health record–derived de-identified database. Eligible pts included those with a CLL diagnosis who started 1L BTKi monotherapy between 01/01/2020 and 08/31/2024. Outcomes included rw time to next tx or death (rwTTNT), time to tx discontinuation or death (rwTTD), and overall survival (rwOS). Landmark tx and survival probabilities were estimated using Kaplan–Meier methods. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazard models, adjusting for age, sex, race/ethnicity, practice type, Eastern Cooperative Oncology Group (ECOG) performance status, immunoglobulin heavy chain variable region (IGHV), and del17p/*TP53* mutation status.

Results: A total of 2515 pts with CLL were included (zanu n=310, acala n=1111, ibr n=1094).1L use of ibr decreased over time, with zanu being most common in 2024 (49% vs 44% acala, 7% ibr). Median age was 73, 74, and 72 years for zanu, acala, and ibr, respectively. More pts with zanu had del17p/*TP53* mutation (16% vs 12% acala, 11% ibr). Median follow-up was 12 months (mos) for zanu, 23 for acala and 33 for ibr. Landmark tx probabilities and 95% CI are in the Table. Median rwTTNT was not reached (NR; 95% CI: NR, NR) for zanu and acala, and was 38.2 mos (95% CI: 33.2, 42.3) for ibr. Median rwTTD was NR (95% CI: NR, NR) for zanu, 43.7 mos (95% CI: 34.4, NR) for acala, and 21.9 mos (95% CI: 18.3, 25.7) for ibr. Pts on zanu had numerically higher probability of not advancing to next line of therapy and not discontinuing tx at 6, 12, and 18 mos than those on acala and ibr (Table). Median rwOS was NR for all groups. Compared to pts on ibr, pts on zanu had statistically significant lower risks of rwTTNT (HR, 0.59; 95% CI, 0.44, 0.79), rwTTD (0.56; 0.44, 0.72), and rwOS (0.46; 0.28, 0.76). Compared to pts on acala, pts on zanu had numerically lower risks of rwTTNT, rwTTD, and rwOS.

Conclusions: Patients with zanu had significantly longer rwTTNT, rwTTD, and rwOS compared to those with ibr and longer trends compared to those with acala. Limitations include limited follow-up time for zanu vs ibr and acala.

Landmark probabilities of not advancing to next treatment or not discontinuing treatment for patients on Bruton tyrosine kinase inhibitors

	Zanubrutinib n=310	Acalabrutinib n=1111	Ibrutinib n=1094
rwTTNT, % (95% CI)			
6 months	91 (87, 94)	88 (86, 90)	85 (83, 87)
12 months	83 (77, 87)	81 (78, 83)	75 (72, 78)
18 months	78 (72, 84)	74 (71, 77)	67 (64, 69)
rwTTD, % (95% CI)			
6 months	85 (80, 88)	81 (78, 83)	75 (72, 77)
12 months	76 (70, 81)	72 (69, 75)	62 (59, 65)
18 months	70 (63, 76)	66 (63, 69)	53 (50, 56)

CI, confidence internval; rwTTNT, real-world time to next treatment or death; rwTTD, real-world time to treatment discontinuation or death