Real-World Comparative Analysis of Treatment Discontinuation with Covalent Bruton Tyrosine Kinase Inhibitors in First-line Chronic Lymphocytic Leukemia (CLL)

Authors

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Background

While covalent Bruton tyrosine kinase inhibitors (cBTKis) are commonly used first-line (1L) therapies for CLL/small lymphocytic lymphoma (SLL), real-world data on treatment patterns remain limited.

Aims

To evaluate real-world treatment persistence and treatment discontinuation associated with 1L cBTKi use in CLL.

Methods

This retrospective observational study used the US IQVIA PharMetrics® closed claims database to identify adult patients (pts) with ≥2 entries of ICD codes for CLL/SLL diagnoses who initiated 1L cBTKi monotherapy (ibrutinib [ibru], acalabrutinib [acala], or zanubrutinib [zanu]) from 01/1/2022 to 02/28/2025; 1L start date was the index date. Eligible pts had continuous enrollment in health insurance for ≥3 months before the start of each cBTKi treatment and were followed until the end of the study period or censoring due to loss to follow-up, whichever occurred first. Baseline pt characteristics and outcomes were examined by each cBTKi. Outcomes included treatment discontinuation (defined as time from index to regimen end date if there was a subsequent therapy, or a gap of ≥120 days between regimen end date and last activity/enrollment date) and treatment persistence (defined as the probability of a pt continuing on treatment). Time to treatment discontinuation (TTD) was analyzed using Kaplan-Meier (KM) estimates. A multivariable Cox proportional hazards model adjusted for age, sex, race, ethnicity, payer type, geographic region, and Charlson Comorbidity Index and was used to estimate the hazard ratio of discontinuation between zanu and acala or ibru. A subgroup analysis was conducted in elderly pts aged ≥65 years.

Results

A total of 1850 pts were included (zanu=608; acala=826; ibru=416). Baseline pt demographic and clinical characteristics were generally comparable between cBTKis, though median age was higher with zanu than acala or ibru (69.0 vs 68.0 vs 67.0 years; *P*=.0007), with a greater proportion of pts aged ≥65 years (73.9% vs 68.9% vs 65.9%; *P*=.0229). Median follow-up

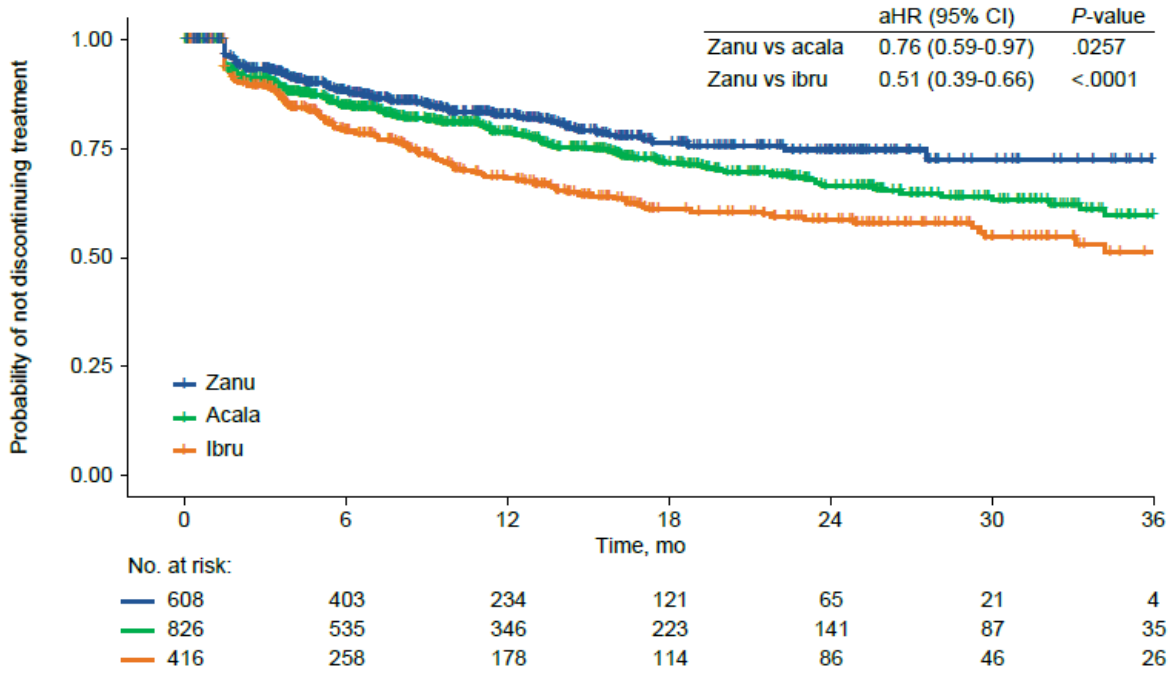
periods were 12 months for zanu, 14 months for acala, and 17 months for ibru. Zanu demonstrated significantly longer TTD (**Figure**) and higher treatment persistence at 6, 12, 18, 24, and 30 months than acala and ibru. At 12 months, treatment persistence was highest with zanu (82.8%; 95% CI, 79.1-85.9), followed by acala (78.7%; 95% CI, 75.4-81.7) and ibru (68.1%; 95% CI, 62.8-72.9; *P*<.0001). Similarly, at 24 months, treatment persistence was highest with zanu (74.7%; 95% CI, 69.3-79.3) than with acala (66.3%; 95% CI, 61.6-70.6) or ibru (58.7%; 95% CI, 52.7-64.3; *P*=.0002). Similar results were observed in the elderly pt subgroup. Multivariable analysis showed that the risk of treatment discontinuation was significantly lower with zanu than acala (adjusted hazard ratio [aHR]=0.76; 95% CI, 0.59-0.97; *P*=.0257) or ibru (aHR=0.51; 95% CI, 0.39-0.66; 66; *P*<.0001). Similar results were seen in pts ≥65 years (zanu vs acala: aHR=0.74; 95% CI, 0.55-0.98; *P*=.0364; zanu vs ibru: aHR=0.48; 95% CI, 0.36-0.66; *P*<.0001).

Summary/Conclusion

In this real-world study, zanu demonstrated significantly lower risk of treatment discontinuation and greater treatment persistence than acala or ibru in 1L CLL, especially in pts aged ≥65 years. While this study provides comparative insights into real-world treatment discontinuation, additional studies with longer follow-up are needed to better understand the reasons for and consequences of treatment discontinuation in 1L CLL.

Figure. Kaplan-Meier Curve of TTD

A. Overall Population



B. ≥65 Years Subgroup