Real-World Comparative Analysis of Treatment Discontinuation (TD) with Covalent Bruton Tyrosine Kinase Inhibitors (cBTKis) in First-Line (1L) Chronic Lymphocytic Leukemia (CLL)

Authors

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Abstract

CONTEXT:

cBTKis are common 1L CLL/small lymphocytic lymphoma (SLL) therapies; real-world data on treatment patterns remain limited.

DESIGN/SETTING/PATIENTS:

This retrospective observational study included adult patients with ≥2 CLL/SLL diagnosis code entries who started 1L cBTKi monotherapy (ibrutinib, acalabrutinib, or zanubrutinib) in the US IQVIA PharMetrics® database 01/01/2022-02/28/2025; 1L start was the index date.

MAIN OUTCOME MEASURES:

Baseline characteristics and outcomes were examined by cBTKi. Outcomes were TD (1L start to end or ≥120-day gap with no treatment record) with hazard ratios (HRs) per multivariable Cox proportional hazards model adjusting for baseline characteristics, probability of continuing treatment (TP), and time to TD (TTD) by Kaplan-Meier method. Patients ≥65 years were also analyzed.

RESULTS:

Overall, 1850 patients were included (zanubrutinib=608; acalabrutinib=826; ibrutinib=416). Baseline demographic and clinical characteristics were comparable between cBTKis; median age was higher with zanubrutinib than acalabrutinib or ibrutinib (69.0 vs 68.0 vs 67.0 years; *P*=.0007), with more patients ≥65 years (73.9% vs 68.9% vs 65.9%; *P*=.0229). Median zanubrutinib, acalabrutinib, and ibrutinib follow-up was 12, 14, and 17 months, respectively. Zanubrutinib demonstrated significantly longer TTD and higher TP at 6, 12, 18, 24, and 30 months than acalabrutinib or ibrutinib. At 12 months, TP was highest with zanubrutinib (82.8%; 95% CI, 79.1-85.9), followed by acalabrutinib (78.7%; 95% CI, 75.4-81.7), and ibrutinib (68.1%; 95% CI, 62.8-72.9; *P*<.0001). Similarly, at 24 months, TP was highest with zanubrutinib (74.7%; 95% CI, 69.3-79.3), compared with acalabrutinib (66.3%; 95% CI, 61.6-70.6) or ibrutinib (58.7%; 95% CI, 52.7-64.3; *P*=.0002). Elderly patients had similar results. TD risk was significantly lower with zanubrutinib than acalabrutinib (adjusted HR [aHR]=0.76; 95% CI, 0.59-0.97; *P*=.0257) or

ibrutinib (aHR=0.51; 95% CI, 0.39-0.66; *P*<.0001). Similar results were seen in patients ≥65 years (zanubrutinib vs acalabrutinib: aHR=0.74; 95% CI, 0.55-0.98; *P*=.0364; zanubrutinib vs ibrutinib: aHR=0.48; 95% CI, 0.36-0.66; *P*<.0001).

CONCLUSIONS:

In this 1L CLL real-world study, zanubrutinib demonstrated significantly lower TD risk and greater TP than acalabrutinib or ibrutinib, especially in patients ≥65 years. Studies with longer follow-up are needed to better understand the reasons for and consequences of 1L CLL TD.