Real-world treatment patterns and outcomes of zanubrutinib in chronic lymphocytic leukemia and small lymphocytic leukemia (CLL/SLL)

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Background: Zanubrutinib (zanu) is a next-generation selective Bruton's tyrosine kinase inhibitor (BTKi) with superior efficacy over first generation ibrutinib (ibru) in CLL/SLL patients (pts). Herein we present real-world treatment patterns based on a formulary change from ibrutinib to zanubrutinib in pts with CLL/SLL in an integrated community oncology practice.

Methods: We retrospectively analyzed CLL/SLL pts 18 years and older who received at least 3 months of zanubrutinib from October 1, 2018 to September 15, 2023 at Kaiser Permanente Northern California. Treatment patterns, treatment-emergent adverse events (TEAEs: AEs reported during BTKi use), treatment-limiting adverse events (TLAEs: AEs leading to BTKi discontinuation), and mortality were reported.

Results: A total of 281 pts received zanu (median age: 71 years; 64% male); 190 pts switched from ibru (ibru-zanu), and 91 pts received zanu only. Most pts were White (75%) followed by Black (10%). Compared with ibru-zanu pts, zanu-only pts were older (median age 74 vs 69 years) and had more comorbidities but were comparable in sex, race, and insurance type. The primary reasons for switching to zanu were formulary change (73%) and progression (15%). Median follow-up time after initiation of first BTKi was longer in the ibru-zanu group (Table). Similar TEAE rates were seen with use of both BTKi therapies, with lower TLAE rates with zanu (Table). Most common TLAE were atrial fibrillation and fatigue for ibru, and cytopenias and rash/bruising for zanu. Cardiac TLAE and non-TLAE rates overall were higher with ibru than zanu, and the rates decreased while on zanu after switching from ibru (Table). Dose modification occurred in 34 pts on ibru and 50 pts on zanu (18 ibru-zanu pts, 32 zanu-only pts), with reductions primarily for grade 1-2 AEs. Of the 281 pts who received zanu, 79% remain on treatment at the end of data collection; 13 pts died (8 from infection, including 5 from COVID), with no reports of treatment-related deaths.

Conclusions: In the real-world setting post-formulary change, zanu is effective and safe in pts with or without prior ibru use. Zanu use had lower cardiotoxicity and TLAE rates than ibru though data was limited by a difference in follow-up time. Similar results were seen in zanu-only pts despite being older and having more comorbidities, with discontinuation most often due to grade <3 AEs.

	While on Ibrutinib (n=190)	While on Zanubrutinib (n=281)	After Ibru-Zanu Switch (n=190)	After Initiating Zanu Only (n=91)
Median Follow Up, mos (range)	46 (15,115)	23.7 (3.3,26)	24.4 (5.5,26)	8.2 (3.3,25)
TEAE, n (%)	69 (36.3)	88 (31.3)	56 (29.5)	32 (35.2)
TLAE, n (%)	21 (11.1)	22 (7.8)	14 (7.4)	8 (8.8)
Cardiotoxicity, n (%)				
TLAE	8 (4.2)	2 (0.7)	2 (1.1)	0 (0.0)
Non-TLAE	18 (9.5)	6 (2.1)	5 (2.6)	1 (1.1)
Other TLAE, n (%)	19 (10.0)	23 (8.2)	14 (7.4)	9 (9.9)
CTCAE grade of TLAE <3, n (%)	14 (7.4)	19 (6.8)	11 (5.8)	8 (8.8)