Real-world treatment switching and sequencing to next line of therapy of zanubrutinib, acalabrutinib, and ibrutinib in CLL/SLL

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Background: Evaluating use of Bruton tyrosine kinase inhibitors (BTKis) for the treatment of CLL/SLL is crucial to understand real-world outcomes of these therapies in diverse populations. The objective of this study was to evaluate real-world switching and sequencing to next line of therapy in patients (pts) initiating BTKis as first-line (1L) or second-line (2L) CLL/SLL treatment.

Methods: A retrospective study was conducted using IntegraConnect PrecisionQ to identify adult pts with ≥1 diagnosis for CLL/SLL initiating zanubrutinib (zanu), acalabrutinib (acala), or ibrutinib (ibru) in 1L or 2L between 1/1/2020-2/28/2023 (index period). Index date was defined as date of BTKi initiation. Pts were required to be continuously enrolled for ≥30 days pre- and post-index date. Treatment switching was measured as pts initiating another treatment within same line or advancing to next line of therapy within 90 days. Sequencing to next line of therapy was calculated from time to next treatment Kaplan-Meier curve, censoring patients at end of follow-up, and reported as proportion of pts receiving next line of therapy at 180 days.

Results: 2,816 pts initiated a 1L BTKi (zanu=157; acala=1,238; ibru=1,421) and 1,253 initiated a 2L BTKi (zanu=107; acala=672; ibru=474). No major differences were observed in baseline demographic and clinical characteristics among 1L and 2L BTKi cohorts. Median follow-up in 1L was 123 days for zanu, 406days for acala, and 637 days for ibru. Regardless of line of therapy, switching rate at ≤60 days and 61-89 days was statistically significantly lower for pts receiving zanu vs acala and ibru (P<0.0001, both 1L and 2L) (Table). Proportion of pts receiving next line of therapy at 180 days was lower for zanu vs acala and ibru (1L P=0.2958; 2L P<0.0001) (Table).

Conclusions: Zanu pts had significantly lower switching rate within 90 days and lower proportion of pts receiving next line of therapy at 180 days when compared with acala and ibru in 1L and 2L. Longer follow-up and larger zanu sample size are required for a comprehensive assessment of treatment outcomes associated with use of BTKis in CLL/SLL.

Table. Treatment switching and proportion of pts receiving next line of therapy for pts initiating BTKis in 1L and 2L

1L	**Zanu** (n=157)	**Acala** (n=1238)	**Ibru** (n=1421)
Switching (%)*			
≤60 days	10.2%	17.1%	13.1%
61-89 days	0.0%	3.4%	2.5%
% of pts receiving next line of therapy at 180 days	13.9%	24.5%	21.1%
2L	**Zanu** (n=107)	**Acala** (n=672)	**Ibru** (n=474)
Switching (%)*			
≤60 days	7.5%	10.7%	17.1%
61-89 days	0.0%	2.5%	4.0%
% of pts receiving next line of therapy at 180 days*	9.1%	18.6%	29.2%

***P<.0001**