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POSTER ABSTRACTS

905.OUTCOMES RESEARCH-LYMPHOID MALIGNANCIES

Real-World Use and Outcomes of Therapies, Including Venetoclax-Based Treatments, after Discontinuation of a Covalent BTK Inhibitor in Patients with Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

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Background
Current treatment guidelines for chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) support the use of covalent BTK inhibitor (cBTKi)-based regimens in the front-line setting. Optimal treatment sequencing following the discontinuation of cBTKi therapy, however, remains unknown. Venetoclax-based regimens, such as the combination of venetoclax plus rituximab, are commonly employed in the treatment of relapsed/refractory CLL/SLL; however, published clinical trial evidence is limited in the post-cBTKi setting due to the small numbers of patients treated with venetoclax-based therapies after cBTKi. This real-world study evaluated patient characteristics, treatment patterns, and clinical outcomes associated with immediate subsequent treatment, including the use of venetoclax-based treatment, after initial cBTKi discontinuation among US patients with CLL/SLL.

Methods
This descriptive, retrospective observational study used the nationwide Flatiron Health electronic health record (EHR)-derived de-identified database. Patients with CLL/SLL aged 18 years or older were included who received at least one cBTKi (ibrutinib, zanubrutinib, or acalabrutinib) and at least one additional line of treatment immediately after their initial cBTKi treatment discontinuation from December 01, 2011, through March 31, 2022. Initial cBTKi treatment could be first line or second or later line of therapy. Patient characteristics and outcomes (time to treatment discontinuation or death [TTD-D], time to next treatment or death [TTNT-D], and overall survival [OS]) were reported. Kaplan Meier method was used for time-to-event outcomes, which were measured from the start of the post-cBTKi treatment.

Results
In this study, n=1,243 patients were analyzed with a median age of 72 years (range, 37-86) at post-cBTKi treatment initiation (Table 1). Most patients received their immediate post-cBTKi treatment in the second (61%) or third line (28%) setting. Twenty-three percent (n=288) of patients received venetoclax-containing regimens as the immediate post-cBTKi therapy, with 10% (n=120) who received venetoclax monotherapy (VenMono), 5% (n=63) venetoclax plus rituximab (VenR), and 8% (n=105) venetoclax plus other (e.g., chemoimmunotherapy, obinutuzumab). In the entire post-cBTKi cohort, the median TTD-D and TTNT-D were 6.5 (95% CI, 5.8-7.5) and 18.8 (95% CI, 16.1-21.7) months, respectively (Table 2). The median TTD-D and TTNT-D in the cohort that included all venetoclax-containing treatments were 12.9 (95% CI, 10.6-16.5) and 30.1 (95% CI, 23.8-39.4) months, respectively. For patients who received VenMono or VenR, the median TTD-D was 10.6 (95% CI, 7.5-16.0) months and median TTNT-D was 29.5 (95% CI, 18.6-39.4) months. Median OS was not reached for any of the cohorts investigated.

Conclusions
The findings of this study suggest that the outcomes observed in clinical trials of venetoclax-containing regimens, where patient populations may differ, may not be routinely extrapolated to patients who received a prior cBTKi. In addition, outcomes for patients treated in the post-cBTKi setting appear to be suboptimal overall. These data suggest the need for additional treatment options and sequencing data to determine the best treatment strategy following the discontinuation of initial cBTKi therapy.

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Table 1. Patient characteristics

Characteristic[a]	Overall post-cBTKi *N=1243*	Non ven-containing post-cBTKi *N=955*	All ven-containing post-cBTKi *N=288*	VenMono OR venR as post-cBTKi[b] *N=183*
Age, median (range)	72 (37, 86)	72 (37, 85)	71 (40, 86)	73 (40, 86)
Male sex, n (%)	793 (64)	600 (63)	193 (67)	123 (67)
Received post-cBTKi treatment in community setting, n (%)	1026 (83)	782 (82)	244 (85)	164 (90)
ECOG PS 0-1[c], n/N (%)	844/988 (85)	634/753 (84)	210/235 (89)	129/144 (90)
Deletion of 17p present[c], n/N (%)	234/1080 (22)	157/813 (19)	77/267 (29)	47/165 (28)
IgHV unmutated[c], n/N (%)	388/624 (62)	291/474 (61)	97/150 (65)	55/85 (65)
Rai stage at initial diagnosis[c], n/N (%)				
0	271/791 (34)	209/606 (34)	62/185 (34)	36/111 (32)
I	183/791 (23)	137/606 (23)	46/185 (25)	29/111 (26)
II	105/791 (13)	80/606 (13)	25/185 (14)	13/111 (12)
III	86/791 (11)	64/606 (11)	22/185 (12)	14/111 (13)
IV	146/791 (18)	116/606 (19)	30/185 (16)	19/111 (17)
Line of therapy in which post-cBTKi treatment received, n (%)				
2	754 (61)	590 (62)	164 (57)	105 (57)
3	351 (28)	256 (27)	95 (33)	62 (34)
4	87 (7)	65 (7)	22 (8)	11 (6)
5 or greater	51 (4)	44 (5)	7 (2)	5 (3)

[a] characteristic at initiation of post-cBTKi treatment unless otherwise stated; [b] excludes n=105 patients who received venetoclax in combination regimens other than those included in this sub-group; [c] number of patients with non-missing data used as denominator when calculating the proportion; N, denominator; ven, venetoclax

Table 2. Clinical outcomes

Endpoint	Overall post-cBTKi *N=1243*	Non ven-containing post-cBTKi *N=955*	All ven-containing post-cBTKi *N=288*	VenMono OR venR as post-cBTKi[a] *N=183*
TTD-D, median months (95% CI)	6.5 (5.8, 7.5)	5.2 (4.7, 6.0)	12.9 (10.6, 16.5)	10.6 (7.5, 16.0)
TTNT-D, median months (95% CI)	18.8 (16.1, 21.7)	15.7 (13.4, 18.8)	30.1 (23.8, 39.4)	29.5 (18.6, 39.4)
OS rate at 4 years[b], rate (95% CI)	0.71 (0.67, 0.75)	0.69 (0.64, 0.74)	0.76 (0.69, 0.82)	0.76 (0.67, 0.82)

[a] excludes n=105 patients who received venetoclax in combination regimens other than those included in this sub-group; [b] median OS was not reached for any of the cohorts investigated; ven, venetoclax

Figure 1

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