Real-World Treatment Switching and Sequencing to Next Line of Therapy of Zanubrutinib, Acalabrutinib, and Ibrutinib in CLL/SLL

Javier Pinilla-Ibarz,[1] Mei Xue,[2] Elizabeth Wu,[3] Kaitlyn Esselman,[3] Wesley Furnback,[3] Swetha Challagulla,[2] Keri Yang[2]

[1]Moffitt Cancer Center, Tampa, FL, USA; [2]BeiGene, San Mateo, CA, USA; [3]Real Chemistry, New York, NY, USA

INTRODUCTION

- Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) account for 25% of all leukemia cases and although indolent, are considered incurable[1,2]
- 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

OBJECTIVE

- The objective of this study was to evaluate real-world switching and sequencing to next line of therapy in patients initiating BTKis as first-line (1L) or second-line (2L) CLL/SLL treatment

METHODS

Data Source

- A retrospective study was conducted using the Integra Connect database, which includes electronic medical records from community-based oncology practices
- The study period was from December 1, 2019, to March 31, 2023, with an index period between January 1, 2020, and February 28, 2023
- Patients were indexed on the date of BTKi initiation during the index period

Inclusion Criteria

- Age ≥18 years with ≥1 diagnosis for CLL or SLL
- Initiated acalabrutinib, ibrutinib, or zanubrutinib in the 1L or 2L setting during the index period
- Continuous enrollment in the database for ≥30 days prior to and after the index date

Cohorts

- Cohorts were developed based on treatment regimens and stratified by line of therapy (1L and 2L)
  - Acalabrutinib
  - Ibrutinib
  - Zanubrutinib

Study Measures

- Demographics, clinical characteristics, and comorbidities were measured at baseline
- Treatment switching was measured as patients 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 the time-to-next treatment Kaplan-Meier curve, censoring patients at end of follow-up, and reported as the proportion of patients receiving next line of therapy at 180 days

RESULTS

- A total of 2816 and 1253 patients initiated a 1L or 2L BTKi during the index period, respectively
- In 1L, ibrutinib (50.5%) was the most common BTKi followed by acalabrutinib (44.0%) and zanubrutinib (5.6%)
- In 2L, acalabrutinib (53.6%) was the most commonly utilized BTKi followed by ibrutinib (37.8%) and zanubrutinib (8.54%)
- In 1L, median (IQR) follow-up was 123 (63, 335) days for zanubrutinib, 406 (196, 659) days for acalabrutinib, and 637 (326, 921) days for ibrutinib (*P*<.0001)
- In 2L, median (IQR) follow-up was 133 (62, 385) days for zanubrutinib, 503 (265, 799) days for acalabrutinib, and 524 (259, 856) days for ibrutinib (*P*<.0001)
- There were no significant differences across the three groups for age, sex, payer type, or Rai stage at baseline among 1L patients (**Table 1**). There was a significant (*P*<.0001) difference in CLL vs SLL and zanubrutinib had the highest percentage of SLL patients (26.75%)
- Mean age at index was significantly different across the three BTKis (*P*=.0037) with zanubrutinib having the highest mean age (**Table 2**). The percentage of CLL vs SLL patients was also significantly (*P*<.0001) different among 2L patients with zanubrutinib having the highest percentage (24.3%) of SLL patients

Table 1. Baseline Characteristics for Patients Initiating a BTKi in 1L

Variable	1L (n=2816) Acalabrutinib (n=1238)	Ibrutinib (n=1421)	Zanubrutinib (n=157)	*P* Value
Age at index				.9168
Mean (SD), years	70.1 (10.4)	70.1 (10.4)	70.4 (11.2)	
Median (IQR), years	71 (63, 78)	70 (63, 78)	72 (65, 78)	
Sex, n (%)				.2586
Male	762 (61.6)	881 (62)	104 (66.2)	
Female	460 (37.2)	532 (37.4)	52 (33.1)	
Payer type, n (%)				.1667
Commercial	208 (17.7)	204 (15.1)	36 (23.1)	
Medicare/Medicaid	508 (43.2)	595 (44.1)	61 (39.1)	
Other	433 (36.8)	524 (38.9)	57 (36.5)	
Self pay	27 (2.3)	25 (1.9)	2 (1.3)	
CLL/SLL, n (%)				<.0001
CLL	1104 (89.2)	1260 (88.7)	115 (73.3)	
SLL	134 (10.8)	161 (11.3)	42 (26.8)	
Rai stage, n (%)				.238
0	126 (10.2)	116 (8.2)	11 (7.0)	
I	99 (8.0)	93 (6.5)	11 (7.0)	
II	58 (4.7)	78 (5.5)	5 (3.2)	
III	74 (6.0)	85 (6.0)	3 (1.9)	
IV	102 (8.2)	117 (8.2)	4 (2.6)	
N/A	779 (62.9)	932 (65.6)	123 (78.3)	

IQR, interquartile range; SD, standard deviation.

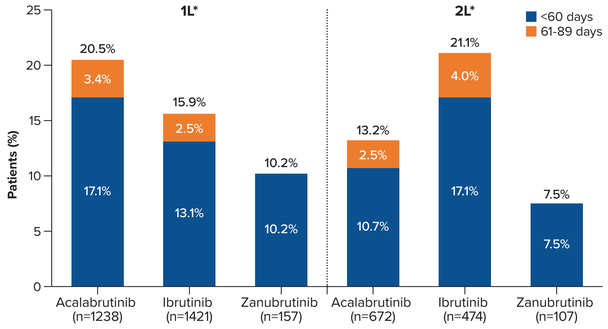
Table 2. Baseline Characteristics for Patients Initiating a BTKi in 2L

Variable	2L (n=1253) Acalabrutinib (n=672)	Ibrutinib (n=474)	Zanubrutinib (n=107)	*P* Value
Age at index				.0037
Mean (SD), years	68.2 (10.1)	68.7 (9.6)	71.7 (10.2)	
Median (IQR), years	68.5 (62, 76)	69 (62, 76)	71 (65, 80)	
Sex, n (%)				.8045
Male	414 (61.6)	283 (59.7)	65 (60.8)	
Female	252 (37.5)	188 (39.7)	42 (39.3)	
Payer type, n (%)				.0663
Commercial	106 (16.4)	52 (11.5)	21 (20)	
Medicare/Medicaid	275 (42.4)	186 (41.2)	47 (44.8)	
Other	256 (39.5)	206 (45.6)	37 (35.2)	
Self pay	11 (1.7)	8 (1.8)	0 (0)	
CLL/SLL, n (%)				<.0001
CLL	602 (89.6)	376 (79.3)	81 (75.7)	
SLL	70 (10.4)	98 (20.7)	26 (24.3)	
Rai stage, n (%)				.0532
0	54 (8.0)	21 (4.4)	5 (4.7)	
I	51 (7.6)	36 (7.6)	12 (11.2)	
II	45 (6.7)	20 (4.2)	4 (3.7)	
III	54 (8.0)	28 (5.9)	4 (3.7)	
IV	61 (9.1)	50 (10.6)	4 (3.7)	
N/A	407 (60.6)	319 (67.3)	78 (72.9)	

IQR, interquartile range; SD, standard deviation.

- Regardless of line of therapy, switching rate at ≤60 days and 61-89 days was significantly lower for patients receiving zanubrutinib vs acalabrutinib and ibrutinib (*P*<.0001, both 1L and 2L) (**Figure 1**)
- In 1L, the percentage of patients switching before 90 days was lowest for zanubrutinib (10.2%) compared to acalabrutinib (20.5%) and ibrutinib (15.6%)
- Zanubrutinib also had the lowest switch rate before 90 days (7.5%) compared to 13.2% for acalabrutinib and 21.1% for ibrutinib among 2L patients

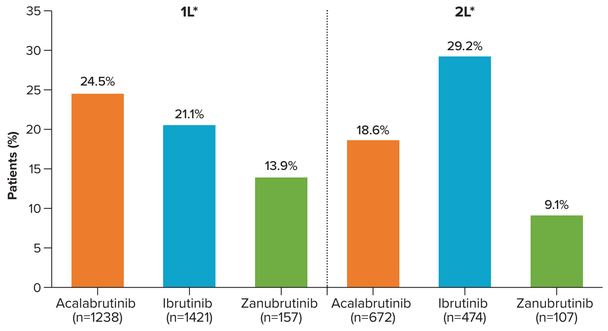
Figure 1. Treatment Switching for Patients Initiating a BTKi in 1L or 2L



*P<.0001

- The proportion of patients receiving the next line of therapy at 180 days for 1L and 2L BTKis are shown in **Figure 2**
- The proportion of patients receiving next line of therapy at 180 days was lower for zanubrutinib vs acalabrutinib and ibrutinib (1L *P*=.2958; 2L *P*<.0001)
- Among 1L patients, the proportion of patients receiving the next line of therapy at 180 days was 13.9% for zanubrutinib compared to 24.5% for acalabrutinib and 21.1% for ibrutinib
- In 2L, the proportion of patients of receiving the next line of therapy at 180 days was 9.1% for zanubrutinib compared to 18.6% for acalabrutinib and 29.2% for ibrutinib

Figure 2. Proportion of Patients Receiving Next Line of Therapy at 180 Days 1L or 2L BTKi



*P<.0001

CONCLUSIONS

- Zanubrutinib patients had significantly lower switching rates within 90 days and lower proportion of patients receiving next line of therapy at 180 days when compared with acalabrutinib and ibrutinib in 1L and 2L
- Longer follow-up and a larger zanubrutinib sample size are required for a comprehensive assessment of treatment outcomes associated with use of BTKis in CLL/SLL

DISCUSSION

- This study highlighted the real-world advantages of zanubrutinib compared to other BTKis in patients with CLL/SLL
- Future studies with extended follow-up are necessary to facilitate evaluation of emerging therapies and to assess long-term real-world outcomes

LIMITATIONS

- While this study included a diverse cross-section of CLL/SLL patients in the United States, it is crucial to recognize that the results may not be applicable to all populations
- Although real-world data have gained acceptance as a reliable source for understanding actual practice patterns, it may present inherent data limitations related to the completeness of the data source

REFERENCES

1. Siegel RL, et al. *CA Cancer J Clin.* 2022;72(1):7-33.
2. Mukkamalla SKR, et al. Chronic Lymphocytic Leukemia. In: StatPearls. Treasure Island (FL): StatPearls Publishing; March 7, 2023.

DISCLOSURES

JP: Consultancy: Novartis, AbbVie, AstraZeneca, Takeda, Merck, Beigene, Eli Lilly, Janssen; Speaker's Bureau: AbbVie, Janssen, Takeda, AstraZeneca; Resesarch Funding: MEI, TG Therapeutics. **MX, SC, KY:** Employment: Beigene. **EW, KE, WF:** Employment: Real Chemistry

ACKNOWLEDGEMENTS

This study was sponsored by BeiGene, Ltd. Editorial support was provided by Elizabeth Hermans, PhD, of BeiGene, and funded by BeiGene.

CORRESPONDENCE: Javier.Pinilla@moffitt.org

Presented at the 2024 Society of Hematologic Oncology; September 4-7, 2024, Houston, TX
Previously presented at EHA 2024; June 13-16, 2024; Madrid, Spain/Virtual Conference