EE694

Evaluation of Healthcare Resource Utilization and Cost Among Patients Receiving Ibrutinib Versus Acalabrutinib as First-Line Treatment for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: a Commercial Claims Database Analysis

Benyam Muluneh,[1] Jinghua He,[2] Zhijie Ding,[2] Alex Bokun,[2] Zaina Qureshi[2]

[1]Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; [2]Janssen Scientific Affairs, Horsham, PA, USA

INTRODUCTION

- Targeted therapies, including Bruton tyrosine kinase inhibitors (BTKis), have transformed the treatment landscape in chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL)[1]
- Ibrutinib, the first BTKi approved by U.S. Food and Drug Administration for CLL/SLL treatment, has demonstrated sustained efficacy, including a well-established safety profile, in patients in the first line (1L) and relapsed/refractory settings[2-4]
- Acalabrutinib, another BTKi, was also approved for relapsed/refractory CLL/SLL and later as a 1L treatment in 2019[5]
- There is a lack of real-world studies comparing healthcare resource utilization (HRU) and costs for patients with CLL/SLL treated with 1L single-agent ibrutinib or acalabrutinib

OBJECTIVE

- To compare HRU and costs for patients with CLL/SLL who received 1L single-agent ibrutinib or acalabrutinib in the United States

METHODS

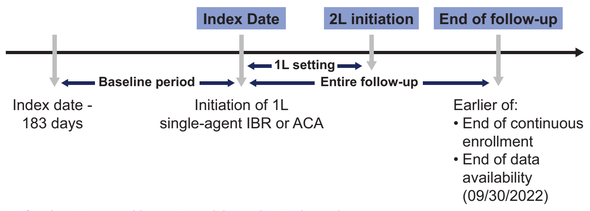
Data Source

- This study included data from IQVIA PharMetrics®Plus, a US commercial claims database

Study Design

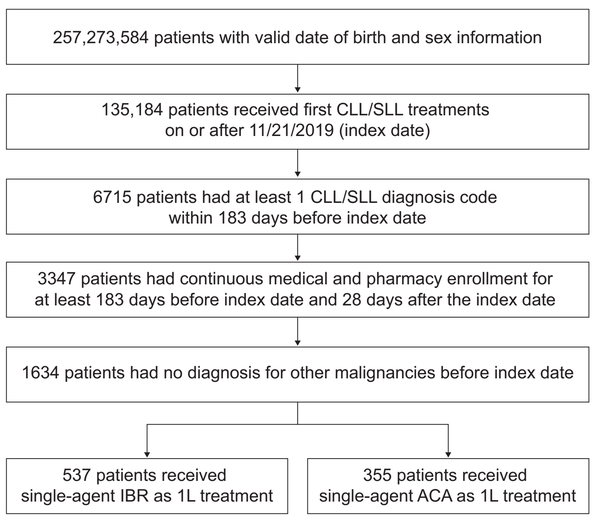
- A retrospective cohort study of patients with CLL/SLL who received 1L treatment with single-agent ibrutinib or acalabrutinib between November 21, 2019, and September 30, 2022 (**Figure 1**)
  - Index date: date of initiating 1L single-agent ibrutinib or acalabrutinib
  - Baseline period: index date 183 days before to 1 day before index date
  - Follow up period: index date to the end of data availability or continuous medical/pharmacy enrollment, whichever occurred first
  - Detailed inclusion/exclusion criteria are summarized in **Figure 2**
  - Outcomes of interest (CLL/SLL-related health encounters, CLL/SLL-related cost) were assessed during 1L treatment and the entire follow-up period
- CLL/SLL-related outcomes were determined based on claims with a diagnosis of CLL/SLL listed in the first diagnostic field

Figure 1. Study design



1L, first-line; 2L, second-line; ACA, acalabrutinib; IBR, ibrutinib.

Figure 2. Patient selection criteria



1L, first-line; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma.

Statistical Analysis

- Descriptive analysis
  - Continuous variables were summarized with means (SD) or medians (interquartile ranges), where appropriate
  - Categorical variables were summarized with counts and percentages
  - Both HRU and costs were summarized per-patient per-month (PPPM), calculated as the number of events or costs incurred over the study period divided by the patient-months of the observation
  - All cost values were adjusted to 2022 US dollar values based on Consumer Price Index
- Comparative analysis
  - A propensity score model was developed using all baseline variables (**Table 1**)
  - Propensity-score weighting was used to balance baseline characteristics between the ibrutinib cohort and acalabrutinib cohort
  - The balance of baseline characteristics was assessed by using standardized mean differences (SMD) where differences of < 10% were considered negligible
  - HRU was compared between the treatment cohorts using rate ratios
  - Costs was compared between the treatment cohorts using linear regression

B-CELL MALIGNANCIES

RESULTS

- A total of 537 and 355 patients were included in the ibrutinib and acalabrutinib cohorts, respectively
  - Mean observed 1L treatment duration was 1.2 years and 0.8 years for ibrutinib and acalabrutinib, respectively
  - Mean follow-up time was 1.4 years and 0.9 years for ibrutinib and acalabrutinib, respectively
- Both cohorts had similar baseline demographic and clinical characteristics (**Table 1**)
  - Mean age at index date was 64 years and approximately 33% of patients were women, 53% were commercially insured, and 65% had a preferred provider organization (PPO) plan
  - The mean Quan-Charlson Comorbidity Index (Q-CCI) score was 2.7 and mean congestive heart failure, hypertension, age, diabetes mellitus, prior stroke or TIA or thromboembolism, vascular disease, age, sex category (CHA2DS2-VASc) score was 1.7 in both cohorts
  - Individual comorbidity conditions, including atrial fibrillation appeared similarly between the cohorts
- All baseline variables were well balanced after propensity score weighting (**Table 1**)

Table 1. Baseline characteristics before and after propensity score weighting[a]

	Before PS weighting			After PS weighting		
	IBR	ACA	SMD	IBR	ACA	SMD
Age at index date, years, mean (SD)	64.0 (10.4)	64.3 (10.2)	3.1	63.9 (10.3)	64.0 (10.2)	1.0
Women, n (%)	181 (33.7)	118 (33.2)	1.0	170 (32.1)	115 (31.8)	0.5
Insurance type, n (%)						
HMO	137 (25.5)	84 (23.7)	4.3	133 (25)	89 (24.6)	1.1
PPO	339 (63.1)	245 (69)	12.5	342 (64.3)	234 (64.8)	0.9
Other	61 (11.4)	26 (7.3)	13.9	56 (10.6)	38 (10.6)	0.0
Payor type, n (%)						
Commercial	280 (52.1)	192 (54.1)	3.9	288 (54.2)	195 (54)	0.5
Medicare advantage	108 (20.1)	62 (17.5)	6.8	99 (18.7)	66 (18.3)	1.0
Self-insured	119 (22.2)	78 (22)	0.5	115 (21.7)	80 (22.1)	1.1
Medicare supplemental	30 (5.6)	23 (6.5)	3.7	29 (5.4)	20 (5.6)	0.6
Index year, n (%)						
2020	287 (53.4)	73 (20.6)	72.4	217 (40.9)	148 (40.9)	0.1
2021	178 (33.1)	141 (39.7)	13.7	191 (35.9)	130 (36)	0.2
2022	72 (13.4)	141 (39.7)	62.4	123 (23.2)	83 (23.1)	0.3
Baseline comorbidities, n (%)						
Q-CCI, mean (SD)	2.7 (1.2)	2.7 (1.3)	3.0	2.7 (1.2)	2.7 (1.2)	0.6
CHA2DS2-VASc, mean (SD)	1.7 (1.5)	1.7 (1.5)	3.4	1.7 (1.5)	1.7 (1.5)	1.6
Cardiovascular diseases[b]	114 (21.2)	78 (22.0)	1.8	114 (21.4)	78 (21.7)	0.6
Atrial fibrillation	30 (5.6)	22 (6.2)	2.6	31 (5.9)	27 (7.4)	6.0
Atrial flutter	6 (1.1)	3 (0.8)	2.8	6 (1.1)	5 (1.5)	3.5
Bleeding/hemorrhage	20 (3.7)	16 (4.5)	3.9	21 (4)	15 (4.1)	0.4
Gastrointestinal disease[c]	92 (17.1)	62 (17.5)	0.9	90 (17)	62 (17.3)	0.9
Baseline CLL/SLL related symptoms, n (%)						
Anemia	167 (31.1)	124 (34.9)	8.2	170 (32)	123 (34)	4.2
Neutropenia	17 (3.2)	8 (2.3)	5.6	15 (2.8)	10 (2.9)	0.4
Thrombocytopenia	103 (19.2)	81 (22.8)	8.9	110 (20.6)	72 (20.1)	1.3
Lymphadenopathy	247 (46)	174 (49)	6.0	248 (46.6)	164 (45.6)	2.0
Fatigue/weakness	137 (25.5)	93 (26.2)	1.6	130 (24.4)	94 (26.1)	4.0
Lymphocytosis	111 (20.7)	87 (24.5)	9.2	121 (22.7)	78 (21.6)	2.6
Night sweats	25 (4.7)	18 (5.1)	1.9	29 (5.5)	24 (6.8)	5.4
Weight loss	42 (7.8)	20 (5.6)	8.7	37 (7.0)	30 (8.3)	5.0
Hepatomegaly	11 (2.0)	2 (0.6)	13.1	8 (1.5)	5 (1.5)	0.2
Splenomegaly	120 (22.3)	70 (19.7)	6.5	108 (20.4)	71 (19.7)	1.9
Hepatosplenomegaly	13 (2.4)	14 (3.9)	8.7	12 (2.3)	9 (2.4)	0.8
Baseline medication, n (%)						
H2-receptor antagonists	15 (2.8)	7 (2.0)	5.4	13 (2.5)	8 (2.2)	1.6
Anticoagulants	40 (7.4)	28 (7.9)	1.6	39 (7.3)	30 (8.2)	3.5
ACE inhibitors	181 (33.7)	127 (35.8)	4.3	181 (34.1)	117 (32.3)	3.8
Diuretics	83 (15.5)	52 (14.6)	2.3	83 (15.7)	65 (18)	6.2
Beta blockers	98 (18.3)	80 (22.5)	10.7	102 (19.3)	79 (21.9)	6.4
Anti-hyperlipidemic	198 (36.9)	142 (4.0)	6.4	204 (38.3)	136 (37.8)	1.0
Baseline CLL/SLL-related HRU and cost						
Hospital admission, n (%)	46 (8.6)	36 (10.1)	5.4	45 (8.4)	36 (10.0)	5.4
Office visit count, PPPM, mean (SD)	2.2 (1.5)	2.5 (1.7)	15.6	2.3 (1.56)	2.3 (1.59)	1.5
Outpatient visit count, PPPM, mean (SD)	2.9 (2.4)	3.3 (2.3)	15.7	3.0 (2.5)	3.0 (2.3)	1.1
Inpatient cost, PPPM,[d] mean (SD)	1432 (8559)	1947 (13,041)	4.7	1307 (8097)	1688 (11,220)	8.6
Physician office visit cost, PPPM,[d] mean (SD)	387 (408)	455 (598)	13.3	395 (397)	415 (522)	8.2
Outpatient visit cost, PPPM,[d] mean (SD)	2698 (4532)	3128 (4812)	9.2	2628 (4482)	3133 (5015)	4.4

[a]Geographical region category is not shown in the table, but was included in PS weighting. [b]Acute myocardial infarction, old myocardial infarction, stable angina, unstable angina, peripheral vascular disease, congestive heart failure, and coronary artery disease. [c]Heartburn, gastroesophageal reflux disease, dyspepsia, esophagitis, gastritis, duodenitis, gastrointestinal bleeding, unspecified, melena, hematemesis, ulcers. [d]PPPM reported in US dollars.
ACA, acalabrutinib; CHA2DS2-VASc, congestive heart failure, hypertension, age, diabetes mellitus, prior stroke or TIA or thromboembolism, vascular disease, age, sex category; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; HMO, health maintenance organization; IBR, ibrutinib; PPO, preferred provider organization; PPPM, per-patient per-month; PS, propensity score; Q-CCI, Quan-Charlson Comorbidity Index; SMD, standardized mean difference.

- The ibrutinib cohort had significantly lower mean PPPM CLL/SLL-related physician office visits (0.57 vs. 0.76) and outpatient visits (0.80 vs. 1.07) during the entire follow-up period then acalabrutinib cohort (**Table 2**)
- The adjusted rate ratio (aRR) after propensity score weighting was 0.83 ($P < 0.05$) and 0.82 ($P < 0.01$), respectively (**Table 3**)
  - Similar findings were seen in the ibrutinib versus acalabrutinib cohorts during 1L treatment (**Tables 2 and 3**)
- In adjusted analyses, the ibrutinib cohort had significantly lower mean PPPM CLL/SLL-related total costs during the entire follow-up period compared with the acalabrutinib cohort ($13,657 and $15,864, respectively, $P = 0.04$) (**Table 3**)

Table 2. CLL/SLL related healthcare resource utilization

	Encounter type, PPPM	IBR Mean (SD)	ACA Mean (SD)	Adjusted rate ratio[a]	*P* value
Entire follow-up	Hospital admission	0.03 (0.1)	0.02 (0.09)	1.21	0.67
	Length of stay, days	0.10 (0.39)	0.17 (1.52)	0.04[b]	0.46
	Office visit	0.57 (0.46)	0.76 (0.58)	0.83	0.03*
	Outpatient visit (including ER)	0.8 (0.82)	1.07 (0.92)	0.83	0.01*
1L treatment	Hospital admission	0.03 (0.13)	0.03 (0.13)	0.90	0.76
	Length of stay, days	0.11 (0.46)	0.20 (1.54)	0.08[b]	0.14
	Office visit	0.62 (0.56)	0.83 (0.71)	0.81	0.01*
	Outpatient visit (including ER)	0.86 (0.9)	1.09 (1.04)	0.85	0.02*

*$P < 0.05$. [a]After propensity score weighting with ACA as the reference group. [b]Adjusted mean difference.
1L, first-line; ACA, acalabrutinib; ER, emergency room; IBR, ibrutinib; PPPM, per-patient per-month.

Table 3. CLL/SLL related costs after propensity score weighting with acalabrutinib cohort as the reference group

	Cost categories, PPPM[a]	IBR Mean (SD)[a]	ACA Mean (SD)[a]	Adjusted mean difference[b]	*P* value
Entire follow-up	CLL/SLL treatment	$13,114 (6108)	$15,072 (7190)	-802	0.07
	BTKi	$12,296 (6039)	$13,630 (4647)	-408	0.30
	Other CLL/SLL treatment	$818 (2794)	$1442 (4899)	-394	0.09
	Medical	$543 (1451)	$792 (3101)	-154	0.23
	Inpatient	$121 (1042)	$259 (2846)	-94	0.37
	Physician office visit	$89 (115)	$113 (107)	-10	0.21
	Outpatient visit	$312 (791)	$420 (1283)	-70	0.30
	Total	$13,657 (6343)	$15,864 (7930)	-956	0.04*
1L treatment	CLL/SLL treatment	$13,308 (5909)	$14,497 (5233)	-467	0.25
	Medical	$622 (1698)	$877 (3376)	-183	0.22
	Inpatient	$150 (1281)	$304 (2991)	-140	0.26
	Physician office visit	$98 (128)	$120 (113)	-9	0.20
	Outpatient visit	$351 (885)	$453 (1616)	-54	0.48
	Total	$13,930 (6174)	$15,374 (6254)	-649	0.13

* $P < 0.05$. [a]Reported in US dollars. [b]After propensity score weighting with acalabrutinib as the reference group.
1L, first-line; ACA, acalabrutinib; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; IBR, ibrutinib; PPPM, per-patient per-month.

LIMITATIONS

- The majority of patients included in this study had commercial insurance and were relatively young
- Results may not be directly generalizable to uninsured and underserved populations or older adults
- Inherent limitations of claims data include potential inaccurate coding errors leading to misclassification of treatment and clinical outcomes
- Identified treatment and clinical events do not include those reimbursed outside insurance coverage or through other payers
- Cost information was imputed based on insurance claims data from the IQVIA PharMetrics®Plus database, and may not be representative of other insurance plans or patients studied in other databases

CONCLUSIONS

- To our knowledge, this is one of the largest studies describing HRU and cost of 1L CLL BTKi treatments utilizing a US commercial claims database
- Compared with single-agent acalabrutinib, 1L use of single-agent ibrutinib for CLL/SLL was associated with significantly fewer CLL/SLL-related physician office visits, outpatient visits, and lower total cost
- These real-word findings, in combination with previous studies showing higher adherence[6, 7] and longer time to next treatment[8] for 1L ibrutinib, support the use of ibrutinib in 1L setting

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References

1. Shadman M. *JAMA*. 2023,329:918-932.
2. IMBRUVICA (ibrutinib). *Prescribing Information*. 2023.
3. Burger JA et al. *N Engl J Med*. 2015;373:2425-37.
4. Munir T et al. *Am J Hematol*. 2019;94:1353 1363.
5. CALQUENCE (acalabrutinib). *Prescribing Information*. 2022
6. Lu X, et al. *Clin Lymphoma Myeloma Leuk*. 2022;22:S280-S281.
7. Lu X, et al. *Patient Prefer Adherence*. 2023;17:2073-2084.
8. Jacobs R, et al. *Future Oncol*. 2023;10.2217/fon-2023-0436.

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