Characteristics and Clinical Outcomes Among Patients Receiving Either Ibrutinib or Anti-CD20 Monotherapy as First-line Treatment for Chronic Lymphocytic Leukemia /Small Lymphocytic Lymphoma: A Retrospective Analysis in Community Oncology Practice

Xiaoxiao Lu[1], Jinghua He[2], Linda Wu[1], Tao Ran[2], Sumeet Panjabi[2], Julie Vose[3]

[1]Janssen Scientific Affairs, LLC, Horsham, PA, USA. [2]Janssen Scientific Affairs, LLC, Titusville, NJ, USA. [1]University of Nebraska Medical Center, Omaha, NE, USA

BACKGROUND

- Treatment of chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) has evolved rapidly in the past decade beyond chemotherapy agents, with the emergence of a number of new treatment options.
- Ibrutinib is an oral, once daily Bruton's tyrosine kinase inhibitor (BTKi) approved for the treatment of adults with CLL/ SLL.[1] It is the only targeted treatment that has demonstrated progression-free survival and overall survival in multiple phase 3 trials across age, fitness, and high-risk markers for CLL/SLL.
- One anti-CD20 monotherapy, obinutuzumab, is NCCN guideline "other recommended" regimen for 1L CLL patients.[2]
- Previous research shows the main reasons for oncologists/hematologists to use anti-CD20 monotherapy as 1L treatment include: frail conditions of patients and desire for low toxicity in these patients; experiences from the past or experiences extrapolated from other indolent lymphatic diseases; desire to delay "aggressive" treatment.

OBJECTIVES

- To describe the demographic and clinical characteristics of CLL/SLL patients who received 1L ibrutinib or anti-CD20 monotherapy
- To compare time-to-next-treatment (TTNT) in these groups, and in two subgroups:
  - Patients with observed high-risk cytogenetic markers (deletion 17p, deletion 11q, or unmutated IGHV)
  - Patients without IGHV testing

METHODS

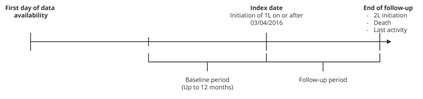
Data source

- The study utilized the Flatiron CLL Core Registry database in the United States (US)
- The dataset consists of de-identified electronic health records enabling a longitudinal data view of cancer patients with resolution at the disease and treatment level.
- Flatiron extracts and processes both structured and unstructured real-world clinical data collected from the electronic health records (EHRs) used by cancer care providers across the US.

Study design

- This was a retrospective cohort study (**Figure 1**)

FIGURE 1: Study design



- CLL patients who received ibrutinib or anti-CD20 monotherapy as their 1L treatment on or after 03/04/2016 (date of approval of ibrutinib for 1L CLL/SLL treatment) were identified and compared. Index date is defined as 1L treatment initiation date.
- Monotherapy was defined as the absence of other antineoplastic agents within 28 days of initiation of ibrutinib or anti-CD20
- The baseline period was defined as a 12-month time window prior to the index date
- Patients were followed from the index date to the earliest of initiation of second-line (2L) therapy, death, or last clinical activity
- TTNT was defined as the interval from the initiation of 1L to the initiation of 2L. Patients were censored when last activity or death was observed prior to the initiation of 2L

Statistical analyses

- Baseline characteristics were reported using means, standard deviations (SDs), and medians for continuous variables, and frequencies and proportions for categorical variables
- Baseline characteristics were summarized by using standard mean difference between the ibrutinib and anti-CD20 cohorts
- Kaplan-Meier (KM) analysis was used to evaluate TTNT from 1L initiation
- TTNT was compared between the 1L users of ibrutinib mono vs. anti-CD20 mono by using COX proportional hazard model
- Missing baseline covariates were imputed by using the multiple imputation (MI) technology
- Baseline differences were adjusted by using propensity score-based inverse probability of treatment weighting (IPTW). Baseline covariate balance after weighting was examined using standardized mean differences (SMD), with absolute SMD values < 0.1 indicative of adequate balance.

B-CELL MALIGNANCIES

RESULTS

Baseline characteristics

- A total of 3,226 CLL/SLL patients were included in the current study (**Figure 2**):
  - 2188 ibrutinib patients
  - 1038 anti-CD20 patients
    - 748 (72.15%) rituximab
    - 290 (27.9%) obinutuzumab
- Patient characteristics before MI & IPTW are summarized in **Table 1**.
  - Compared to anti-CD20 users, CLL patients treated by ibrutinib were slightly younger (mean age of 71.4 years vs. 72.9 years), more likely to be black (9.3% vs. 4.5%), and more likely to have high-risk cytogenetic markers (42.6% vs. 27.9%)
  - The rate of unknown IGHV mutation status is approximately 60% in the included CLL/SLL cohort
  - After IPTW, the imputed baseline characteristics were well balanced between the two comparison groups with all SMD < 10%
- **Table 2** and **Figure 3** summarized comparative analysis results of 1L ibrutinib vs. anti-CD20 regarding TTNT after IPTW
  - Ibrutinib is associated with a significantly 70% lower risk of initiating 2L treatment than anti-CD20 in the overall patients (HR = 0.30, P<0.001).
  - Similar results were found in the subgroups of patients with high-risk cytogenetic markers and those without IGHV testing.

FIGURE 2: Patient eligibility and attrition table

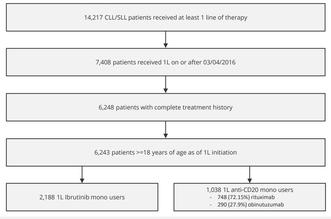


TABLE 1. Baseline demographics and clinical characteristics

		Before weighting				
		Ibrutinib N=2,188		Anti-CD20 N=1,038		Standardized mean difference
		N	%	N	%	
Age at 1L Initiation	Mean (SD)	71.4	9.3	72.9	9.2	16.2%
Gender (n, %)	Female	853	39.0	436	42.0	6.2%
	Male	1,335	61.0	602	58.0	6.2%
Race (n, %)	White	1,593	72.8	771	74.3	3.3%
	Black	204	9.3	47	4.5	19.0%
	Other	208	9.5	106	10.2	2.4%
	Missing/Unknown	183	8.4	114	11.0	8.9%
Region (n, %)	Midwest	363	16.6	128	12.3	12.1%
	Northeast	451	20.6	207	19.9	1.7%
	South	881	40.3	394	38.0	4.7%
	West	289	13.2	194	18.7	15.0%
	Missing/Unknown	204	9.3	115	11.1	5.8%
1L initiation year (N, %)	2016	278	12.7	205	19.8	19.2%
	2017	399	18.2	216	20.8	6.5%
	2018	422	19.3	186	17.9	3.5%
	2019	572	26.1	159	15.3	26.9%
	2020	399	18.2	165	15.9	6.2%
	2021	118	5.4	107	10.3	18.4%
Months between initial diagnosis and 1L initiation	Mean (SD)	50.9	62.9	44.3	59.0	10.8%
Rai stage (n, %)	0	616	28.2	247	23.8	10.0%
	1	298	13.6	104	10.0	11.2%
	2	122	5.6	42	4.0	7.2%
	3	123	5.6	49	4.7	4.1%
	4	152	6.9	81	7.8	3.3%
	Missing/Unknown	877	40.1	515	49.6	19.3%
ECOG PS (n, %)	0	798	36.5	355	34.2	4.8%
	1	525	24.0	253	24.4	0.9%
	2	147	6.7	60	5.8	3.9%
	3+	33	1.5	19	1.8	2.5%
	Missing/Unknown	685	31.3	351	33.8	5.4%
17p Deletion (n, %)	Present	317	14.5	64	6.2	27.6%
	Absent	1,376	62.9	601	57.9	10.2%
	Unknown	495	22.6	373	35.9	29.6%
11q Deletion (n, %)	Present	350	16.0	88	8.5	23.1%
	Absent	1,332	60.9	564	54.3	13.3%
	Unknown	506	23.1	386	37.2	31.0%
IGHV Mutation (n, %)	Unmutated	532	24.3	197	19.0	13.0%
	Mutated	353	16.1	139	13.4	7.7%
	Unknown	1,303	59.6	702	67.6	16.8%
Genetic risk group (n, %)	High	933	42.6	290	27.9	31.1%
	Low	246	11.2	107	10.3	3.0%
	Unknown	1,009	46.1	641	61.8	31.8%
CCI score	Mean (SD)	2.1	1.1	2.1	1.1	8.9%

CCI: Charlson Comorbidity Index; CLL: chronic lymphocytic leukemia; CV: cardiovascular; IPTW: inverse probability treatment weighting MI, multiple imputation; SD: standard deviation; SLL: small lymphocytic lymphoma.

TABLE 2. Comparison of clinical outcomes in patients receiving 1L ibrutinib monotherapy versus anti-CD20 monotherapy

	Median TTNT (months)		Adjusted Hazard Ratio (95% confidence interval) *	p-value
	Ibrutinib	Anti-CD20 Median (range)		
Overall patients (n=3,226)	Not reached	18.3 (14.9-20.9)	0.30 (0.27-0.34)	<0.001
Patients with high-risk cytogenetics (n=1,223)	Not reached	14.5 910.9-20.2)	0.26 (0.21-0.33)	<0.001
Patients without IGHV testing (n=2,005)	Not reached	19.3 (14.9-24.0)	0.30 (0.26-0.36)	<0.001

Abbreviations: TTNT, time to next treatment.
*Adjusted for age at 1L initiation, gender, race, region, disease subtype, index year, Rai Stage, ECOG, CCI, 17p Deletion, 17p Deletion, IGHV mutation

FIGURE 3: Comparison of TTNT between ibrutinib and anti-CD20 monotherapy

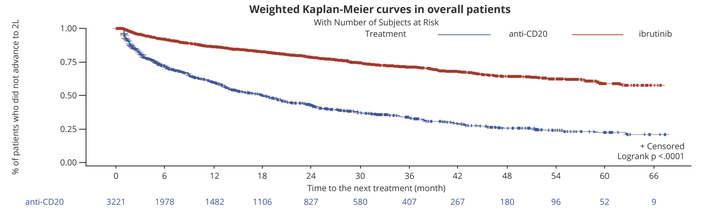


FIGURE 3.2

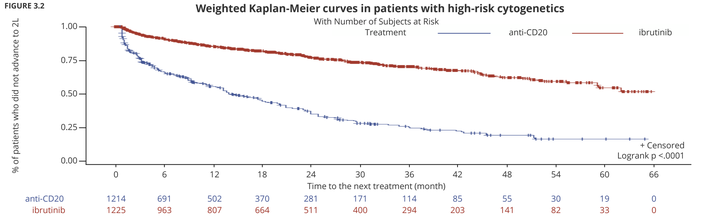
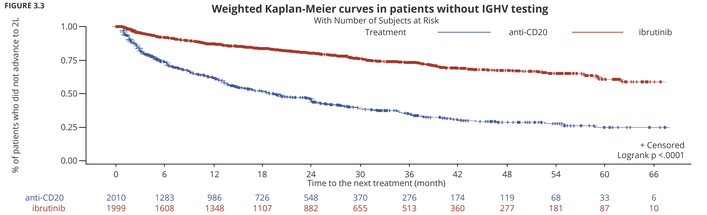


FIGURE 3.3



LIMITATIONS

- The Flatiron database does not capture treatments and healthcare services received outside of the network.
- The Flatiron Health database does not capture information on all comorbidities; therefore, a condition or treatment not reported in the database does not necessarily mean that it is absent for a specific patient but may simply reflect missing information
- The "missing at random" assumption for multiple imputation cannot be validated
- Although a propensity score method was used to adjust for baseline confounders, residual confounding due to unobserved confounders may remain. The current findings should be interpreted as the association instead of causality

CONCLUSIONS

- First-line treatment with ibrutinib monotherapy in CLL/SLL patients was associated with a statistically significantly lower risk of initiating subsequent treatment than anti-CD20 monotherapy
- Similar findings were observed in the subgroups of patients with high-risk cytogenetic markers and patients without IGHV testing, respectively
- IGHV testing in clinical practice remains suboptimal. Improvement of testing rate is warranted in order to optimize clinical and economic outcomes, especially in the novel agent era

ACKNOWLEDGMENTS

Sponsored by Janssen Scientific Affairs, LLC..

Scan the QR code

https://www.congresshub.com/Oncology/SOHO2022/Ibrutinib/Lu-Persistence

The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

REFERENCES:

1. IMBRUVICA (ibrutinib) Full Prescribing Information. Pharmacyclics, LLC, Janssen Biotech, Inc. May 2022. **2.** NCCN Guidelines for Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma V.1.2023

Presented at the 10th Society of Hematologic Oncology (SOHO) Annual Meeting, September 28-October 1, 2022, Houston, TX, USA