Persistence and Time to Next Treatment with Ibrutinib Treatment in Patients with Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Including Patients at High Risk for Atrial Fibrillation or Stroke: A Real-World Study

Anna Narezkina[1], Nausheen Akhter[2], Xiaoxiao Lu[3], Bruno Emond[4], Qing Huang[3], Sumeet Panjabi[3], Annalise Hilts[4], Stephanie Liu[5], Marie-Hélène Lafeuille[4], Patrick Lefebvre[4], Michael Choi[6]

[1]University of California San Diego Health, San Diego, CA, USA. [2]Northwestern Medicine, Chicago, IL, USA. [3]Janssen Scientific Affairs, LLC, Horsham, PA, USA. [4]Analysis Group, Inc., Montréal, Québec, Canada. [5]Analysis Group, Inc., Menlo Park, CA, USA. [6]University of California San Diego Moores Cancer Center, San Diego, CA, USA

BACKGROUND

- Ibrutinib, a once-daily Bruton's tyrosine kinase inhibitor (BTKi),[1] has been used to treat >250,000 patients worldwide[2] and is the only targeted therapy that has demonstrated overall survival benefits compared to chemo- and/or immunotherapy across multiple phase 3 clinical trials in first-line (1L) and relapsed/refractory CLL/SLL[3-5]
- Approved BTKis as a drug class are associated with atrial fibrillation (AF)[6,7]
  - In the ELEVATE-RR trial (in patients treated with ibrutinib or acalabrutinib who had ≥1 previous line of therapy), the rate of any-grade AF was 9.0% and 15.6% for acalabrutinib and ibrutinib, respectively, while a numerically higher rate of grade ≥3 AF was observed with acalabrutinib (4.5%) than with ibrutinib (3.4%), providing further evidence that AF is a class effect of BTKis[8]

OBJECTIVE

- To describe time to next treatment (TTNT) and time to discontinuation (TTD) for patients with CLL/SLL who initiated a 1L or second or later line (2L+) of therapy with ibrutinib or other regimens, in all patients and for subsets of patients with high baseline risk of AF or stroke determined using the CHARGE-AF and CHA_2DS_2-VASc risk scores

METHODS

Data source

- The nationwide Flatiron Health Electronic Health Record-derived de-identified database was used to select patients with CLL/SLL who were initiated on any line of therapy at community and academic medical centers between February 12, 2014 (i.e., the approval date for ibrutinib) and January 31, 2021
- The database also contained elements extracted from structured electronic health records and unstructured information abstracted from physicians' notes and other documentation (e.g., demographics, diagnoses, visits, laboratory tests and vitals, medication administration, prescriptions and orders, performance status, and insurance data)
- The data are de-identified and subject to obligations to prevent re-identification and protect patient confidentiality

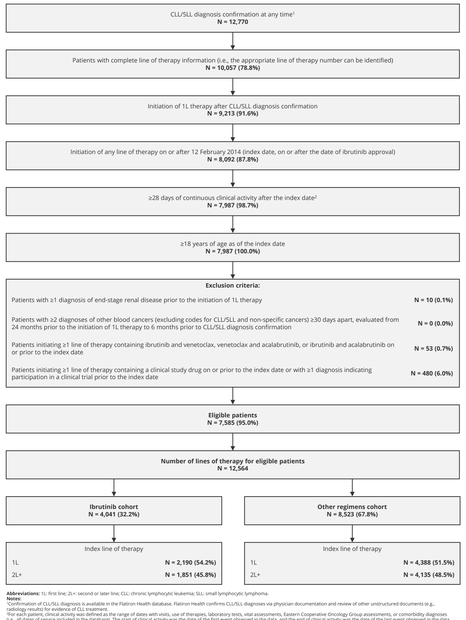
Study design

- A retrospective cohort design was used
- The index date was defined as the date of initiation of a line of therapy containing ibrutinib or other regimen (i.e., chemotherapy only, CIT, immunomodulatory agent, novel targeted agents other than ibrutinib, or anti-CD20 immunotherapy only) on or after February 12, 2014
- A line of therapy was defined as the initiation of a new regimen that ended with either switch to a subsequent treatment regimen; or for patients without a next treatment regimen (1) end of clinical activity (i.e., date of last record of patient activity in the database), (2) death, or (3) end of data availability (i.e., cut-off date of January 31, 2021)
  - Based on the algorithm from Flatiron Health, treatment re-initiation after a gap of >120 days (i.e., after treatment discontinuation) was also considered a new line of therapy
- The baseline period was defined as the up-to-12-month period pre-index date
- The follow-up period spanned from the index date to the earliest among the end of clinical activity, death, or end of data availability

Study population

- The sample selection criteria are presented in **Figure 1**
- Patients were classified into cohorts based on the line of therapy (1L or 2L+) and type of regimen (ibrutinib-based or other regimens)
- For each treatment setting (1L and 2L+) and cohort (ibrutinib or other regimens), the following subgroups of patients were assessed:
  - Patients considered at high risk of AF using CHARGE-AF risk score ≥10.0%[9,10]
    - The CHARGE-AF score was calculated using the following formula: 0.508 × age (5 years) + 0.248 × height (10 cm) + 0.115 × weight (15kg) + 0.197 × systolic blood pressure (20 mm Hg) - 0.101 × diastolic blood pressure (10 mm Hg) + 0.359 × current smoker + 0.349 × antihypertensive medication + 0.237 × diabetes + 0.701 × congestive heart failure + 0.496 × myocardial infarction
  - Patients considered at high risk of stroke using CHA_2DS_2-VASc risk score ≥3 [females] or ≥2 [males][11,12]
    - The CHA_2DS_2-VASc score was calculated based on the following risk factors: age (<65, 65–74, and ≥75 years), sex, hypertension, diabetes mellitus, stroke/transient ischemic attack/thromboembolism, vascular disease, and heart failure; the presence of each risk factor was assigned 1 point, except age ≥75 years and stroke/transient ischemic attack/thromboembolism, which were assigned 2 points

FIGURE 1: Identification of CLL/SLL Patients Treated With Ibrutinib or Other Regimens in Any Line of Therapy



Abbreviations: 1L: first line; 2L+: second or later line; CLL: chronic lymphocytic leukemia; SLL: small lymphocytic lymphoma.
Notes:
[1]Confirmation of CLL/SLL diagnosis is available in the Flatiron Health database. Flatiron Health confirms CLL/SLL diagnoses via physician documentation and review of other unstructured documents (e.g., radiology results for evidence of CLL treatment).
[2]For each patient, clinical activity was defined as the range of dates with visits, use of therapies, laboratory tests, vital assessments, Eastern Cooperative Oncology Group assessments, or comorbidity diagnoses (i.e., all dates of service included in the database). The start of clinical activity was the date of the first event observed in the data, and the end of clinical activity was the date of the last event observed in the data.

Study measures

- TTNT was defined as the time from initiation of a line of therapy to the date of initiation of the next line of therapy (triggered by a change in therapy or the addition of another treatment to the regimen). Patients not using a next line of therapy within the study period, lost to follow-up, or dead at the end of data availability were censored at the end of follow-up
- TTD was defined as the time from starting index therapy to the earliest of: (1) stopping treatment, (2) the day before switching to a next line of therapy, or (3) the end of follow-up if patients did not discontinue treatment

Statistical Analysis

- Characteristics reported during the baseline and follow-up periods were described using means, standard deviations, and medians for continuous variables, and frequencies and proportions for categorical variables
- Kaplan–Meier (KM) methodology was used to describe rates of TTNT, stratified by line of therapy (1L or 2L+), type of regimen (ibrutinib-containing or other regimens), and based on CHARGE-AF and CHA_2DS_2-VASc risk scores (all patients, high risk CHARGE-AF, or high risk CHA_2DS_2-VASc)
- *P*-values for comparisons between cohorts were obtained from analysis of variance tests for continuous variables, chi-squared tests for categorical variables, and log-rank tests for KM rates

RESULTS

Baseline characteristics

- A total of 7,585 eligible patients (12,564 lines of therapy) were eligible for the study (**Figure 1**)
  - The ibrutinib cohort consisted of 4,041 patients, with 2,190 (54.2%) patients in 1L and 1,851 (45.8%) patients in 2L+, while the cohort treated with other regimens included 8,523 patients, with 4,388 (51.5%) patients in 1L and 4,135 (48.5%) in 2L+
- Among the overall patient population and across treatment lines and treatment cohorts, mean age was 70-72 years old, ~37% were females, and the mean Quan-Charlson comorbidity index score was ~2.3 (**Table 1**)
- Across treatment lines and cohorts, there were similar proportions of patients with high risk CHARGE-AF and CHA_2DS_2-VASc scores at baseline (CHARGE-AF: 15.6-20.8% of patients; CHA_2DS_2-VASc: 44.3-50.5% of patients)
- The mean Framingham Heart Study and ASCVD risk scores were also similar across treatment lines and regimens (mean Framingham Heart Study risk score: 9.2-10.1%; mean ASCVD risk score: 18.5-20.0%; **Table 1**)
- Among patients using regimens other than ibrutinib, CIT was generally the most common regimen in both 1L and 2L+ (55.4% and 26.7% of patients in 1L and 2L+, respectively); use of novel targeted therapies other than ibrutinib was less frequent in 1L than in 2L+ (5.9% vs. 22.6%), with the most common agent being venetoclax (1L: 3.8%; 2L+: 13.4%), followed by acalabrutinib (1L: 1.8%; 2L+: 5.1%); anti-CD20 immunotherapy-only regimens were slightly more common in 1L than 2L+ (26.6% vs. 19.2%)
- For both 1L and 2L+ cohorts, the prevalence of high risk 17p deletion at baseline was 2 to 3 times higher for patients treated with ibrutinib (24.0%–25.5%) than for other regimens (7.5%–14.2%; **Table 1**)

TABLE 1. Baseline Characteristics of Patients in the 1L and 2L+ Cohorts[1]

	Ibrutinib				Other regimens			
	All patients	High risk CHARGE-AF	High risk CHA_2DS_2-VASc		All patients	High risk CHARGE-AF	High risk CHA_2DS_2-VASc	
1L cohorts								
	N=2,190	N=439	N=1,080	*P*	N=4,388	N=686	N=1,946	*P*
Age, mean ± SD [median]	70.8 ± 9.5 [72.0]	80.1 ± 2.3 [81.0]	77.7 ± 3.1 [79.0]	*	69.8 ± 9.9 [71.0]	79.5 ± 2.8 [80.0]	77.7 ± 4.2 [79.0]	*
Female, n (%)	845 (38.6)	90 (20.5)	452 (41.9)	*	1,612 (36.7)	113 (16.5)	784 (40.3)	*
Time from CLL/SLL diagnosis confirmation to the initiation of 1L therapy (in months), mean ± SD [median]	50.4 ± 62.3 [29.5]	54.8 ± 75.5 [26.2]	55.8 ± 72.3 [28.8]		42.0 ± 54.2 [22.3]	49.4 ± 63.4 [25.2]	47.9 ± 61.7 [24.5]	*
Quan-CCI, mean ± SD [median]	2.3 ± 0.8 [2.0]	2.5 ± 1.2 [2.0]	2.5 ± 1.1 [2.0]	*	2.3 ± 0.8 [2.0]	2.5 ± 1.1 [2.0]	2.4 ± 1.0 [2.0]	*
IGHV testing, n (%)	479 (21.9)	76 (18.2)	202 (18.7)	*	768 (18.2)	122 (17.9)	312 (16.0)	*
Unmutated IGHV	265 (55.8)	37 (46.8)	107 (53.0)		433 (54.3)	61 (49.6)	156 (50.0)	
Patients with cytogenetic testing, n (%)	998 (45.6)	217 (49.5)	494 (45.7)		1,979 (45.1)	296 (43.1)	851 (43.7)	
17p deletion	242 (24.2)	54 (24.9)	120 (24.3)		148 (7.5)	31 (10.5)	71 (8.3)	
11q deletion	192 (19.2)	46 (21.2)	86 (17.4)		312 (15.8)	45 (15.2)	118 (13.9)	
ASCVD risk score[2] (%), mean ± SD [median]	19.7 ± 11.6 [19.0]	33.2 ± 6.4 [32.0]	27.6 ± 9.2 [26.0]	*	18.9 ± 11.6 [17.0]	33.2 ± 8.7 [35.4]	27.5 ± 9.4 [25.0]	*
Framingham Heart Study risk score[2] (%), mean ± SD [median]	9.8 ± 5.2 [9.9]	15.8 ± 2.8 [15.8]	13.4 ± 4.0 [13.6]	*	9.2 ± 5.1 [9.0]	15.3 ± 2.8 [15.2]	13.1 ± 3.9 [13.1]	*
CV-related comorbidities, n (%)								
Hypertension	328 (15.0)	96 (21.9)	291 (26.9)	*	572 (13.0)	136 (19.8)	471 (24.2)	*
Diabetes	135 (6.2)	46 (10.5)	125 (11.6)	*	229 (5.2)	71 (10.3)	205 (10.5)	*
Hypercholesterolemia	46 (2.1)	13 (3.0)	36 (3.3)		73 (1.7)	17 (2.5)	50 (2.6)	*
Obesity	28 (1.3)	5 (1.1)	18 (1.7)		49 (1.1)	15 (2.2)	33 (1.7)	*
Sleep apnea	31 (1.4)	9 (2.1)	21 (1.9)		48 (1.1)	14 (2.0)	31 (1.6)	
Atrial fibrillation	41 (1.9)	22 (5.0)	32 (3.0)	*	79 (1.8)	38 (5.5)	69 (3.5)	*
Atrial flutter	3 (0.1)	1 (0.2)	3 (0.3)		4 (0.1)	0 (0.0)	2 (0.1)	
Acute coronary syndrome	63 (2.9)	20 (4.6)	48 (4.4)	*	89 (2.0)	39 (5.7)	78 (4.0)	*
Congestive heart failure	27 (1.2)	13 (3.0)	25 (2.3)	*	54 (1.2)	34 (5.0)	51 (2.6)	*
Valvular disease	20 (0.9)	7 (1.6)	14 (1.3)		36 (0.8)	12 (1.7)	26 (1.3)	*
Cerebrovascular disease	15 (0.8)	5 (1.1)	18 (1.7)		31 (0.7)	12 (1.7)	25 (1.3)	*
Length of follow-up (in months), mean ± SD [median]	26.9 ± 18.3 [23.1]	22.9 ± 16.0 [19.5]	24.9 ± 17.3 [21.3]	*	35.0 ± 22.8 [33.6]	27.9 ± 19.9 [25.6]	30.8 ± 21.7 [28.0]	*
2L+ cohorts								
Baseline characteristics	N=1,851	N=324	N=824	*P*	N=4,135	N=862	N=2,089	*P*
Age, mean ± SD [median]	70.2 ± 9.1 [72.0]	80.0 ± 2.3 [80.0]	78.1 ± 4.3 [79.0]	*	72.2 ± 9.1 [73.0]	80.3 ± 2.3 [81.0]	78.3 ± 4.5 [79.0]	*
Female, n (%)	677 (36.6)	71 (21.9)	342 (41.5)	*	1,609 (38.9)	164 (19.0)	895 (42.8)	*
Time from CLL/SLL diagnosis confirmation to the initiation of 1L therapy (in months), mean ± SD [median]	40.5 ± 49.9 [25.2]	47.3 ± 53.8 [28.4]	47.2 ± 55.0 [29.6]	*	43.6 ± 54.6 [25.2]	48.8 ± 61.2 [26.5]	49.6 ± 60.7 [27.5]	*
Quan-CCI, mean ± SD [median]	2.3 ± 0.9 [2.0]	2.3 ± 1.1 [2.0]	2.4 ± 1.1 [2.0]	*	2.4 ± 1.2 [2.0]	2.6 ± 1.5 [2.0]	2.6 ± 1.4 [2.0]	*
IGHV testing, n (%)	146 (7.9)	17 (5.2)	55 (6.7)		304 (7.4)	45 (5.2)	146 (7.0)	
Unmutated IGHV	92 (63.0)	10 (58.8)	35 (63.6)		181 (58.8)	20 (44.4)	84 (57.5)	
Patients with cytogenetic testing, n (%)	329 (17.8)	52 (17.0)	146 (17.7)		722 (17.5)	121 (14.0)	344 (16.5)	
17p deletion	84 (25.5)	14 (26.9)	35 (24.0)		81 (11.2)	17 (13.8)	49 (14.2)	
11q deletion	64 (19.5)	6 (10.5)	21 (14.4)		138 (19.0)	18 (14.6)	70 (20.3)	
ASCVD risk score[2] (%), mean ± SD [median]	18.3 ± 10.6 [15.5]	31.8 ± 6.1 [30.4]	26.4 ± 8.3 [25.0]	*	20.0 ± 10.6 [19.5]	32.3 ± 7.2 [32.7]	26.5 ± 8.3 [25.2]	*
Framingham Heart Study risk score[2] (%), mean ± SD [median]	9.5 ± 4.9 [9.4]	15.6 ± 2.7 [15.3]	13.3 ± 3.6 [13.5]	*	10.1 ± 4.9 [10.1]	15.7 ± 2.9 [15.7]	13.4 ± 3.8 [13.7]	*
CV-related comorbidities, n (%)	705 ± 9.1 [72.0]	80.0 ± 2.3 [80.0]	78.1 ± 4.3 [79.0]	*	72.0 ± 8.8 [73.0]	80.3 ± 2.3 [81.0]	78.3 ± 4.5 [79.0]	*
Hypertension	144 (7.8)	24 (7.4)	123 (14.9)	*	347 (8.4)	104 (12.1)	304 (14.6)	*
Diabetes	60 (3.2)	13 (4.0)	57 (6.9)	*	176 (4.3)	53 (6.1)	163 (7.8)	*
Hypercholesterolemia	30 (1.6)	3 (0.9)	24 (2.9)	*	78 (1.9)	27 (3.1)	55 (2.6)	*
Obesity	16 (0.9)	0 (0.0)	6 (0.7)		41 (1.0)	11 (1.3)	27 (1.3)	
Sleep apnea	10 (0.5)	2 (0.6)	7 (0.8)		49 (1.2)	20 (2.3)	35 (1.7)	*
Atrial fibrillation	36 (1.9)	15 (4.6)	30 (3.6)	*	125 (3.0)	54 (6.3)	95 (4.5)	*
Atrial flutter	6 (0.3)	4 (1.2)	4 (0.5)		11 (0.3)	4 (0.5)	6 (0.3)	
Acute coronary syndrome	26 (1.4)	10 (3.1)	20 (2.4)	*	106 (2.6)	58 (6.7)	96 (4.6)	*
Congestive heart failure	13 (0.7)	12 (3.7)	13 (1.6)	*	54 (1.3)	41 (4.8)	54 (2.6)	*
Valvular disease	14 (0.8)	4 (1.2)	9 (1.1)		47 (1.1)	19 (2.2)	36 (1.7)	*
Cerebrovascular disease	7 (0.4)	1 (0.3)	7 (0.8)		30 (0.7)	10 (1.2)	30 (1.4)	*
Length of follow-up (in months), mean ± SD [median]	27.6 ± 20.8 [22.1]	22.0 ± 17.3 [18.0]	25.0 ± 19.4 [19.8]	*	22.7 ± 19.5 [16.7]	18.4 ± 16.5 [12.4]	21.0 ± 18.6 [14.7]	*

*P<0.05.
Abbreviations: 1L = first line; 2L+ = second line or later; ASCVD = atherosclerotic cardiovascular disease; CLL = chronic lymphocytic leukemia; CV = cardiovascular; IGHV = immunoglobulin heavy chain gene; Quan-CCI = Quan-Charlson comorbidity index; SD = standard deviation; SLL = small lymphocytic lymphoma.
Notes:
[1]Evaluated during the up-to-12-month baseline period, excluding the index date.
[2]The ASCVD risk score is calculated based on sex, age, race, total and high-density lipoprotein (HDL) cholesterol, systolic blood pressure, presence of diabetes, smoking history, and treatment for hypertension.[13]
[3]The Framingham Heart Study AF risk score is based on age, body mass index, systolic blood pressure, use of antihypertensives, presence of heart failure and murmur, and PR interval.[14]

Time to Discontinuation

- Most 1L and 2L+ patients treated with ibrutinib who had ≥12, ≥24, and ≥36 months of follow-up remained persistent on ibrutinib treatment at 12, 24, and 36 months; the proportions of persistent patients at each time point were similar across the overall and high-risk cohorts (**Table 2**)

TABLE 2. TTD Among Patients Treated With Ibrutinib

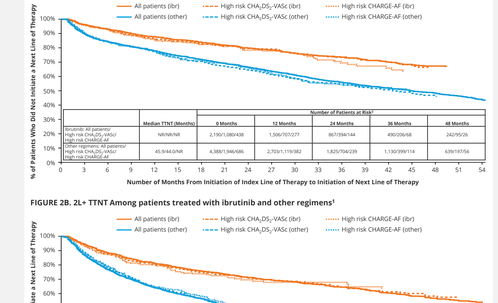
	All patients	High risk CHARGE-AF	High risk CHA_2DS_2-VASc
1L cohorts			
	N=2,190	N=438	N=1,080
TTD (in months), mean ± SD [median]	20.0 ± 23.3 [10.3]	16.1 ± 18.5 [9.2]	18.2 ± 19.4 [11.2]
Patients with ≥12 months of follow-up	N=1,699	N=320	N=808
Persistent on treatment for ≥12 months, n (%)	1,294 (76.2)	217 (67.8)	577 (71.4)
Patients with ≥24 months of follow-up	N=1,045	N=177	N=478
Persistent on treatment for ≥24 months, n (%)	730 (69.9)	110 (62.1)	319 (66.7)
Patients with ≥36 months of follow-up	N=425	N=86	N=262
Persistent on treatment for ≥36 months, n (%)	386 (91.8)	49 (57.0)	156 (59.5)
2L+ cohorts			
	N=1,851	N=324	N=824
TTD (in months), mean ± SD [median]	19.3 ± 19.7 [12.5]	15.4 ± 15.9 [9.5]	17.2 ± 17.6 [10.6]
Patients with ≥12 months of follow-up	N=1,319	N=212	N=563
Persistent on treatment for ≥12 months, n (%)	950 (72.0)	149 (70.3)	391 (69.4)
Patients with ≥24 months of follow-up	N=873	N=113	N=340
Persistent on treatment for ≥24 months, n (%)	566 (64.8)	69 (61.1)	208 (61.2)
Patients with ≥36 months of follow-up	N=589	N=64	N=216
Persistent on treatment for ≥36 months, n (%)	343 (58.2)	39 (60.9)	123 (56.9)

Abbreviations: 1L = first line; 2L+ = second or later line; SD = standard deviation; TTD = time to discontinuation.

Time to Next Treatment

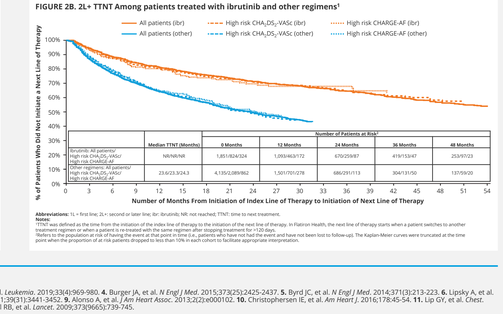
- Median TTNT was longer for patients initiated on ibrutinib (1L and 2L+ median TTNT: not reached) than for patients initiated on other regimens (1L median TTNT: 45.9 months; 2L+ median TTNT: 23.6 months, all *P*<0.05; **Figure 2a and 2b**)
- Similar results were observed when comparing CHA_2DS_2-VASc/CHARGE-AF high-risk patients initiated on ibrutinib (1L and 2L+ median TTNT: not reached) with CHA_2DS_2-VASc /CHARGE-AF high-risk patients initiated on other regimens (1L median TTNT: not reached; 2L+ median TTNT: 24.3 months; all *P*<0.05)
- There was no difference in TTNT between all patients and high-risk cohorts for ibrutinib and other regimens in 1L and 2L+ (all *P*≥0.05)

FIGURE 2A. 1L TTNT Among Patients Treated With Ibrutinib And Other Regimens[1]



	Median TTNT (Months)	Number of Patients at Risk[2]				
		0 Months	12 Months	24 Months	36 Months	48 Months
Ibrutinib: All patients/ High risk CHA_2DS_2-VASc/ High risk CHARGE-AF	NR/NR/NR	2,190/1,080/438	1,506/707/277	867/394/144	490/206/68	242/95/26
Other regimens: All patients/ High risk CHA_2DS_2-VASc/ High risk CHARGE-AF	45.9/44.0/NR	4,388/1,946/686	2,703/1,119/382	1,825/704/239	1,130/399/114	639/197/56

FIGURE 2B. 2L+ TTNT Among patients treated with ibrutinib and other regimens[1]



	Median TTNT (Months)	Number of Patients at Risk[2]				
		0 Months	12 Months	24 Months	36 Months	48 Months
Ibrutinib: All patients/ High risk CHA_2DS_2-VASc/ High risk CHARGE-AF	NR/NR/NR	1,851/824/324	1,093/463/172	670/259/87	419/153/47	253/97/23
Other regimens: All patients/ High risk CHA_2DS_2-VASc/ High risk CHARGE-AF	23.6/23.3/24.3	4,135/2,089/862	1,501/701/278	686/291/113	304/131/50	137/59/20

Abbreviations: 1L = first line; 2L+ = second or later line; ibr: ibrutinib; NR: not reached; TTNT: time to next treatment.
Notes:
[1]TTNT was defined as the time from initiation of the index line of therapy to the initiation of the next line of therapy. In Flatiron Health, the next line of therapy within a patient switches to another treatment regimen or when a patient is re-treated with the same regimen after stopping treatment for >120 days.
[2]Refers to the population at risk of having the event at that point in time (i.e., patients who have not had the event and have not been lost to follow-up). The Kaplan-Meier curves were truncated at the time point when the proportion of at-risk patients dropped to less than 10% in each cohort to facilitate appropriate interpretation.

LIMITATIONS

- The analyses were descriptive and no adjustments were made for differences in baseline characteristics between cohorts; such comparative analyses would have required the identification of a mutually exclusive low-risk cohort, which was not possible given the underreporting of cardiovascular conditions in this database. Furthermore, most reported characteristics directly contributed to risk status assignment and warranted exclusion as covariates. The two potential cohorts for comparison would have also been receiving the same treatment (e.g., high-risk patients treated with ibrutinib vs. low-risk patients treated with ibrutinib), resulting in over-adjusting on covariates associated with the treatment.
- 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
  - Thus, the number of patients with high CHARGE-AF and CHA_2DS_2-VASc, which consider the presence of comorbidities as part of the score, may have been underestimated
- Using a gap of 120 days instead of shorter gaps (e.g., 90 days) for treatment discontinuation may have resulted in a conservative estimate of the proportion of patients who discontinued treatment
- Electronic health record data may contain omissions and inaccuracies, although these would be random and would be expected to similarly affect all cohorts
- Results are only applicable to patients included in the Flatiron Health database, which is more representative of community-based medical practices; therefore, results may not be generalizable to other populations

CONCLUSIONS

- In this study describing the real-world use of ibrutinib in patients with CLL/SLL, patients' increased baseline risk of AF or stroke did not adversely impact TTD and TTNT associated with ibrutinib in any line of therapy
- Additionally, TTNT was significantly longer for patients treated with ibrutinib-based regimens than with other regimens
- Overall, the results of this study show that even patients at high baseline risk for AF or stroke can derive benefit from ibrutinib and that understanding how collaborative mitigation strategies to manage BTKi-associated adverse CV events can help patients continue treatment with ibrutinib is important

ACKNOWLEDGMENTS

Supported by Janssen Scientific Affairs, LLC.

DISCLOSURES

A.N. has received consulting fees from Pharmacyclics, Janssen Scientific Affairs, and Epsilon imaging Inc. B.E., A.H., S.L., M-H.L., and P.L.. are employees of Analysis Group, Inc., which has provided paid consulting services to Janssen Scientific Affairs, LLC. S.P.F. was an employee of Analysis Group, Inc. at the time the study was conducted. S.P., X.L., and Q.H. are employees of Janssen Scientific Affairs, LLC, and stockholders of Johnson & Johnson. M.C. has received research funding from Abbvie, Pharmacyclics, Oncternal, Velosbio, Merck, and Geron. N.A. reports no relevant conflicts of interest related to this work.

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) Prescribing Information. 2020. **2.** Data on file. Based on IQVIA claims, commercial, and clinical trial tracking. **3.** Fraser G, et al. *Leukemia*. 2019;33(4):969-980. **4.** Burger JA, et al. *N Engl J Med*. 2015;373(25):2425-2437. **5.** Byrd JC, et al. *N Engl J Med*. 2014;371(3):213-223. **6.** Lipsky A, et al. *Hematology Am Soc Hematol Educ Program*. 2020;2020(1):336-345. **7.** Sestier M, et al. *Curr Oncol Rep*. 2021;23(10):113. **8.** Byrd JC, et al. *J Clin Oncol*. 2021;39(31):3441-3452. **9.** Alonso A, et al. *J Am Heart Assoc*. 2013;2(2):e000102. **10.** Christophersen IE, et al. *Am Heart J*. 2016;178:45-54. **11.** Lip GY, et al. *Chest*. 2010;137(2):263-272. **12.** Melgaard L, et al. *JAMA*. 2015;314(10):1030-1038. **13.** Goff DC, Jr., et al. *Circulation*. 2014;129(25 Suppl 2):S49-73. **14.** Schnabel RB, et al. *Lancet*. 2009;373(9665):739-745.

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

B-CELL MALIGNANCIES