Comparison of Time to Next Treatment Between Patients With Chronic Lymphocytic Leukemia Initiating First-Line Ibrutinib or Acalabrutinib, **Overall and in a Subgroup With High-Risk Characteristics**

Ryan Jacob Priyanka (

INTRO

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FIGURE 1: S

Ryan Jacobs, ¹ Moshe Y. Levy, ² Victor Yazbeck, ³ Marie-Hélène Priyanka Gogna, ⁴ Rodrigo Maegawa, ⁵ Zaina P. Qureshi, ⁵ Ales	Lafeuille, ⁴ Bruno Emond, ⁴ sandra Ferrajoli ⁶		³ VCU Health, Richmond, VA, USA; ⁴ Analysis Group, ⁶ MD Anderson Cancer Center, Houston, TX, USA
INTRODUCTION	Figure 2: Study population se	lection	RESULTS
 Ibrutinib and acalabrutinib are 2 covalent Bruton tyrosine kinase inhibitors (BTKis) approved for the treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)^{1,2} 	 Inclusion criteria (N = 2849) ≥2 diagnoses for CLL/SLL (ICD-10 CM code: C91.1, C83.0) ≥30 days apart ≥1 order, fill, or administration of ibrutinib or acalabrutinib ≥12 months of data availability before first use of ibrutinib or acalabrutinib (index date); no other antineoplastic agents received during washout period 		 Baseline demographics and clinical characteristics A total of 710 patients initiated 1L ibrutinib and 373 paacalabrutinib (Figure 2)
 Although no head-to-head randomized studies comparing these 2 medications in the first-line (1L) setting currently exist, a previous real-world study of electronic medical records (EMRs) found that patients treated with 1L acalabrutinib were more likely to initiate a next treatment compared with patients treated with 1L ibrutinib³ 	 ≥18 years of age as of index date 	 Exclusion criteria (n = 25) ≥2 diagnoses of other blood cancer ≥30 days apart between 24 months prior to index date and 6 months prior to first 	 In the ibrutinib and acalabrutinib cohorts, mean age w 72.4 years, respectively; <i>P</i> = 0.159) and 61.5% and 61.7 men (<i>P</i> = 0.971); mean Quan-Charlson Comorbidity Inc similar between the 2 cohorts (ibrutinib: 3.1; acalabrut (Supplementary Table 1) Of the 13.2% of patients in the ibrutinib cohort with EC
 Other studies have also found that treatment with 1L ibrutinib was associated with higher adherence and lower healthcare resource utilization and costs compared with 1L acalabrutinib⁴⁻⁶ 	Fligible	 CLL/SLL diagnosis ≥1 diagnosis of end-stage renal disease prior to index date 	 had an ECOG PS score between 0 and 1; in the acalabr PS data were available for 16.1% of patients, of which 9 PS score between 0 and 1 Cytogenetics data were available in 12.7% of patients i
) BIECTIVE		2824	 cohort and 11.3% of patients in the acalabrutinib coho 31 patients in the ibrutinib cohort and 18 patients in the
 To compare time to next treatment (TTNT) between 1L ibrutinib and 1L acalabrutinib among patients with CLL/ SLL in the United States, overall and among a subgroup of 	Patients treated with 1L single-agent ibrutinib n = 1827	Patients treated with 1L single-agent acalabrutinib n = 398	cohort had del(17p)/ <i>TP53</i> mutation or unmutated IGHV evaluated as part of the HRC subgroup Time to next treatment
patients with high-risk characteristics (HRCs; i.e., patients with del(17p)/ <i>TP53</i> mutation or unmutated immunoglobulin heavy chain variable [IGHV]) using academic EMR data	Ibrutinib cohort Patients treated with 1L ibrutinib on or after acalabrutinib approval n = 710	Acalabrutinib cohort Patients treated with 1L acalabrutinib on or after acalabrutinib approval n = 373	 Over a median follow-up of 18.1 and 11.9 months, 42 p the ibrutinib cohort and 28 patients (7.5%) in the acala respectively, initiated a next treatment
METHODS	1L, first-line; CLL, chronic lymphocytic le Classification of Diseases, Tenth Revisio	ukemia; ICD-10-CM, International n, Clinical Modification; SLL, small	 At 12 months, 95.3% of patients in the ibrutinib cohort patients in the acalabrutinib cohort had not initiated a
 Data source This study used structured EMR and unstructured patient chart data from the Acentrus database (November 21, 2018, to April 30, 2022) 	 A subgroup of patients with del(17p)/<i>TP53</i> mutation or ui 	HRCs , defined as those with nmutated IGHV, was also evaluated	these rates remained similar at 24 months, with 91.5% patients without a next treatment in the ibrutinib and cohorts, respectively
 Acentrus included patient records from 15 academic and 12 nonteaching hospital systems across 15 US states and contains information on demographics, visits, diagnoses, laboratory tests, mortality, and medication orders, fills, or 	 Study outcome measures TTNT was defined as the time from the index date to the date of initiation of a next regimen Patients who did not initiate a subsequent regimen 		acalabrutinib were 81% more likely to initiate a next transformed by the second secon
 administrations Eastern Cooperative Oncology Group performance status (ECOG PS) and cytogenetics data were also extracted from patient charts 	were censored at the d availability – Patients with an observ time or with a venetocla	ate of death or the end of data ed within-class BTKi switch at any ax or anti-CD20 add-on within the	Figure 3: Comparison of TTNT between patients treated or 1L acalabrutinib
 Data were de-identified and comply with the patient requirements of the Health Insurance Portability and Accountability Act 	first 6 months were cen – Beyond the first 180 da venetoclax add-ons we treatment	sored at the date of switch/add-on ys post-index, anti-CD20 or re considered to be a next	b did not initi
 In this real-world retrospective study, the index date was defined as the date of initiation of 1L single-agent ibrutinib or acalabrutinib on or after November 21, 2019 (date of acalabrutinib approval), the baseline period was defined as the 12-month period before the index date, and the follow- 	 Patients who switched cancers were censored Statistical analyses Baseline demographics and compared between cohorts 	to agents for nonhematologic at the date of switch I clinical characteristics were s using <i>t</i> -tests for continuous	Adjusted HR (95% CI); 10 10 10 10 1.81 (1.07, 3.06); $P = 0.026^{a}$ Number of months from initiation of index rest to initiation of a subsequent regimen Number of patients
up period was defined as time from the index date to the earliest date of initiation of second-line therapy, death, or end of data availability (Figure 1)	 variables and chi-square ter TTNT was reported using Ka was compared between col 	sts for categorical variables aplan-Meier survival curves and norts using the Cox proportional	at risk," n (%)3 months6 months9 months12 monthsIbrutinib DR64057652946Acalabrutinib30824520415
 Study population The patient selection criteria are presented in Figure 2 	hazards model, adjusting for clinical characteristics (inclu	or baseline demographics and iding ECOG PS and cytogenetics)	1L, first-line; DR, dose reduction; ECOG PS, Eastern Cooperative Oncology status; HR, hazard ratio; IGHV, immunoglobulin heavy chain variable; NR, r next treatment; Quan-CCI, Quan-Charlson Comorbidity Index. ^a P < 0.05. HRs and P values were calculated using a Cox proportional hazar for the following baseline covariates: age, say, region, race, year of index of
FIGURE 1: Study design Inde Start of data Initiation of 1L ibru	ex date: utinib or acalabrutinib Ea	End of follow-up period: rliest of initiation of 2L therapy,	fibrillation, chronic pulmonary disease, metastases, corticosteroid use, and vascular disease, hypertension, ECOG PS score, as well as del(17q), del(11c <i>TP53</i> , and trisomy 12 mutation status. ^b Refers to the population at risk of having the event at that point in time (i
			 had the event and have not been lost to follow-up). Among patients who received a next treatment, the maswitched to venetoclax (59.5% in the ibrutinib cohort a acalabrutinib cohort) (Table 1)
12-month baseline/washout period No antineoplastic agents (to confirm identification of 1L therapy) 1L, first-line; 2L, second-line.	Follow-up period 1L therapy duration		REFERENCES: 1. IMBRUVICA (ibrutinib) [prescribing information]. South San Fran AstraZeneca Pharmaceuticals LP; 2022. 3. Jacobs R et al. <i>Future Or</i> 2023;26(12 suppl):188. 6. Rogers KA et al. <i>Value Health</i> . 2023;26(12
B-cell Malignancies			Originally presente Poster presented at the European H

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 Study outcome measures TTNT was defined as the time date of initiation of a next rest 	e from the index date to the	 After adjusting for baseline characteristics, patients acalabrutinib were 81% more likely to initiate a nex with patients treated with ibrutinib (adjusted hazar P = 0.026) (Figure 3)
 Patients who did not init were censored at the da availability 	tiate a subsequent regimen ite of death or the end of data	Figure 3: Comparison of TTNT between patients trea or 1L acalabrutinib
 Patients with an observe time or with a venetoclas first 6 months were cens Beyond the first 180 day 	d within-class BTKi switch at any k or anti-CD20 add-on within the fored at the date of switch/add-on ys post-index_anti-CD20 or	in itiate 80- 100 % 80- 100 %
 venetoclax add-ons wer treatment Patients who switched to the treatment 	e considered to be a next o agents for nonhematologic	60 - 50 - 40 - 40 - 30 - 30 - 20 - Adjusted HR (95% CI);
cancers were censored a	at the date of switch	$\begin{array}{c c} \mathbf{\dot{P}} & \mathbf{\dot{P}} \\ \mathbf{\dot{P}}$
• Baseline demographics and	clinical characteristics were	Number of months from initiation of index to initiation of a subsequent regin
compared between cohorts variables and chi-square tes • TTNT was reported using Ka	using <i>t</i> -tests for continuous ts for categorical variables plan-Meier survival curves and	Number of patients at risk, ^b n (%)3 months6 months9 months1Ibrutinib DR640576529Acalabrutinib308245204
was compared between coh hazards model, adjusting for clinical characteristics (inclue	orts using the Cox proportional r baseline demographics and ding ECOG PS and cytogenetics)	1L, first-line; DR, dose reduction; ECOG PS, Eastern Cooperative Oncol- status; HR, hazard ratio; IGHV, immunoglobulin heavy chain variable; N next treatment; Quan-CCI, Quan-Charlson Comorbidity Index. ^a P < 0.05. HRs and P values were calculated using a Cox proportional h for the following baseline covariates: age, sex, region, race, year of ind fibrillation, chronic pulmonary disease, metastases, corticosteroid use
late: ib or acalabrutinib Ear mber 21, 2019 de	End of follow-up period: liest of initiation of 2L therapy, ath, or end of data availability	vascular disease, hypertension, ECOG PS score, as well as del(17q), del <i>TP53</i> , and trisomy 12 mutation status. ^b Refers to the population at risk of having the event at that point in tin had the event and have not been lost to follow-up).
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> Time to initiation of a next treatment was shorter in the acalabrutinib cohort (mean [median]: 6.2 [4.6] months) than in the ibrutinib cohort (mean [median]: 9.2 [6.8] months)

patients initiated 1L

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e majority of patients ort and 50.0% in the

 Table 1: Treatment regimen received following 1L ibrutinib or acalabrutinib

	lbrutinib N = 710	Acalabrutinib N = 373
Patients with a next treatment, n (%)	42 (5.9)	28 (7.5)
TTNT (months), mean ± SD [median]	9.2 ± 7.6 [6.8]	6.2 ± 4.6 [4.6]
Next treatment regimen received, n (%)		
Venetoclax	25 (59.5)	14 (50.0)
Obinutuzumab	1 (2.4)	3 (10.7)
Rituximab	2 (4.8)	0
Chlorambucil	2 (4.8)	1 (3.6)
Lenalidomide	3 (7.1)	0
Bendamustine + rituximab	4 (9.5)	0
Venetoclax + obinutuzumab	0	3 (10.7)
Venetoclax + idelalisib	1 (2.4)	0
Venetoclax + chlorambucil + rituximab	0	1 (3.6)
BTKi + venetoclax	3 (7.1)	5 (17.9)
BTKi + obinutuzumab	0	1 (3.6)
BTKi + lenalidomide	1 (2.4)	0

1L, first-line; BTKi, Bruton tyrosine kinase inhibitor; SD, standard deviation; TTNT, time to next treatment.

Among patients with HRCs, 5 patients (16.1%) in the ibrutinib cohort and 5 patients (27.8%) in the acalabrutinib cohort initiated a next treatment

In the ibrutinib and acalabrutinib cohorts, 81.9% and 50.3% of patients had not initiated a next treatment at 12 months, respectively; at 24 months, these estimates were 75.1% and 50.3%, respectively

In adjusted analyses, patients with HRCs treated with acalabrutinib were >5 times more likely to initiate a next treatment compared with patients treated with ibrutinib (adjusted HR = 5.82; *P* = 0.036) (**Figure 4**)

Figure 4: Comparison of TTNT between patients treated with 1L ibrutinib or 1L acalabrutinib among patients with HRCs



1L, first-line; DR, dose reduction; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; HRCs, high-risk characteristics; NR, not reached; TTNT, time to next treatment; Quan-CCI, Quan-Charlson Comorbidity Index.

^a*P* < 0.05. HRs and *P* values were calculated using a Cox proportional hazards model adjusting for the following baseline covariates: age, sex, Quan-CCI, hypertension, and ECOG PS score. ^bRefers 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).

Francisco, CA: Pharmacyclics LLC; 2024. 2. CALQUENCE (acalabrutinib) [prescribing information]. Wilmington, DE: *re Oncol*. 2024;20(1):39-53. 4. Lu X et al. *Patient Prefer Adherence*. 2023;17:2073-2084. 5. Muluneh B et al. *Value Health*. 26(12 suppl):63.

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LIMITATIONS





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Acentrus is a provider-based data source, meaning that records are only available to the extent that visits are part of the network of academic and nonteaching hospital systems included in the data

A 12-month washout period was used to identify the use of ibrutinib or acalabrutinib in the 1L setting, which has been used extensively in real-world studies, but could have included patients in longer remission who had received a previous line of therapy

Patients were assumed to be using their medication based on prescription fills, but may not always have adhered to their treatment regimen as prescribed

Reasons for starting a next treatment were not available in Acentrus; however, assumptions regarding the definition of TTNT were made to ensure that the reason was most likely related to disease progression

Results may not be generalizable to all patients treated with 1L ibrutinib or acalabrutinib or to patients treated outside of academic or nonteaching hospital systems in the United States

CONCLUSIONS



Over a median follow-up of 12 to 18 months, this real-world study of patients with CLL/SLL treated with 1L single-agent ibrutinib or acalabrutinib supports previous results, suggesting that while most patients benefit from BTKis, a significantly greater proportion of patients treated with 1L acalabrutinib initiated a next treatment compared with those treated with 1L ibrutinib



Results were consistent in the subgroup of patients with HRCs



These results demonstrate the impact of using ibrutinib in the 1L setting and highlight the importance of these data to support clinical decision-making in improving patient outcomes in the real-world setting

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Comparison of Time to Next Treatment Between Patients With Chronic Lymphocytic Leukemia Initiating First-Line Ibrutinib or Acalabrutinib, Overall and in a Subgroup With High-Risk Characteristics

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SUPPLEMENTAL METHODS

SUPPLEMENTAL TABLE 1: Baseline demographics and clinical characteristics

	lbrutinib N = 710	Acalabrutinib N = 373	P value
Baseline demographics			
Age at index date, mean ± SD [median], years	71.5 ± 10.4 [73.0]	72.4 ± 9.8 [72.0]	0.159
Sex, n (%)			
Men	437 (61.5)	230 (61.7)	0.971
Women	273 (38.5)	143 (38.3)	0.971
Insurance coverage, n (%)			
Medicare	196 (27.6)	104 (27.9)	0.923
Managed care	61 (8.6)	34 (9.1)	0.772
Medicaid	15 (2.1)	0 (0.0)	0.005*
Other	252 (35.5)	137 (36.7)	0.687
Unknown	186 (26.2)	98 (26.3)	0.978
US region, n (%)			
West	213 (30.0)	138 (37.0)	0.546
South	S 212 (29.9)	118 (31.6)	0.019*
Midwest	188 (26.5)	86 (23.1)	0.218
Northeast	21 (3.0)	9 (2.4)	0.604
Unknown	76 (10.7)	22 (5.9)	0.009*
Race, n (%)	, , , , , , , , , , , , , , , , , , , ,	(313)	
White	320 (45.1)	150 (40.2)	0.125
Black	25 (3.5)	19 (5.1)	0.213
Asian	13 (1 8)	7 (1 9)	0.958
Other	352 (49 6)	197 (52 8)	0 311
Year of index date, n (%)			
2019	45 (6 3)	7 (1 9)	0.001*
2020	408 (57 5)	119 (31 9)	<0.001*
2020	217 (30.6)	200 (53 6)	<0.001*
2027	40 (5 6)	47 (12 6)	<0.001*
Clinical characteristics	40 (0.0)	47 (12.0)	0.001
O_{uan} (CL mean + SD [median]	3 1 + 1 7 [2 0]	3 0 + 1 7 [2 0]	0 597
Comorbidities n (%)	5.1 ± 1.7 [2.0]	J.0 ± 1.7 [2.0]	0.337
Hypertension	29 <i>4 (1</i> 1 <i>1</i>)	120 (32 2)	0 003*
Chronic nulmonary disease	94 (13 2)	32 (8 6)	0.003*
Renal disease	75 (10.6)	48 (12 9)	0.025
Perinheral vascular disease	54 (7 6)	15 (4 0)	0.230
Atrial fibrillation	50 (7 0)	37 (9 9)	0.022
Valvular disease	39 (5 5)	18 (4 8)	0.050
Metastatic cancer	17 (2 /)	17 (4 6)	0.040
Baseline use of other medications n (%)		17 (-1.0)	0.052
Corticosteroide	103 (14 5)	75 (20 1)	0 010*
Antiplatolots	50 (7 0)	12 (2 5)	0.017*
Patients with ECOC DS information on (0()	04 (12 2)	13(3.3)	0.01/*
0.1	94 (13.2)		0.203
0-1	90(12.7)	55 (14.7)	0.342
Z-4	4 (0.6)	5(1.3)	0.181
Patients with cytogenetics information, n (%)	90 (12.7)	42 (11.3)	0.499
Patients with unmutated IGHV	14 (2.0)	10(2.7)	0.451
Patients with del(17p)/mutation	19 (2.7)	9 (2.4)	0.795

**P* < 0.05.

ECOG PS, Eastern Cooperative Oncology Group performance status; IGHV, immunoglobulin heavy chain variable; Quan-CCI, Quan-Charlson Comorbidity Index; SD, standard deviation.