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Real-World Treatment Outcomes Among Relapsed/Refractory Patients With Mantle Cell Lymphoma Treated With Ibrutinib or Acalabrutinib

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OBJECTIVE

To describe and compare persistence, TTNT, and health care costs among patients with MCL treated with ibrutinib or acalabrutinib in 2L+ settings

CONCLUSIONS

This study provides insights into real-world persistence, TTNT, and health care costs for patients with MCL who started 2L+ treatment with single-agent ibrutinib or acalabrutinib

In this real-world population study, similar treatment persistence and TTNT were observed in patients treated with ibrutinib or acalabrutinib

Costs were generally similar for both cohorts, and no significant differences were observed in all-cause and MCL-related costs

Ibrutinib has dosing advantages due to once-daily administration and flexible management guidelines,[12] which may translate into real-world benefits

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INTRODUCTION

- Mantle cell lymphoma (MCL) is a rare and aggressive subtype of non-Hodgkin lymphoma characterized by the malignant transformation of B lymphocytes at the outer edge of the lymph nodes (mantle zone) due to acquired genetic mutations[1,2]
- The introduction of Bruton's tyrosine kinase inhibitor (BTKi) therapies such as ibrutinib and acalabrutinib have revolutionized treatment for MCL[3]
- The clinical efficacy of ibrutinib[4-8] and acalabrutinib[9,10] for second-line or greater (2L+) MCL treatment was established in several separate clinical trials, with emerging data on the comparative efficacy and safety of these agents based on indirect comparisons[11]
- However, comparative real-world data are limited for patients treated with different BTKis in 2L+ settings

METHODS

Data Source

- Data from Optum's de-identified Clinformatics® Data Mart Database (04/30/2017–12/31/2021) were used (~15–19 million annual covered lives across all 50 states)
- The data are de-identified in compliance with Health Insurance Portability and Accountability Act (HIPAA) and comprise inpatient and outpatient medical claims, pharmacy claims, and estimated costs of medical services

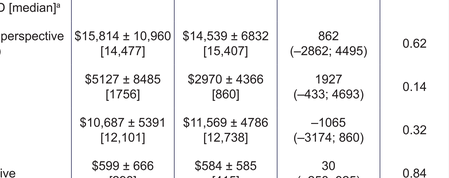
Patients and Study Outcomes

- Patients were classified into either the ibrutinib or acalabrutinib cohorts based on whichever therapy was received first in the 2L+ setting (**Supplemental Figure S1**)
  - The index date was defined as the initiation date of 2L single-agent ibrutinib or acalabrutinib following first MCL diagnosis
- In sensitivity analyses, subgroups were evaluated on having no prior line of therapy (LOT) with a BTKi or treatment with chemoimmunotherapy (CIT) in first-line (1L) treatment
- Persistence and time to next treatment (TTNT) were evaluated among patients with sufficient potential follow-up (index date ≥15 months before end of data, with ≥60 days of continuous enrollment post-index) to observe discontinuation
- Persistence to 2L+ treatment with the index agent was defined as having no gap for >90 days between consecutive days of supply of ibrutinib/acalabrutinib during the index LOT
- TTNT was defined as the time from the index date to the start of the patient's next LOT
- All-cause and MCL-related costs were evaluated during the index LOT and were reported per patient per month
  - Patient, payer, and comprehensive (ie, the sum of patient and payer) costs were reported
  - Costs were adjusted to 2021 United States dollar (USD) using the medical care component of the Consumer Price Index

Statistical Analysis

- Descriptive and univariate statistics were used to assess baseline characteristics and comparisons between 2 cohorts, respectively (**Supplemental Methods**)
- Persistence and TTNT were compared between the ibrutinib and acalabrutinib cohorts using Cox proportional hazards models among the overall population, patients with no prior LOT with a BTKi, and patients treated with CIT in 1L
- All-cause and MCL-related costs during the LOT were compared using ordinary least squares regression models
- Baseline characteristics were added as covariates in the Cox proportional hazards and ordinary least squares regression models (**Supplemental Methods**)
  - 95% CIs and *P* values were obtained from nonparametric bootstrap procedures with 500 replications

Figure 1. Retrospective Study Design



RESULTS

- 50 patients with MCL receiving ibrutinib and 48 patients with MCL receiving acalabrutinib in 2L+ were included in the study, with the majority initiating treatment in 2L in both cohorts (**Supplemental Figure S1**)
- For the ibrutinib cohort, mean age was 76.3 years, 42.0% were female, and mean Quan Charlson Comorbidity Index (CCI) score was 4.6; for the acalabrutinib cohort, mean age was 76.4 years, 35.4% were female, and mean Quan-CCI score was 3.6
- The median duration of the index LOT was 10.2 months for the ibrutinib cohort and 8.7 months for the acalabrutinib cohort

Table 1. Baseline[a] Characteristics

	Ibrutinib cohort N=50	Acalabrutinib cohort N=48	*P* value
Female, n (%)	21 (42.0)	17 (35.4)	0.50
Age,[b] years, mean ± SD [median]	76.3 ± 8.8 [78.0]	76.4 ± 8.3 [78.0]	0.99
Region,[b] n (%)			
South and West	39 (78.0)	30 (62.5)	0.09
Northeast and Midwest	11 (22.0)	18 (37.5)	0.09
Race,[b] n (%)			
White	37 (74.0)	35 (72.9)	0.90
Non-White[c]	13 (26.0)	13 (27.1)	0.90
Time between the first MCL diagnosis observed in the data and initiation of ibrutinib/acalabrutinib therapy in 2L+, months, mean ± SD [median]	32.7 ± 31.5 [21.0]	33.5 ± 28.9 [25.2]	0.89
Year of initiation of ibrutinib/acalabrutinib therapy in 2L+, n (%)			
2017–2019	31 (62.0)	14 (29.2)	<0.01*
2020–2021	19 (38.0)	34 (70.8)	<0.01*
Prior treatment with CIT in any LOT, n (%)	37 (74.0)	28 (58.3)	0.10
Quan-CCI, mean ± SD [median]	4.6 ± 2.6 [4.0]	3.6 ± 2.0 [3.0]	0.03*
History of atrial fibrillation, n (%)	8.0 (16.0)	10.0 (20.8)	0.54
Total all-cause costs, 2021 USD, mean ± SD [median]			
Comprehensive perspective[d]	$13,243 ± 16,561 [5827]	$9832 ± 11,480 [6094]	0.24
Payer perspective[d]	$13,009 ± 16,416 [5654]	$9555 ± 11,344 [5993]	0.23
Patient perspective[d]	$234 ± 275 [146]	$277 ± 328 [135]	0.48

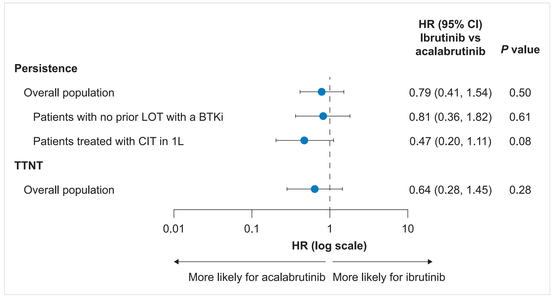
*P<0.05.
[a]Baseline characteristics were evaluated during the 6 months preceding the index LOT. Categories with <11 patients were combined with other categories to ensure patient confidentiality.
[b]Evaluated at the initiation of index LOT.
[c]Non-White=Black, Hispanic, Asian, or other.
[d]The payer perspective was defined as the sum of the paid amount and the coordination of benefits amount. The patient perspective was defined as the sum of deductible amount, copay amount, and coinsurance amount. The comprehensive perspective was defined as the sum of the patient perspective and payer perspective. Costs were adjusted to 2021 USD using the medical care component of the Consumer Price Index.

- Among patients with sufficient follow-up post-index (n=43, ibrutinib; n=24, acalabrutinib), 62.8% and 75.0% of patients discontinued ibrutinib and acalabrutinib, respectively. Median time between 2L+ initiation and end of follow-up was 17.8 months for the ibrutinib cohort and 20.8 months for the acalabrutinib cohort; median time to discontinuation was 8.9 and 5.7 months, respectively
- A smaller proportion of patients in the ibrutinib cohort had a next treatment (39.5% vs 62.5%)
- TTNT was also assessed in previously mentioned subgroups; given the limited number of patients with a next treatment, not all subgroups were reported in order to preserve patient confidentiality

Table 2. Fewer Patients Discontinued Ibrutinib Than Acalabrutinib, With a Longer Median Time to Discontinuation and TTNT

	Ibrutinib	Acalabrutinib
Treatment Discontinuation		
Patients discontinuing treatment, n/N (%)		
Overall	27/43 (62.8)	18/24 (75.0)
No prior LOT with a BTKi	25/40 (62.5)	11/16 (68.8)
Treated with CIT in 1L	17/31 (54.8)	13/17 (76.5)
Median time to discontinuation, months		
Overall	8.9	5.7
No prior LOT with a BTKi	8.9	6.9
Treated with CIT in 1L	9.3	4.4
TTNT		
Patients with next treatment, n/N (%)		
Overall	17/43 (39.5)	15/24 (62.5)
Median TTNT, months, n/N (%)		
Overall	46.1	10.7

Figure 2. Trends in Ibrutinib Cohort Were Favorable With a Lower Likelihood of Treatment Discontinuation or Need for Next Treatment Compared With Acalabrutinib Cohort



HR, hazard ratio.
*P<0.05.

Table 3. Patients in the 2L+ Ibrutinib and Acalabrutinib Cohorts Generally Had Similar MCL-Related Costs (differences in all-cause costs were not significant)

	Ibrutinib N=50	Acalabrutinib N=48	Adjusted mean monthly cost difference (95% CI)	*P* value
All-cause costs, 2021 USD, mean ± SD [median][a]				
Comprehensive perspective (patient + payer)	$18,098 ± 11,873 [16,325]	$15,626 ± 7599 [16,060]	1816 (–2167; 5472)	0.36
Medical[b]	$7181 ± 9397 [2883]	$3748 ± 4676 [1408]	3019 (269; 6141)	0.02*
Pharmacy	$10,917 ± 5444 [12,255]	$11,878 ± 5115 [12,820]	–1203 (–3445; 853)	0.28
Patient perspective	$665 ± 675 [389]	$632 ± 583 [458]	33 (–262; 323)	0.83
Medical[b]	$123 ± 168 [65]	$89 ± 152 [47]	21 (–45; 93)	0.51
Pharmacy	$542 ± 640 [162]	$543 ± 590 [296]	12 (–288; 290)	0.92
MCL-related costs, 2021 USD, mean ± SD [median][a]				
Comprehensive perspective (patient + payer)	$15,814 ± 10,960 [14,477]	$14,539 ± 6832 [15,407]	862 (–2862; 4495)	0.62
Medical[b]	$5127 ± 8485 [1756]	$2970 ± 4366 [860]	1927 (–433; 4693)	0.14
Pharmacy	$10,687 ± 5391 [12,101]	$11,569 ± 4786 [12,738]	–1065 (–3174; 860)	0.32
Patient perspective	$599 ± 666 [298]	$584 ± 585 [415]	30 (–258; 325)	0.84
Medical[b]	$81 ± 138 [23]	$64 ± 140 [17]	13 (–42; 79)	0.63
Pharmacy	$519 ± 645 [151]	$520 ± 592 [240]	16 (–283; 297)	0.90

*P<0.05.
[a]Costs per patient per month.
[b]Medical costs included costs for outpatient visits, inpatient admissions, emergency room visits, hospice admissions, and other services.

Main Limitations

- Reasons for discontinuation or switching to a next treatment could not be determined
- A claim for a medication did not necessarily indicate its use
- Claims data may contain omissions and inaccuracies but should have no impact on conclusions since all cohorts are equally affected

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SUPPLEMENTAL METHODS

Data Considerations

- Data are de-identified and comply with HIPAA; therefore, no institutional review board approval was needed

Study Design and Population

- The index date was defined as the date of initiation of 2L+ single-agent ibrutinib or acalabrutinib following the first MCL diagnosis
  - The identification of 1L treatment was ascertained based on a washout period of 6 months without any use of antineoplastic agents
- Patients were classified into either the ibrutinib or acalabrutinib cohorts based on whichever therapy was received first in the 2L+ setting
- Subgroups based on having no prior LOT with a BTKi or treatment with CIT in 1L were further analyzed

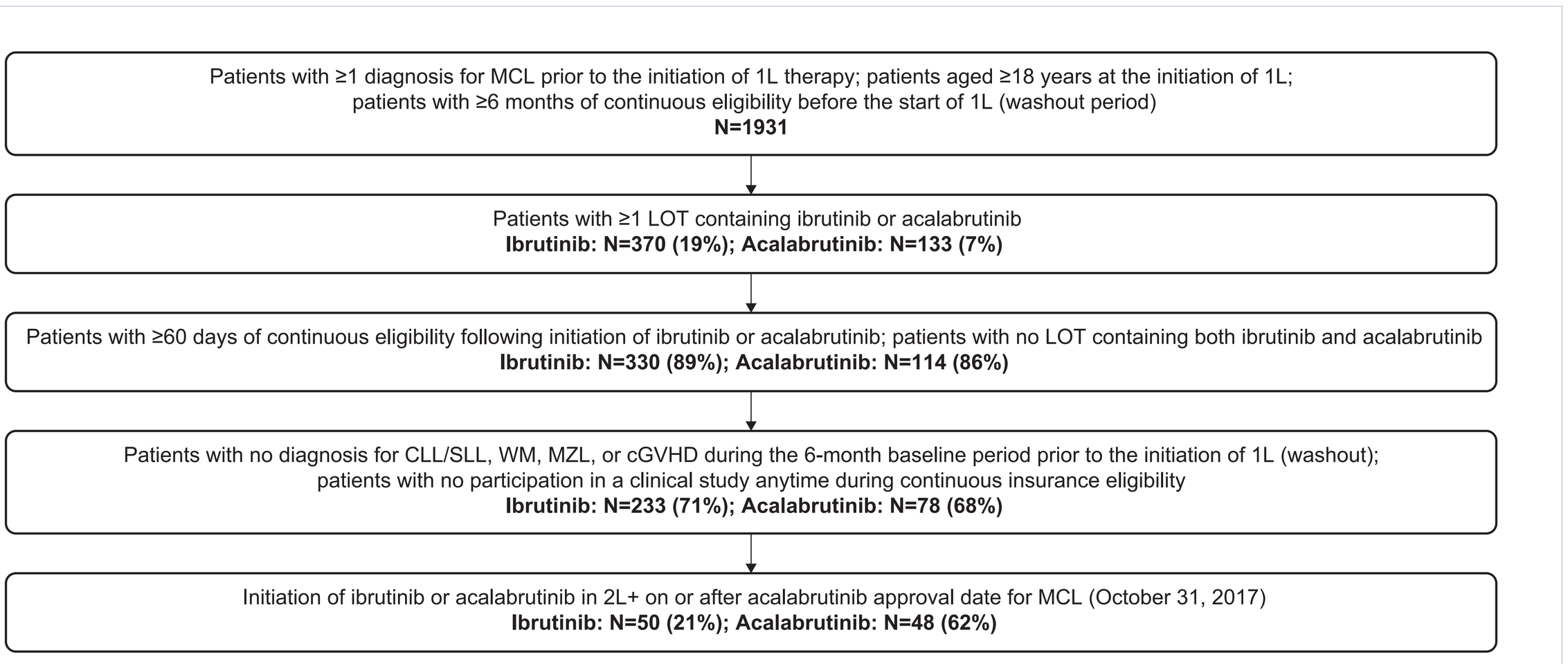
Statistical Methods

- Baseline characteristics were described using means, standard deviations, and medians for continuous variables and frequencies and proportions for categorical variables
  - Comparisons between the ibrutinib and acalabrutinib cohorts were conducted using univariate statistical tests (ie, t-test for continuous variables and chi-square test for categorical variables)
- In addition to the cohort indicator (ibrutinib vs acalabrutinib), the following baseline characteristics were added as covariates in the models: age, sex at birth, region, race, LOT of index treatment, type of therapy used in prior lines (CIT vs other), Quan-CCI, all-cause total monthly health care costs (comprehensive perspective), and baseline atrial fibrillation

Limitations

- A 6-month washout period for antineoplastic agents prior to the initiation of 1L therapy was imposed to ensure that 1L therapy for MCL was captured; however, for regimens with fixed durations that may have had a treatment-free interval lasting more than 6 months, the LOT number could have been misclassified
- Multivariable model adjustment may be subject to residual confounding due to unmeasured confounders
- The analyses were conducted in a cohort of commercially insured and Medicare Advantage patients and may not be generalizable to patients with other types of insurance (eg, Medicaid) or uninsured patients
- The statistical power of this study was limited by the small sample size

Figure S1. Identification of Patients With MCL Treated With Ibrutinib or Acalabrutinib



[a]MCL diagnoses were identified using ICD-9-CM code 200.4, and ICD-10-CM code C83.1.
cGVHD, chronic graft versus host disease; CLL, chronic lymphocytic leukemia; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; MZL, marginal zone lymphoma; SLL, small lymphocytic lymphoma; WM, Waldenström macroglobulinemia.