Clinical Outcomes Among Patients With Relapsed/Refractory Mantle Cell Lymphoma Receiving Zanubrutinib or Acalabrutinib in Real-World Practice in the United States

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Jing-Zhou Hou,[1]* Javier Munoz,[2]* Gregory A. Maglinte,[3] Manasi Suryavanshi,[3] John Li,[4] Beverly Chigarira,[4] Lindsay Aton,[4] Lisa Morere,[4] Melissa Hagan,[3] Rhys Williams,[3] Rushir Choksi,[1] Yucai Wang[5]

[1]UPMC, Pittsburgh, PA, USA; [2]Mayo Clinic, Phoenix, AZ, USA; [3]BeOne Medicines, Ltd, San Carlos, CA, USA; [4]Integra Connect, West Palm Beach, FL, USA; [5]Mayo Clinic, Rochester, MN, USA

CONCLUSIONS

- In this real-world comparative effectiveness analysis of patients with R/R MCL, zanubrutinib was associated with longer treatment duration and a trend toward longer time to subsequent therapy and overall survival compared with acalabrutinib
- Collectively, these data highlight the need for further comparative studies with larger cohort sample sizes and longer follow-up to further evaluate outcomes and optimize treatment sequencing strategies in R/R MCL

INTRODUCTION

- Mantle cell lymphoma (MCL) is a rare and clinically heterogeneous subtype of B-cell non-Hodgkin lymphoma (NHL) that represents approximately 5-6% of NHL cases[1]
- MCL is characterized by an aggressive clinical course in most patients with repeated relapses and remains incurable with standard therapies
- The second-generation Bruton tyrosine kinase inhibitors (BTKis) zanubrutinib and acalabrutinib have substantially improved survival outcomes and have become the established therapies for relapsed or refractory (R/R) MCL[2]
- However, head-to-head clinical trials comparing the efficacy of second-generation BTKis are lacking
- The objective of this study was to describe baseline characteristics and compare treatment outcomes among patients with R/R MCL receiving zanubrutinib or acalabrutinib in real-world practice

METHODS

Study Design

- This is a retrospective, observational study of adult patients with R/R MCL initiating second-line or later (2L+) zanubrutinib or acalabrutinib treatment in the United States
  - Study period: January 1, 2018-July 31, 2025
  - Follow-up period: January 1, 2018-October 31, 2025
    - The index date was the start date of 2L+ acalabrutinib or zanubrutinib treatment
  - Patients with prior ibrutinib use were included if ibrutinib was discontinued due to toxicity or adverse events
- Descriptive statistics were used to summarize baseline and clinical characteristics. The frequency and proportion of patients with R/R MCL within each parameter were described
- Outcome measures included time to treatment discontinuation (TTD), time to next treatment (TTNT), and overall survival (OS)
  - The event date was the date of discontinuing a BTKi or death for TTD, and the date of starting a subsequent line of treatment (LoT) or death for TTNT
  - The probabilities of not discontinuing treatment, not advancing to the next LoT from zanubrutinib or acalabrutinib initiation, and OS were estimated using the Kaplan-Meier method

RESULTS

Patient Characteristics

- A total of 184 patients with R/R MCL were included (**Table 1**)
  - Among the study population, 93 (50.5%) received zanubrutinib and 91 (49.5%) received acalabrutinib
- Most patients were male (76.1%), non-Hispanic (77.2%), White (84.2%), and Medicare/Medicaid insured (42.9%); the median age at index was 72.0 years (66.0-80.0)
- Overall, patients had more severe stages of disease at diagnosis (stage IV, 64.1%)
  - The most common prior therapy included anti-CD20 monoclonal antibodies (48.4%) and chemotherapy (38.6%)
- The median (range) follow-up was 18.8 months (0.9-89.0)
  - The median (range) follow-up for zanubrutinib was 17.3 months (3.0-53.0) and for acalabrutinib was 20.2 months (0.9-89.0)

Table 1. Demographic Characteristics

	Baseline		
	Overall (N=184)	Acalabrutinib (n=91)	Zanubrutinib (n=93)
Age at MCL diagnosis, years			
Median (IQR)	68 (61-75)	69 (60-77)	68 (63-74)
Age at index, years			
Median (IQR)	72 (66-80)	72 (64-80)	72 (67-78)
Sex (n, %)			
Female	44 (23.9%)	21 (23.1%)	23 (24.7%)
Male	140 (76.1%)	70 (76.9%)	70 (75.3%)
Race (n, %)			
White	155 (84.2%)	74 (81.3%)	81 (87.1%)
Black/African American	6 (3.3%)	2 (2.2%)	4 (4.3%)
Asian	5 (2.7%)	3 (3.3%)	2 (2.2%)
Not documented/unknown/other	18 (9.8%)	12 (13.2%)	6 (6.5%)
Ethnicity (n, %)			
Hispanic	10 (5.4%)	4 (4.4%)	6 (6.5%)
Non-Hispanic	142 (77.2%)	69 (75.8%)	73 (78.5%)
Not documented/unknown/other	32 (17.4%)	18 (19.8%)	14 (15.1%)
Payer (n, %)			
Commercial	34 (18.5%)	16 (17.6%)	18 (19.4%)
Medicare/Medicaid	79 (42.9%)	39 (42.9%)	40 (43%)
Self-pay/other/unknown	71 (38.6%)	36 (39.6%)	35 (37.6%)
Year of treatment initiation (n, %)			
2018	8 (4.3%)	8 (8.8%)	0 (0%)
2019	13 (7.1%)	13 (14.3%)	0 (0%)
2020	17 (9.2%)	12 (13.2%)	5 (5.4%)
2021	22 (12%)	16 (17.6%)	6 (6.5%)
2022	23 (12.5%)	12 (13.2%)	11 (11.8%)
2023	37 (20.1%)	15 (16.5%)	22 (23.7%)
2024	30 (16.3%)	8 (8.8%)	22 (23.7%)
2025	34 (18.5%)	7 (7.7%)	27 (29%)
Disease stage at dx (n, %)			
I	5 (2.7%)	1 (1.1%)	4 (4.3%)
II	7 (3.8%)	3 (3.3%)	4 (4.3%)
III	33 (17.9%)	16 (17.6%)	17 (18.3%)
IV	118 (64.1%)	58 (63.7%)	60 (64.5%)
Not available/unknown	21 (11.4%)	13 (14.3%)	8 (8.6%)
Prior therapy			
CD20 monoclonal antibody	89 (48.4%)	43 (47.3%)	46 (49.5%)
Chemotherapy	71 (38.6%)	35 (38.5%)	36 (38.7%)
Proteasome inhibitor	4 (2.2%)	2 (2.2%)	2 (2.2%)
IMID	2 (1.1%)	1 (1.1%)	1 (1.1%)
BCL2i	0 (0%)	0 (0%)	0 (0%)
CAR T cell	12 (6.5%)	6 (6.6%)	6 (6.5%)
Other	6 (3.3%)	4 (4.4%)	2 (2.2%)

Abbreviations: BCL2i, B-cell lymphoma 2 inhibitor; dx, diagnosis; IQR, interquartile range; MCL, mantle cell lymphoma.

Real-World Effectiveness Outcomes

- Median TTD was 17.8 months (95% confidence interval [CI]: 14.7-not reached [NR]) for zanubrutinib and 9.6 months (95% CI: 6.5-15.4) for acalabrutinib (hazard ratio [HR, 95% CI]: 0.59 [0.4-0.87], *P*<.01) (**Figure 1**)
  - The primary reasons for discontinuation of zanubrutinib or acalabrutinib were unknown (10.8% vs 26.4%), toxicity (11.8% vs 11.0%), disease progression (6.5% vs 5.5%), and death (2.2% vs 4.4%), respectively (**Figure 2**)
- Median TTNT was 18.2 months (95% CI: 15.4-NR) for zanubrutinib and 15.4 months (95% CI: 9.6-26.6) for acalabrutinib (HR [95% CI]: 0.74 [0.49-1.11], *P*=.15) (**Figure 3**)
- The 12- and 18-month survival probabilities in the zanubrutinib group were 85% (77-93) and 75% (66-87), respectively, compared with 77% (68-86) and 69% (59-80) in the acalabrutinib group (HR [95% CI]: 0.78 [0.45-1.35], *P*=0.37) (**Table 2**)

Figure 1. Time to Discontinuation

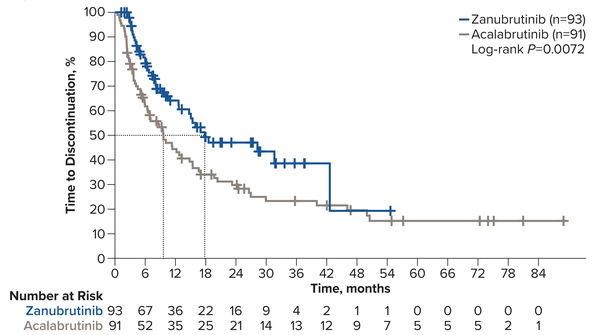
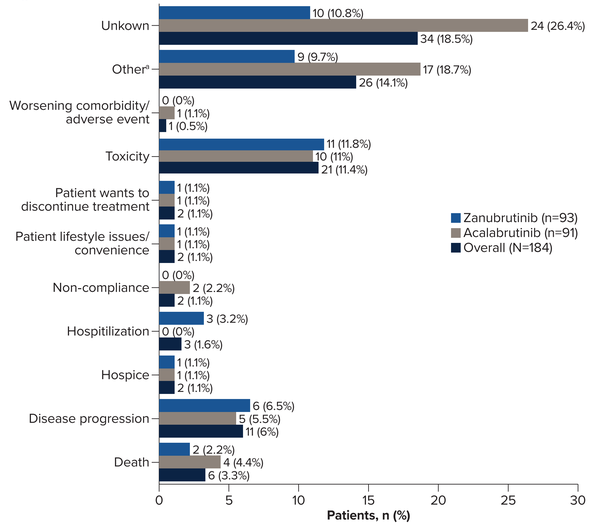


Figure 2. Reasons for Discontinuation



[a]Other refers to patient discharge and patient transfer care.
Abbreviations: 2L, second line; 3L, third line; AE, adverse event; BTKi, Bruton tyrosine kinase inhibitor.

Figure 3. Time to Next Treatment

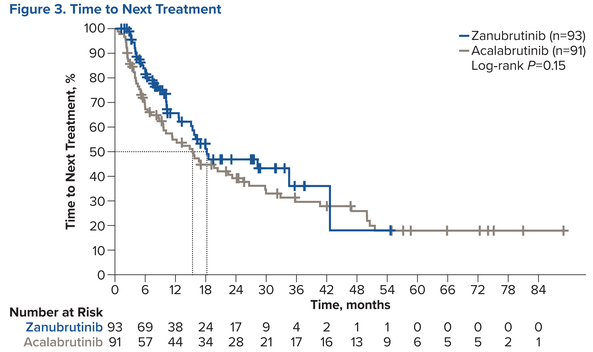


Figure 4. Overall Survival

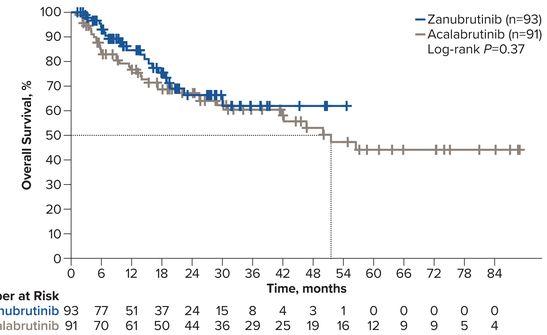


Table 2. Probability of Not Discontinuing Treatment, Not Advancing to the Next LoT, and Survival at 6, 12, 18, and 24 Months

		Zanubrutinib	Acalabrutinib (ref)
Time to discontinuation, % (95% CI)	6 months	80 (72-89)	62 (52-73)
	12 months	64 (54-76)	44 (35-56)
	18 months	49 (38-63)	34 (25-46)
	24 months	47 (36-61)	30 (21-42)
Time to next treatment, % (95% CI)	6 months	83 (75-91)	67 (58-78)
	12 months	66 (56-77)	55 (45-67)
	18 months	51 (40-65)	45 (35-57)
	24 months	47 (36-61)	39 (30-51)
Overall survival, months, % (95% CI)	6 months	93 (88-99)	83 (75-91)
	12 months	85 (77-93)	77 (68-86)
	18 months	75 (66-87)	69 (59-80)
	24 months	66 (55-80)	67 (58-78)

Abbreviation: LoT, line of treatment.

LIMITATIONS

- The results of this study should be interpreted cautiously considering the limitation of small sample size, and the variable follow-up time given the difference in regulatory milestones and clinical adoption
- This analysis was based on structured data, which may be subject to coding errors and incomplete or miscategorized capture of clinical information
- Data were sourced exclusively from the Integra network; information may be missing or incomplete for patients who left the network or received care elsewhere. For instance, the Integra Network captures electronic health record data from oncology-based practices, and comorbidities may not be adequately captured
- Results may not be generalizable to populations outside the Integra Network, to uninsured patients, or to patients treated outside of community hospitals in the US

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DISCLOSURES

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*CO-AUTHORSHIP
CORRESPONDENCE: Jing-Zhou Hou, houj@upmc.edu

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