Risk of Tumor Lysis Syndrome Among Patients With Chronic Lymphocytic Leukemia or Mantle Cell Lymphoma Treated With Venetoclax-Based Regimens: A Real-World Study

CLL-737

Alessandra Ferrajoli,[1] Lili Zhou,[2] Ayad K. Ali,[2] Gabriel Man,[2] Qianhong Fu,[2] Wassim Aldairy[2]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]BeOne Medicines, Ltd, San Carlos, CA, USA

CONCLUSIONS

- This real-world study reported the occurrence of TLS in patients treated with venetoclax and showed that TLS generally occurred shortly after treatment initiation
- The risk appeared to be relatively higher in patients with MCL (8.6%) than in those with CLL (5.6%)
- These findings underscore the importance of close monitoring during venetoclax therapy, particularly during the dose ramp-up period, and provide real-world evidence to inform TLS risk management in routine clinical practice

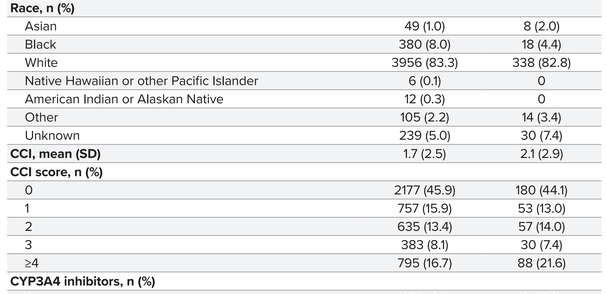
INTRODUCTION

- Tumor lysis syndrome (TLS) is a life-threatening oncological emergency caused by the rapid destruction of malignant cells and can result in renal failure, cardiac arrhythmias, or death[1]
- Venetoclax is a B-cell lymphoma 2 (BCL2) inhibitor that promotes apoptosis in BCL2-dependent cells by restoring activation of the intrinsic apoptotic pathway[2]
  - Consistent with its mechanism of action, venetoclax can induce rapid tumor cell death, thus contributing to the risk of TLS, an adverse event that has been observed in clinical trials[3,4]
- The incidence of TLS events in clinical trials of venetoclax in patients with B-cell malignancies ranged from 1.8% to 3.0%[5]
  - However, real-world data on TLS in patients treated with venetoclax remain limited
- Effective management of TLS relies on risk stratification, early detection, and prompt intervention[1]; therefore, a comprehensive understanding of TLS risk in real-world settings is essential
- This study aimed to describe the incidence of TLS in patients with chronic lymphocytic leukemia (CLL) or mantle cell lymphoma (MCL) treated with venetoclax in routine clinical practice in the United States

METHODS

- Deidentified data from patients with CLL or MCL who initiated venetoclax between April 11, 2016, and December 31, 2024, were identified from the TriNetX Dataworks-USA Network electronic health record database (**Figure 1**)
- Patient demographics, comorbidities, and concomitant medications were described
- The primary outcome was the 3-month TLS risk following venetoclax initiation
  - TLS was identified using two definitions
    1. The presence of *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)* diagnosis code E88.3
    2. Receipt of rasburicase treatment
  - Both laboratory and clinical TLS were identified using the specified definitions
  - A 3-month follow-up was selected to encompass the dose ramp-up period in patients with CLL or MCL
  - Time to event and follow-up were recorded
    - Follow-up was defined as the earliest recorded date of TLS, death, 3 months after index, loss to follow-up, or end of study period (ie, December 31, 2025)
  - Death was considered as a competing risk for the TLS outcome
- The secondary outcome was the cumulative incidence of mortality in patients experiencing TLS, defined as the presence of a TLS diagnosis within the same month as death or the month prior, with no trauma-related diagnosis recorded during the same period
  - Death due to causes other than TLS was treated as a competing event

Figure 1. Patient Attrition Flowchart



[a]The earliest date of venetoclax treatment was identified as the index date.
Abbreviations: CLL, chronic lymphocytic leukemia; *ICD-9, International Classification of Diseases, Ninth Revision; ICD-10, International Classification of Diseases, Tenth Revision; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; ICD-O, International Classification of Diseases for Oncology;* MCL, mantle cell lymphoma; TLS, tumor lysis syndrome.

RESULTS

Baseline Demographics and Characteristics of Patients who Initiated Venetoclax

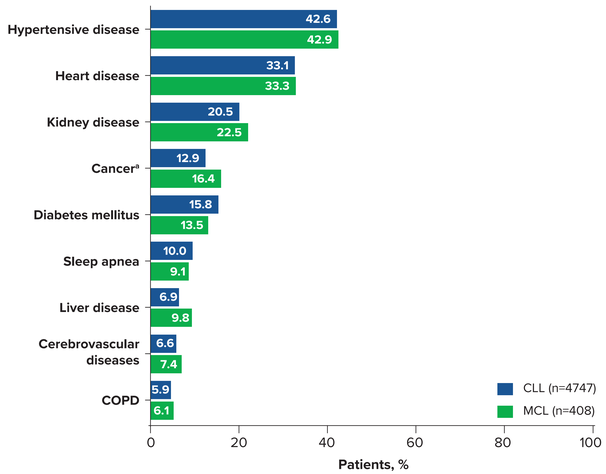
- A total of 4747 patients with CLL and 408 patients with MCL initiated venetoclax therapy and were included in this analysis (**Table 1**)
- Among patients with CLL, 68.7% were aged ≥65 years; among those with MCL, 67.2% were aged ≥65 years
  - Most were White (CLL, 83.3%; MCL, 82.8%) and male (CLL, 66.3%; MCL, 71.1%)
- Approximately 54.1% of patients with CLL and 55.9% of patients with MCL had Charleson Comorbidity Index of ≥1
- The most common comorbidity was hypertensive disease (CLL, 42.6%; MCL, 42.9%) (**Figure 2**)
- Venetoclax was administered in combination with either rituximab or obinutuzumab in 44.3% and 40.7% of patients with CLL and MCL, respectively
- Baseline antihyperuricemic prophylaxis with either allopurinol or febuxostat was observed in 58.2% of patients with CLL and 63.7% of patients with MCL

Table 1. Baseline Characteristics

	Patients with CLL (n=4747)	Patients with MCL (n=408)
Age, median (IQR), years	69 (62-76)	69 (62-76)
Male sex, n (%)	3148 (66.3)	290 (71.1)
Race, n (%)		
Asian	49 (1.0)	8 (2.0)
Black	380 (8.0)	18 (4.4)
White	3956 (83.3)	338 (82.8)
Native Hawaiian or other Pacific Islander	6 (0.1)	0
American Indian or Alaskan Native	12 (0.3)	0
Other	105 (2.2)	14 (3.4)
Unknown	239 (5.0)	30 (7.4)
CCI, mean (SD)	1.7 (2.5)	2.1 (2.9)
CCI score, n (%)		
0	2177 (45.9)	180 (44.1)
1	757 (15.9)	53 (13.0)
2	635 (13.4)	57 (14.0)
3	383 (8.1)	30 (7.4)
≥4	795 (16.7)	88 (21.6)
CYP3A4 inhibitors, n (%)		
Strong	288 (6.1)	31 (7.6)
Moderate	1205 (25.4)	154 (37.7)
Treatment type, n (%)		
Venetoclax monotherapy	2643 (55.7)	242 (59.3)
Venetoclax in combination with rituximab or obinutuzumab[a]	2104 (44.3)	166 (40.7)
Allopurinol or febuxostat prophylaxis, n (%)	2765 (58.2)	260 (63.7)

[a]Identified as any use of rituximab or obinutuzumab within 120 days before or after the index date.
Abbreviations: CCI, Charleson Comorbidity Index; CLL, chronic lymphocytic leukemia; MCL, mantle cell lymphoma.

Figure 2. Baseline Comorbidities With a Prevalence ≥5%

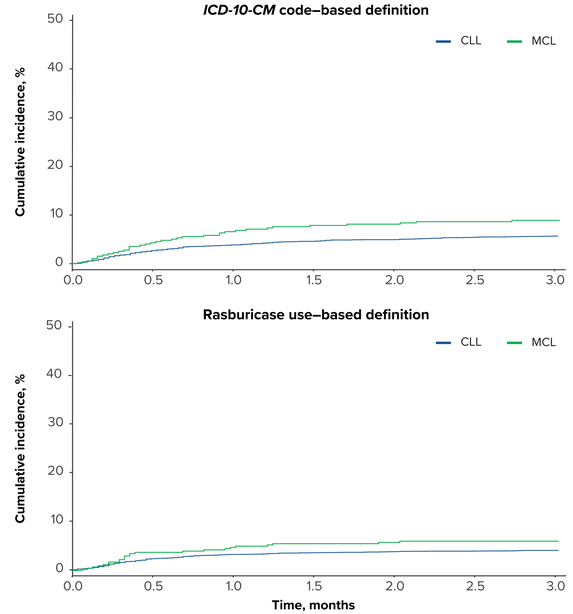


[a]Excluding B-cell malignancies.
Abbreviations: CLL, chronic lymphocytic leukemia; MCL, mantle cell lymphoma; COPD, chronic obstructive pulmonary disease.

TLS and Mortality in Patients With TLS Following Venetoclax Treatment

- The cumulative incidence of TLS with death as a competing event in both patients with CLL and MCL is displayed in **Figure 3**

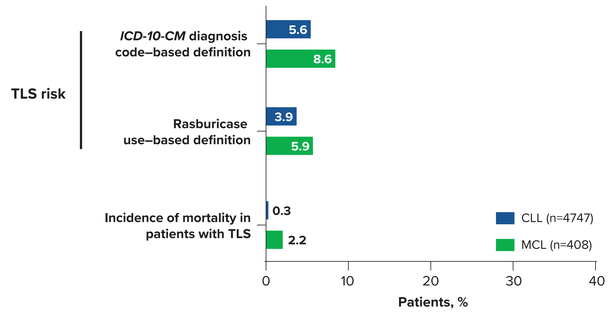
Figure 3. Cumulative Incidence of TLS



Abbreviations: CLL, chronic lymphocytic leukemia; *ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification;* MCL, mantle cell lymphoma; TLS, tumor lysis syndrome.

- Using the *ICD-10-CM* diagnosis code–based definition, TLS occurred within 3 months of venetoclax initiation in 5.6% of patients with CLL and 8.6% of patients with MCL (**Figures 4**)
  - Median time to onset was 17 and 16 days, respectively (**Table 2**)
- Using the definition based on rasburicase use, TLS incidence was 3.9% in patients with CLL and 5.9% in patients with MCL
  - Median time to onset was 13.5 and 10.5 days, respectively
- All-cause mortality occurred in 0.3% (n=12) of patients with CLL and 2.2% (n=9) of patients with MCL who were identified as having TLS
  - Median time to mortality was 47 and 43 days after the start of therapy with venetoclax, respectively

Figure 4. TLS Risk and Incidence of Mortality in Patients With TLS



Abbreviations: CLL, chronic lymphocytic leukemia; *ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification;* MCL, mantle cell lymphoma; TLS, tumor lysis syndrome.

Table 2. Summary of TLS Outcomes

3-month TLS risk	Patients with CLL (n=4747)	Patients with MCL (n=408)
***ICD-10-CM* diagnosis code–based definition**		
Time to event, median (IQR), days	17.0 (7.0-37.0)	16.0 (8.0-31.0)
Incidence rate (95% CI), events per 100 patient-months	2.0 (1.8-2.3)	3.4 (2.4-4.7)
Rasburicase use–based definition		
Time to event, median (IQR), days	13.5 (7.0-26.0)	10.5 (7.0-29.5)
Incidence rate (95% CI), events per 100 patient-months	1.4 (1.2-1.6)	2.3 (1.5-3.4)
Incidence of mortality in patients with TLS[a]		
Time to event, median (IQR), days	47.0 (36.0-59.5)	43.0 (29.0-50.0)
Incidence rate (95% CI), events per 100 patient-months	0.1 (0.1-0.2)	0.8 (0.4-1.6)

[a]Includes all-cause mortality; cause of death was not available in the data source.
Abbreviations: CLL, chronic lymphocytic leukemia; *ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification;* MCL, mantle cell lymphoma; TLS, tumor lysis syndrome.

REFERENCES

1. Zivin SP, et al. *Semin Intervent Radiol.* 2015;32(1):3-9.
2. Lew TE, Seymour JF. *J Hematol Oncol.* 2022;15(1):75.
3. Roberts AW, et al. *N Engl J Med.* 2016;374(4):311-322.
4. Seymour JF, et al. *Lancet Oncol.* 2017;18(2):230-240.
5. Seymour JF, et al. *Blood.* 2020;136(suppl 1). Abstract 2231.

ACKNOWLEDGMENTS

This study was sponsored by BeOne Medicines, Ltd. Medical writing support was provided by Amy Ryan, PhD, of Nucleus Global, an Inizio company, and supported by BeOne Medicines.

DISCLOSURES

AF: Payment for educational event: AstraZeneca; Participation on a Data Safety Monitoring Board or Advisory Board: AstraZeneca, BeOne Medicines, Ltd. **LZ:** Employment and may own stock: BeOne Medicines, Ltd. **AKA:** Employment and owns stock: BeOne Medicines, Ltd. **GM:** Employment and may own stock: BeOne Medicines, Ltd. **QF:** Employment and owns stock: BeOne Medicines, Ltd (self), AbbVie (spouse). **WA:** Employment and may own stock: BeOne Medicines, Ltd.

CORRESPONDENCE: Alessandra Ferrajoli, aferrajo@mdanderson.org

Presented at the 2026 Society of Hematologic Oncology (SOHO) Annual Congress; September 9-12, 2026; Houston, TX, USA