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Risk of Tumor Lysis Syndrome (TLS) Among Patients With Chronic Lymphocytic Leukemia (CLL) or Mantle Cell Lymphoma (MCL) Treated With Venetoclax: A Real-World Study

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CONTEXT: Venetoclax, a BCL2 inhibitor, has been associated with TLS in clinical trials, with incidence ranging from 1.8%-3.0%. However, data on TLS among patients receiving venetoclax in routine clinical practice are limited.

OBJECTIVE: To describe the real-world incidence of TLS among patients with CLL or MCL treated with venetoclax in the US.

DESIGN: Deidentified data from patients initiating venetoclax from 4/2016-12/2024 were identified within the TriNetX Dataworks-USA Network electronic health record database. A 3-month follow-up was selected to encompass the dose ramp-up period. TLS was identified by the presence of *ICD-10-CM* diagnosis code E88.3 or receipt of rasburicase treatment.

MAIN OUTCOMES: The primary outcome was 3-month TLS risk following venetoclax initiation. The secondary outcome was incidence of all-cause mortality in patients experiencing TLS, defined as presence of TLS diagnosis within the same month as death or the month prior, with no trauma-related diagnosis recorded during the same period.

RESULTS: 4747 patients with CLL and 408 with MCL initiated venetoclax therapy. Of patients with CLL, 68.7% were aged ≥65 years; 54.1% had ≥1 comorbidity. Of those with MCL, 67.2% were aged ≥65 years; 55.9% had ≥1 comorbidity. Venetoclax was administered in combination with rituximab or obinutuzumab in 44.3% of patients with CLL and 40.7% with MCL; antihyperuricemic prophylaxis (allopurinol or febuxostat) was administered in 58.2% and 63.7%, respectively. Among patients identified according to *ICD-10* code, TLS incidence within 3 months of venetoclax initiation was 5.6% and 8.6% in patients with CLL and MCL, respectively (median time to onset, 17 and 16 days). Among patients identified based on rasburicase use, TLS incidence was 3.9% and 5.9%, respectively (median time to onset, 14 and 11 days). In patients who had TLS, all-cause mortality occurred in 0.3% (MCL) and 2.2% (CLL) at a median time of 47 and 43 days.

CONCLUSIONS: This real-world study demonstrated that TLS risk was common among patients receiving venetoclax and generally occurred shortly after treatment initiation. Risk appeared to be relatively higher among patients with MCL vs CLL. These findings underscore the importance of close monitoring during venetoclax therapy, particularly during dose ramp-up. Adapted from ©EHA2026.