

Risk of infections in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) receiving first-line treatment: a real-world study

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ABSTRACT

Background: Patients with CLL/SLL are at increased risk for infections due to treatment-related immunosuppression and disease-related immune dysregulation. As covalent Bruton tyrosine kinase inhibitors (cBTKi) become widely used in the first-line setting, it is important to understand their impact on infection risk.

Methods: We conducted a retrospective cohort study of patients with previously untreated CLL/SLL (Jan 2019-Dec 2024) using the Symphony Health Solutions database. Patients were categorized into three groups based on management: (1) cBTKi as monotherapy (ibrutinib, acalabrutinib, or zanubrutinib), (2) chemotherapy/immunotherapy (CIT), and (3) observation. The primary outcomes were 24-month incidence rates of infections, including overall (non-COVID-19) infections, serious infections, shingles, COVID-19, invasive fungal infections, and pneumonia. Infection rates among the groups were compared using Chi-square tests, with statistical significance set at $p < .05$. Additionally, we recorded the rate of shingles vaccination in patients aged ≥ 65 years.

Results: Among 112,966 patients included in this study, 15,565 received cBTKi monotherapy, 15,463 received CIT, and 81,938 remained on observation. Mean age was similar across groups (68-69 years), with a male predominance (55-59%). The incidence of non-COVID-19 infections was higher in the CIT (36.4%) versus both cBTKi (28.1%; OR 1.46, 95% CI 1.39-1.53; $p < .0001$) and observation (28.1%; OR 1.46, 95% CI 1.41-1.51; $p < .0001$). Serious infections were also more frequent with CIT (11.7%) compared to cBTKi (6.0%; OR 2.05, 95% CI 1.87-2.23) and observation (7.6%; OR 1.59, 95% CI 1.51-1.69; all $p < .0001$). Pneumonia (18.0% in CIT vs 14.1% in cBTKi and 11.9% in observation; OR 1.34 vs cBTKi, 1.63 vs observation) and COVID-19 infections (14.1% vs 11.2% and 10.8%; OR 1.30 vs cBTKi, 1.36 vs observation) were more frequent in the CIT group (all $p < .0001$). Invasive fungal infections were rare ($< 1\%$ in all groups). Shingles vaccination among patients aged ≥ 65 years remained low across all groups (17.6% cBTKi vs 18.1% in CIT vs 19.6% in observation).

Conclusions: In this large real-world study, the rates of overall infections and serious infections at 24 months were lower in patients treated with cBTKi and in patients on observation when compared to patients treated with CIT.