Serious infections in patients with CLL/SLL treated with combination venetoclax and obinutuzumab compared with those treated with zanubrutinib: a real-world study

Authors: Nicole Lamanna[1], Jamie Colasurdo,[2] Lili Zhou,[2] Wassim Aldairy,[2] Qianhong Fu,[2] Shaohui Sun,[3] Jiazheng Zhang,[3] Ayad K. Ali[2]

Affiliations: [1]Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY; [2]BeiGene USA, Inc, San Mateo, CA; [3]BeiGene (Beijing) Co, Ltd, Beijing, China

Background: Given the compromised immune systems of patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), there has always been concern about the association between CLL/SLL-directed therapies and serious infection risks, prompting the need for treatments with lower risks.

Aims: Using the Symphony Health Solutions database, this real-world study described and compared the rates of serious infections 12 and 18 months following the initiation of venetoclax + obinutuzumab (VO) and zanubrutinib in patients with CLL/SLL.

Methods: Patients diagnosed with CLL/SLL who received VO from Apr 2016 to Aug 2022 or zanubrutinib from Nov 2019 to Aug 2023 were included. For the VO cohort, patients were required to have initiated obinutuzumab within 90 days after first venetoclax prescription. The index date was defined as the date of the first venetoclax prescription in the VO cohort and the first zanubrutinib prescription in the zanubrutinib cohort. Given the inherent differences between time-limited and continuous therapy, the proportions of serious infections were evaluated at 12- and 18-month follow-up periods after treatment initiation. Serious infections were defined by the use of intravenous antibiotics/antivirals within 15 days during hospitalization. Inverse probability of treatment weighting (IPTW) Cox proportional hazards models were used to balance baseline confounders (age, sex, race and ethnicity, Charlson Comorbidity Index, and region) between VO and zanubrutinib cohorts and to compare hazard ratios (HRs).

Results: A total of 2,104 patients with CLL/SLL received VO, and 2,650 patients received zanubrutinib. During the 12-month follow-up, 7.9% of the VO cohort and 4.8% of the zanubrutinib cohort developed serious infections. Compared with zanubrutinib-treated patients, those treated with VO had a higher risk of serious infections (HR, 1.57; 95% CI, 1.23-1.99). The proportions and risks of serious infections were also higher in the VO cohort vs the zanubrutinib cohort during the 18-month follow-up (10.1% vs 5.6%; HR, 1.72; 95% CI, 1.38-2.13). Kaplan-Meier curves demonstrated a consistently higher proportion of serious infections in the VO cohort vs the zanubrutinib cohort.

Summary/Conclusion: This real-world study showed that patients diagnosed with CLL/SLL treated with VO had a higher risk of serious infections than those treated with zanubrutinib. In patients with a higher risk of infections, zanubrutinib could be considered as a treatment option in lieu of VO.

Table. Serious Infections During 12- and 18-Month Follow-Up Period

	Venetoclax + Obinutuzumab (n=2,104)	Zanubrutinib (n=2,650)
12-month follow-up		
n (%)	167 (7.9)	128 (4.8)
Event rate (per 100 patient-months) (95% CI)	0.70 (0.60-0.81)	0.42 (0.35-0.49)
IPTW-weighted HR (95% CI)	1.57 (1.23-1.99)	Reference
18-month follow-up		
n (%)	212 (10.1)	149 (5.6)
Event rate (per 100 patient-months) (95% CI)	0.60 (0.52-0.69)	0.34 (0.28-0.40)
IPTW-weighted HR (95% CI)	1.72 (1.38-2.13)	Reference