Risk of Infections in Patients With Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma Receiving First-Line Treatment: A Real-World Study

CLL-756

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

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

CONCLUSIONS

- In this large real-world study, patients treated with covalent BTK inhibitors or managed with observation experienced lower rates of overall and serious infections at 24 months compared with those receiving CIT
- The shingles vaccination rate in patients with CLL/SLL was low (≈15%, regardless of treatment type) vs that in the general population (≈30%)[1]
- These data suggest that covalent BTK inhibitors may offer a more favorable safety profile compared with CIT; additionally, shingles vaccination rates remain suboptimal across all treatments and education efforts are needed to improve vaccination rates in patients with CLL/SLL

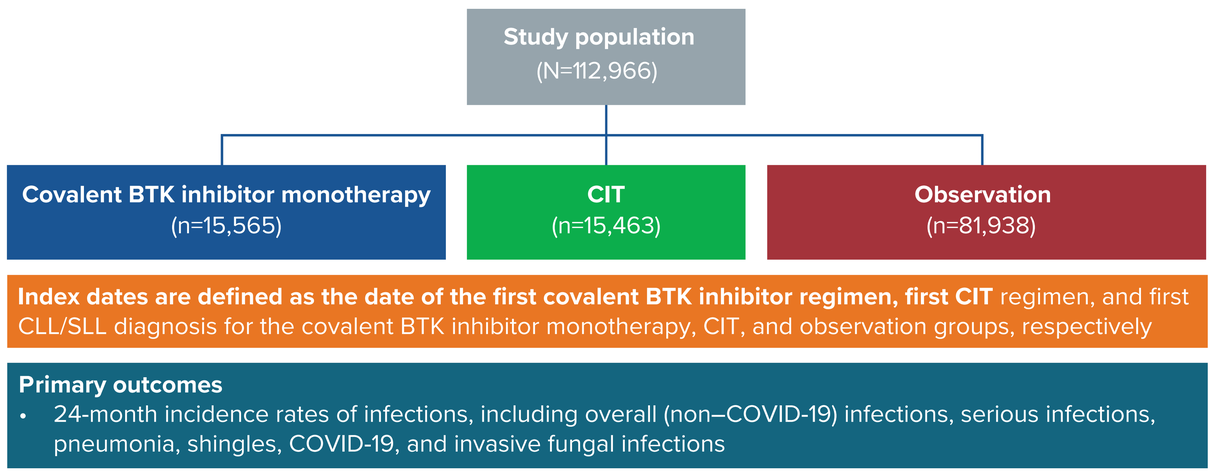
INTRODUCTION

- Patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) are at an increased risk of infections due to treatment-related immunosuppression and disease-related immune dysregulation[2]
- As covalent Bruton tyrosine kinase (BTK) inhibitors become widely used in the first-line (1L) setting, it is important to understand their impact on infection risk[2,3]
- This real-world study described and compared the rates of infections at 24 months following the initiation of covalent BTK inhibitors, chemotherapy/immunotherapy (CIT), or no treatment (observation only) in patients with CLL/SLL

METHODS

- A retrospective cohort study of patients with CLL/SLL (January 2019-December 2024) was conducted using the Symphony Health Solutions database
- The Symphony Health Solutions database contains deidentified and tokenized information that allows linkage of patient-level data from various sources, such as hospital claims, physician offices, and prescription data, with record dates as recent as 1 month prior
- Patients were categorized into three groups based on the management of their CLL/SLL (**Figure 1**)
  1. **1L covalent BTK inhibitor monotherapy:** ibrutinib, acalabrutinib, or zanubrutinib
  2. **1L CIT:** chemotherapies (eg, bendamustine, chlorambucil) or immunotherapies (eg, anti-CD20 or anti-CD52 antibodies)
  3. **Observation:** Watch and Wait (no CLL/SLL-directed therapies after cancer diagnosis)
- The primary outcomes were 24-month incidence rates of infections, including overall (non–COVID-19) infections, serious infections, pneumonia, shingles, COVID-19, and invasive fungal infections
- Overall (non–COVID-19) infections, pneumonia, shingles, COVID-19, and invasive fungal infections were defined as infections that had at least one medical encounter related to the respective condition; serious infections were defined as infections treated with intravenous antibiotics or antivirals during hospitalization
- Infection rates in the groups were compared using χ^2 tests, with statistical significance set at $P<.05$; odds ratio (OR) was also calculated
- The rate of shingles vaccination history was assessed in the overall patient population as well as in those aged ≥50 and ≥65 years, respectively

Figure 1. Study Design



Abbreviations: BTK, Bruton tyrosine kinase; CIT, chemotherapy/immunotherapy; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma.

RESULTS

Baseline Demographics

- Of 112,966 patients included in this study, 15,565 received covalent BTK inhibitor monotherapy, 15,463 received CIT, and 81,938 remained on observation
- Baseline demographics are shown in **Table 1**
  - Mean age was similar across groups (68-69 years), with a male predominance (55%-59%)
  - Approximately 20% of patients had missing data for race/ethnicity; of those with available data, the majority were non-Hispanic White (82%-84%)

Table 1. Baseline Demographics

	Covalent BTK inhibitor monotherapy (n=15,565)	CIT (n=15,463)	Observation (n=81,938)
Age at index date, years			
Mean (SD)	69 (8.2)	68 (9.2)	68 (9.0)
Median	72	71	72
Sex, n (%)			
Female	6317 (40.6)	6745 (43.6)	37,273 (45.5)
Male	9248 (59.4)	8718 (56.4)	44,665 (54.5)
Race and ethnicity, n (%)	**(n=12,415)**	**(n=12,166)**	**(n=64,343)**
White, non-Hispanic	10,308 (83.0)	10,165 (83.6)	54,561 (81.8)
Black, non-Hispanic	1250 (10.1)	1030 (8.5)	5154 (8.0)
Asian, non-Hispanic	193 (1.6)	179 (1.5)	900 (2.4)
Hispanic	627 (5.1)	749 (6.2)	3535 (5.5)

Fewer than 1% of the values for age and sex are missing.
Abbreviations: BTK, Bruton tyrosine kinase; CIT, chemotherapy/immunotherapy.

Incidence of Infections

- The 24-month incidence rates of infections are shown in **Table 2**
  - The incidence of non–COVID-19 infections was higher in the CIT group (36.4%) vs both the covalent BTK inhibitor group (28.1%; OR, 1.46; 95% CI, 1.39-1.53; $P<.0001$) and observation group (28.1%; OR, 1.46; 95% CI, 1.41-1.51; $P<.0001$)
  - The cumulative incidence curve also showed that non–COVID-19 infections were consistently highest in the CIT group, followed by the covalent BTK inhibitor and observation groups (**Figure 2**)
  - Serious infections were also more frequent with CIT (11.7%) compared with covalent BTK inhibitor monotherapy (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 $P<.0001$), consistent with the cumulative incidence curve (**Figure 3**)
  - Pneumonia (18.0% with CIT vs 14.1% with covalent BTK inhibitor and 11.9% with observation) and COVID-19 infections (14.1% vs 11.2% and 10.8%, respectively) were more frequent in the CIT group (all $P<.0001$); invasive fungal infections were rare (<1%) in all groups

Shingles Vaccination History

- Shingles vaccination rates were low across all groups (14.5% in the covalent BTK inhibitor group, 14.8% in the CIT group, 16.1% in the observation group; **Table 3**)
  - In patients aged ≥65 years, the rate remained low (17.6%, 18.1%, and 19.6% in the covalent BTK inhibitor, CIT, and observation groups, respectively)

Table 2. Infection Rates at the 24-Month Follow-Up

	Covalent BTK inhibitor monotherapy (n=15,565)	CIT (n=15,463)	Observation (n=81,938)	OR (CIT vs covalent BTK inhibitor)	OR (CIT vs observation)
Overall infections, excluding COVID-19, n (%)	4376 (28.1)	5632 (36.4)	23,053 (28.1)	1.46 (95% CI, 1.40-1.54); $P<.0001$	1.46 (95% CI, 1.41-1.52); $P<.0001$
Serious infections, n (%)	937 (6.0)	1801 (11.7)	6245 (7.6)	2.06 (95% CI, 1.90-2.23); $P<.0001$	1.60 (95% CI, 1.51-1.69); $P<.0001$
Pneumonia	2195 (14.1)	2784 (18.0)	9739 (11.9)	1.34 (95% CI, 1.26-1.42); $P<.0001$	1.63 (95% CI, 1.55-1.70); $P<.0001$
COVID-19	1745 (11.2)	2177 (14.1)	8838 (10.8)	1.30 (95% CI, 1.21-1.39); $P<.0001$	1.36 (95% CI, 1.29-1.43); $P<.0001$
Shingles	360 (2.3)	518 (3.4)	1499 (1.8)	1.46 (95% CI, 1.28-1.68); $P<.0001$	1.86 (95% CI, 1.68-2.06); $P<.0001$
Invasive fungal infection	115 (0.7)	144 (0.9)	316 (0.4)	1.26 (95% CI, 0.99-1.62); $P=.0625$	2.43 (95% CI, 1.99-2.96); $P<.0001$

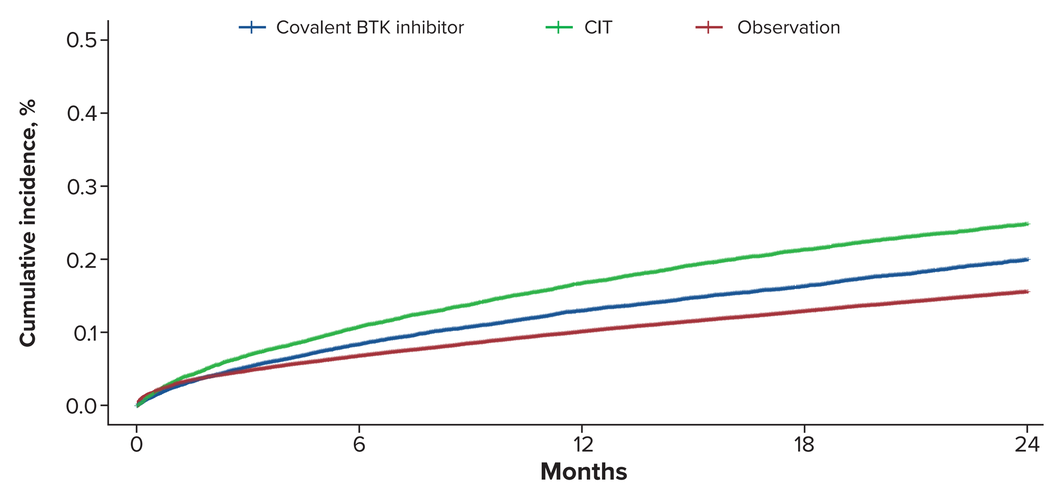
Abbreviations: BTK, Bruton tyrosine kinase; CIT, chemotherapy/immunotherapy; OR, odds ratio.

Table 3. Shingles Vaccine History

	Covalent BTK inhibitor monotherapy (n=15,565)	CIT (n=15,463)	Observation (n=81,938)
Received shingles vaccine, n (%)			
Overall	2250 (14.5)	2295 (14.8)	13,195 (16.1)
Aged ≥50 years	2247 (14.8)	2290 (15.5)	13,187 (16.8)
Aged ≥65 years	2036 (17.6)	2033 (18.1)	11,757 (19.6)

Shingles vaccination was identified from either procedure code 90750, 90736, or 90396 or the product names Shingrix or Zostavax within 1 year prior to index date.
Abbreviations: BTK, Bruton tyrosine kinase; CIT, chemotherapy/immunotherapy.

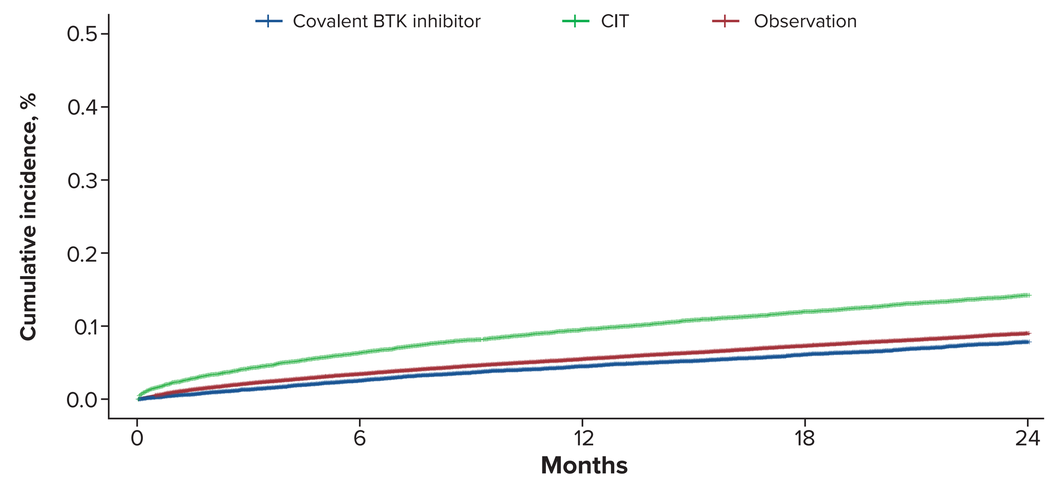
Figure 2. Cumulative Incidence Curve of Non–COVID-19 Infections



No. at risk					
Covalent BTK inhibitor	15,565	12,328	10,097	8578	6966
CIT	15,463	12,229	10,066	8197	6675
Observation	81,938	70,672	61,321	51,965	43,040

Abbreviations: BTK, Bruton tyrosine kinase; CIT, chemotherapy/immunotherapy.

Figure 3. Cumulative Incidence Curve of Serious Infections



No. at risk					
Covalent BTK inhibitor	15,565	12,937	10,813	9329	7700
CIT	15,463	12,581	10,564	8724	7185
Observation	81,938	72,436	63,215	53,805	44,711

Abbreviations: BTK, Bruton tyrosine kinase; CIT, chemotherapy/immunotherapy.

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DISCLOSURES

VB: No disclosures; **LZ, WA:** Employment and may own stock: BeOne Medicines Ltd; **AKA:** Employment and owns stock: BeOne Medicines Ltd; **QF:** Employment and may own stock: BeOne Medicines Ltd, Amgen, AbbVie; **AF:** Consulting or advisory role: Janssen, AstraZeneca, BeOne Medicines Ltd, Genentech; Research funding: GenMab, Genentech, Lilly.

CORRESPONDENCE: Vanthana Bharathi, VBharathi@mdanderson.org

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