REAL-WORLD TREATMENT PATTERNS, ADHERENCE AND HEALTHCARE RESOURCE UTILIZATION FOR CHRONIC LYMPHOCYTIC LEUKEMIA /SMALL LYMPHOCYTIC LYMPHOMA AMONG VETERANS IN THE UNITED STATES

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BACKGROUND

- Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) are the most common types of leukemia in adults in the US
- The US veteran population, predominantly older males, are at high risk for CLL/SLL, especially with prior exposure to Agent Orange or other herbicides during military service
- With the increasing availability of novel agents and associated improved survival, there is a need to assess the real-world evidence of CLL/SLL burden in US veterans, and the clinical and economic outcomes associated with current treatments

OBJECTIVE

- To examine the clinical burden, costs and healthcare resource utilization of US veterans with CLL/SLL

METHODS

- **Study design:** Retrospective, observational study
- **Data source:** Veteran Health Administration dataset
- **Study period**: October 2014 - September 2019
- **Study population:**
  - Adults who were newly diagnosed with CLL/SLL
  - Index date: the first CLL/SLL diagnosis date during the identification period (April 2014 - July 2018)
  - Aged ≥18 years at index date
  - ≥2 diagnosis of CLL/SLL (ICD-9-CM: 204.1, 200.8 or ICD-10-CM: C91.1, C83.0) on different days during the identification period
  - Continuous enrollment of 6 months pre- and 3 months post-index date
  - ≥ 1 CLL/SLL treatment on or after the index date
  - No CLL/SLL treatment any time prior to the index date

- **Treatment regimens and patterns:**
  - Classified according to NCCN guidelines and identified using HCPCS and NDC codes
  - 5 mutually exclusive categories of CLL/SLL treatment regimen:
    - **Bendamustine-based (alone or in combination) therapy**
    - **Other chemotherapies**
    - **Ibrutinib**
    - **Rituximab-monotherapy**
    - **Other regimens**
  - Treatment patterns evaluated by frequency and duration of treatment regimen, and by lines of therapy

- **Adherence:**
  - <u>Treatment duration:</u> The total number of days from the first day of a line of therapy to the last drug prescription date, plus derived days of supply for injectable drugs or days of supply for oral drugs of the respective line of therapy
  - <u>Discontinuation:</u> Defined as a treatment gap of more than 90 days from the last day of supply
  - <u>Switching:</u> Any new WM treatment >60 days after the start of a line of therapy
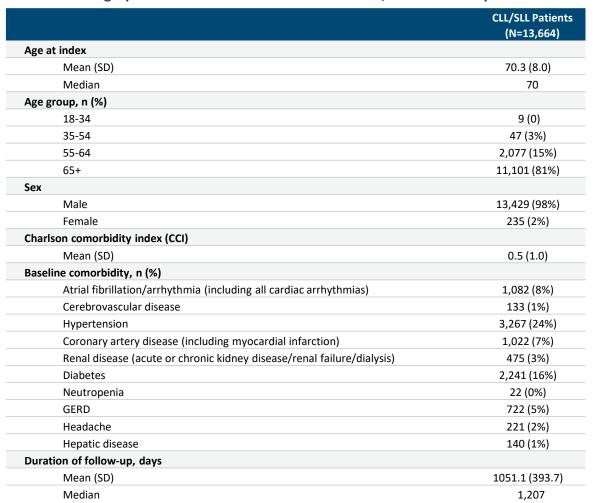
- **Economic outcomes:**
  - Healthcare resource utilization: Frequency and duration of inpatient hospital admissions, outpatient visits, and pharmacy visits
  - Total costs: Calculated as the sum of inpatient, outpatient, and pharmacy costs per-patient-per-month (PPPM)

RESULTS

- **Patient characteristics:**
  - Of 13,664 veteran patients diagnosed with CLL/SLL, 79% were in watch-and-wait
  - Final study population consisted of 2,861 patients who received ≥1 line of CLL/SLL therapy (mean duration = 465 days)
  - Most patients were elderly (median age= 70 years), white (83%), and male (98%)
  - Approximately 39% of veterans had concurrent use of proton pump inhibitors at baseline

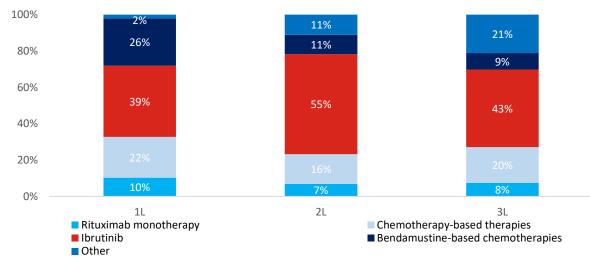**Table 1. Demographic and Clinical Characteristics of CLL/SLL Patient Population**

	CLL/SLL Patients (N=13,664)
Age at index	
Mean (SD)	70.3 (8.0)
Median	70
Age group, n (%)	
18-34	9 (0)
35-54	47 (3%)
55-64	2,077 (15%)
65+	11,101 (81%)
Sex	
Male	13,429 (98%)
Female	235 (2%)
Charlson comorbidity index (CCI)	
Mean (SD)	0.5 (1.0)
Baseline comorbidity, n (%)	
Atrial fibrillation/arrhythmia (including all cardiac arrhythmias)	1,082 (8%)
Cerebrovascular disease	133 (1%)
Hypertension	3,267 (24%)
Coronary artery disease (including myocardial infarction)	1,022 (7%)
Renal disease (acute or chronic kidney disease/renal failure/dialysis)	475 (3%)
Diabetes	2,241 (16%)
Neutropenia	22 (0%)
GERD	722 (5%)
Headache	221 (2%)
Hepatic disease	140 (1%)
Duration of follow-up, days	
Mean (SD)	1051.1 (393.7)
Median	1,207

Abbreviations: GERD, gastroesophageal reflux disease; SD, standard deviation;

- **Treatment patterns:**
  - Average time to treatment initiation from diagnosis to first-line therapy was 315 days
  - 770 (26.9%) patients who received first-line (1L) therapy further received second-line (2L) therapy (mean duration of treatment=318 days), and 199 (7.0%) patients received third-line (3L) therapy (mean duration of treatment=229 days)
  - Ibrutinib was the most common treatment regimen across all lines of therapy (1L: 39%; 2L: 55%; 3L: 43%) (**Figure 1**)

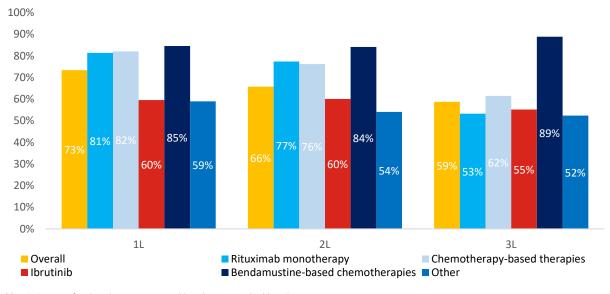**Figure 1. Treatment Patterns Among CLL/SLL patients by Line of Therapy**

Abbreviations: 1L, first-line therapy; 2L, second-line therapy; 3L, third-line therapy

RESULTS

- **Treatment discontinuation:**
  - Overall, treatment discontinuation rates were high across current regimens in each line of therapy (1L: 73% [mean duration: 354 days], 2L: 66% [mean duration: 241 days], 3L: 59% [mean duration:190 days]) (**Figure 2**)
  - Discontinuation rates were generally highest for bendamustine-based chemotherapies, with 85%, 84% and 89% discontinuing in 1L, 2L, and 3L, respectively
  - Ibrutinib accounts for over half of total patient discontinuations during treatment; discontinuation rates at 60%, 60%, and 55% in 1L, 2L, and 3L, respectively
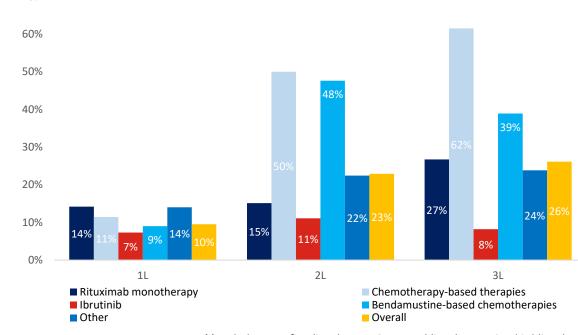
Figure 2. Treatment Discontinuation Rates by Line of Therapy

Abbreviations: 1L, first-line therapy; 2L, second-line therapy; 3L, third-line therapy

- **Treatment switch:** The overall treatment switching rate was highest in 3L (26%), followed by 23% in 2L and 10% in 1L therapies (**Figure 3**)

Figure 3. Treatment Switch Rates by Line of Therapy

Abbreviations: 1L, first-line therapy; 2L, second-line therapy; 3L, third-line therapy
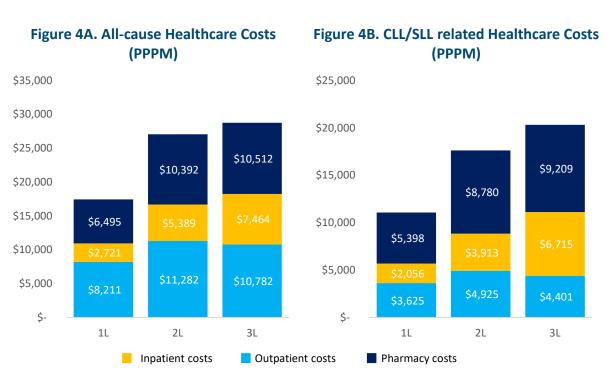
- **Healthcare resource utilization and costs:**
  - The CLL/SLL-related hospitalization rate was 39%, with an average LOS of 7 days (**Table 2**)
  - Total PPPM all-cause- and CLL/SLL-related costs were $26,709 and $17,233, respectively; these costs were increased by line of therapy (**Figure 4A and Figure 4B**)
  - Controlling for patient clinical and demographic covariates, treatment discontinuation and treatment switching were statistically significant predictors of higher inpatient admissions and LOS of hospitalizations

RESULTS

Table 2. All-Cause Health Resource Utilization

Frequency (Per-Patient Per-Month)	Overall Treated (N=2,861)	1L (n=2,861)	2L (n=770)	3L (n=199)
Outpatient visits (Mean ± SD)	7.69 ± 5.07	5.62 ± 2.74	6.07 ± 5.58	6.19 ± 3.06
Inpatient admissions (Mean ± SD)	0.05 ± 0.30	0.02 ± 0.18	0.07 ± 0.43	0.08 ± 0.37
Pharmacy visits (Mean ± SD)	5.74 ± 5.06	4.05 ± 3.06	4.93 ± 4.40	5.19 ± 4.00
Duration of hospitalization (Length of stay, days) (Mean ± SD)	1.04 ± 3.66	0.64 ± 2.71	1.14 ± 3.78	1.46 ± 4.80

Figure 4A. All-cause Healthcare Costs (PPPM)

Figure 4B. CLL/SLL related Healthcare Costs (PPPM)

DISCUSSION

- This study evaluated the real-world utilization of treatment regimens by line of therapy in newly diagnosed CLL/SLL patients in the US. Results reflected the variation of real-world treatment patterns from clinical treatment guidelines
- Study limitations were inherent to the use of claims databases in an observational study design
- Future studies are needed to further understand factors associated with treatment selection and outcomes

CONCLUSION

- **This real-world data demonstrated significant clinical and economic burden associated with CLL/SLL among the US veterans**
- **Furthermore, the suboptimal adherence, as reported by high treatment discontinuation rates and its impact on increasing costs and healthcare resource use, highlights the real-world unmet needs of CLL/SLL management in the veteran population**