Burden of Chronic Lymphocytic Leukemia in the United States: A Review of Literature

Bisen R, Thakur L, Bisen V, Shivsingwale G

SRS HEOR (A Division of SRS Pharmaceuticals Pvt. Ltd., MH, India)

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BACKGROUND

- Chronic lymphocytic leukemia (CLL) is the most prevalent leukemia in the Western world, accounting for more than one-third (37%) of all newly diagnosed leukemia cases in the United States (US).[1,2]
- Because improving survival has increased the incidence of CLL in the United States, a comprehensive understanding of the CLL burden is essential for future disease management.

OBJECTIVES

- To conduct a targeted literature review with the objective of identifying published evidence on the epidemiology, clinical, humanistic, and economic burden associated with CLL in the United States.

METHODS

- Literature search from recent years (2017-2022) was performed in EMBASE®, and MEDLINE® databases. Studies published in the English language reporting on epidemiology and burden associated with CLL patients were included.
- All the records retrieved from the literature search were screened against the pre-defined inclusion and exclusion criteria (**Table 1**), first based on the title and abstract and then on the full-text citations. Data was extracted from the full-text articles that were included.

Table 1. The predefined inclusion and exclusion criteria of the TLR

Criteria	Inclusion Criteria	Exclusion Criteria
Population	Patients with CLL, SLL	Patients with conditions other than CLL & SLL
Interventions	No restrictions by interventions	None
Comparators	No restrictions by comparators	None
Outcomes	Epidemiology: Incidence, prevalence, survival, mortality, and severity of disease Clinical burden: Comorbidities, rate of hospitalizations, symptoms, complications, and disability Humanistic burden: HRQoL, ADL, caregiver health and caregiver QoL, treatment satisfaction Economic burden: Cost of medical care (hospital admission, outpatient visit, and medication use) and nonmedical costs (transportation and caregiver costs), resource use.	Studies reporting outcomes other than those listed in the inclusion criteria
Study Design	Studies reported above outcomes	Animal/in vitro studies, review, editorial, letters, or case studies
Geographic Location	USA	Other than inclusion criteria

Key: ADL, activities of daily living; CLL, chronic lymphocytic leukemia; HRQoL, health-related quality of life; QoL, quality of life; SLL, small lymphocytic leukemia

RESULTS

- Thirty studies were identified from 2,363 citations, with the majority reported economic burden (n=13), followed by epidemiology (n=12), clinical burden (n=8), and humanistic burden (n=1).

❑ Epidemiology

- Based on SEER data, the rate of new cases of CLL was 4.7 per 100,000 per year (from SEER 12) (**Figure 1**), and 5-year relative survival was 87.9% (from SEER 17 2012-2018). The following published literature showed increase in CLL incidence over the period (1990-2019), which was associated with aging population.

Incidence

- In 2019, global CLL cases exceeded 1,034,000, with a 155% increase since 1990. The highest incidence was in the United States, China, and India. Smoking, high BMI, and workplace exposure to chemicals contributed to CLL cases and deaths.[3]
- Cases of CLL increased 187% from 7,300 in 1998 to 20,940 in 2018, which was highly associated to the aging of the US population. CLL death rate reduced by 18% from 1.7/100,000 in 1998 to 1.4/100,000 in 2018.[4]

Survival rates

- 5-year relative survival rates: 75-84 years (76.5%), ≥85 years (55.2%).[5]
- 5-year and 10-year age-adjusted relative survival rates ranged between 73.7% and 89.4%, and from 51.6% to not reached for different calendar periods (1985–1989 to 2010–2014).[6]

Incidence of second primary malignancies (SPM)

- The 3-year cumulative incidence rate was 16% for non-melanoma skin cancer and 7% for other SPM in CLL patients. Smoking associated with increased SPM risk, higher CD8 count associated with lower SPM risk.[7]
- CLL patients faced a 20% increased risk of SPMs. Highest SPM risk occurred 2-5 months after CLL diagnosis and in patients aged 50-79.[8]

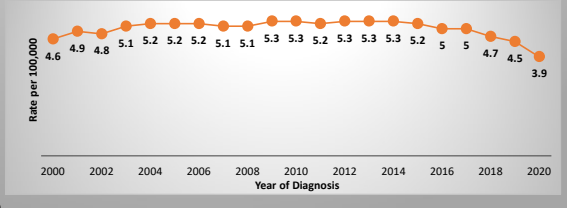


Figure 1. Recent trends in SEER age-adjusted incidence rates

❑ Clinical burden

- Comorbidities had a larger impact on survival in patients aged <65 years compared to ≥65 years, while CLL and CLL-related complications (infections and second cancers) were the increased cause of death in CLL patients.[9, 10]
- The main pulmonary symptoms were dyspnea (71%), cough (68%), and sputum (34%), while the main thoracic complications were pneumonia (62.8%), pleural effusion (31.8%), and bronchopulmonary leukemic infiltrate.[11]

❑ Humanistic burden

- Goyal et al. reported that baseline cancer-specific stress (measured by the Impact of Event Scale – Revised) was associated with higher 5-month predicted cognitive-affective depressive symptoms, negative mood scores, and lower mental health quality of life (HQoL), but not with predicted 5-month fatigue interference, sleep problems, or physical HQoL. In relapsed/refractory CLL patients, worse psychological outcomes at 5 months were associated with higher levels of baseline cancer-specific stress, but not with physical outcomes.[12]

❑ Economic Burden

- CLL imposed a high economic burden associated with inpatient, pharmaceutical, adverse events, and indirect costs. Oral targeted therapies are projected to increase the lifetime cost of CLL treatment from $147,000 (in 2011) to $604,000 (by 2025).

Cost data

- During front-line therapy, ibrutinib (Ibr) patients had significantly fewer visits with all-cause outpatient visits, shorter inpatient lengths of stay, and incurred lower all-cause medical cost and higher all-cause pharmacy cost as compared with chemoimmunotherapy (CIT) or bendamustine/rituximab (BR) as represented in **Figure 2a and 2b**.[13,14]
- Patients with treatment failure (TF) in CLL had higher total per patient per month healthcare costs ($3,006 vs. $2,448) and the average TF cost was $3,011 per patient per month.[15]
- Total hospitalization cost, including both the initial admission and 90-day readmission, was similar in CLL and non-CLL patients, with costs of $48,302 versus $48,060 and $14,262 versus $14,471, respectively.[17]
- The mean monthly all-cause costs were $8,798 for all causes and $6,241 for CLL-related visits during the follow-up period. Office visits ($2,166), inpatient admissions ($2,066), and outpatient prescription drugs ($2,003) were the largest cost drivers. [2]

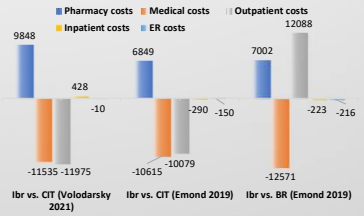


Figure 2a. Mean monthly cost difference (MMCD), $ between Ibr vs. CIT/BR

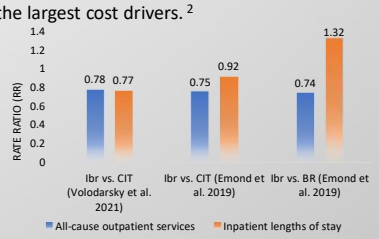
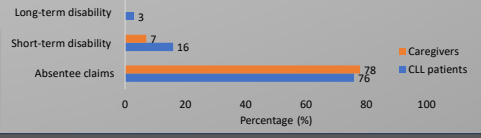


Figure 2b. Comparison of healthcare resource utilization between Ibr vs. CIT/BR

Resource use data

- Patients with private insurance had numerically lower mean all-cause hospitalizations (0.039) and emergency room (ER) visits (0.023) per-patient-per-month (PPPM) than patients with public or other insurance.[16]
- Average length of stay (LoS) of inpatient hospitalization was 6.3 days, with mean costs per hospitalization of $19,566. [19]
- CLL/SLL-related hospitalization rate was 39%, with an average length of stay of 7 days. Total PPPM all-cause and CLL/SLL-related costs were $26,709 and $17,233, respectively.[20]
- The mean monthly per-patient costs during the post-index date follow-up were $3,784 for all-cause and $1,885 for CLL-related events. The mean monthly all-cause costs and mean LoS per admission increased with the number of adverse events.[21]
- Adherent CLL patients treated with Ibr had fewer mean all-cause hospitalizations (adherent PPPM = 0.03, non-adherent PPPM = 0.08). All-cause total medical costs were significantly lower in the adherent cohort compared to the non-adherent cohort (MMCD = -$1,747.77).[22]
- Among eligible CLL patients, higher proportions had absentee claims (76%) and average illness-related absentee hours were higher in patients than caregivers (9.5 vs. 6.9) as depicted in **Figure 3.** [18]

Figure 3. Proportions of absentee claims and disabilities among CLL patients and caregivers



CONCLUSIONS

CLL is a prevalent leukemia type that primarily affects the elderly. This literature review demonstrates an alarming increase in CLL incidence, as well as improved survival rates. This growing tendency, however, comes at a huge financial cost to both patients and healthcare systems. Future study must address the humanistic burden of CLL, including its influence on patients' life beyond the economic element. Understanding both the economic and humanistic aspects of CLL will aid in the development of more comprehensive strategies for effectively managing and treating this disease.

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