POST-2020 REAL-WORLD EVIDENCE ON PHARMACOTHERAPIES FOR CHRONIC LYMPHOCYTIC LEUKEMIA: A SCOPING REVIEW

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INTRODUCTION

- Chronic Lymphocytic Leukemia (CLL) is a slow-processing leukemia, with 22760 new cases and 4350 deaths annually.
- The targeted therapies, especially B-cell lymphoma 2 inhibitors (BCL2i) and Bruton's Tyrosine Kinase Inhibitors (BTKi), are transforming the treatment landscape for CLL. The five-year relative survival reached 90.2% (National Cancer Institute, 2026).
- Marchetti et al. (2022) reviewed real-world evidence (RWE) studies from 2010 to 2020. Most patients were treated with BTKi, especially ibrutinib. Discontinuation rates were higher than clinical trials, but the median overall survival or progression-free survival was not reached in most studies.
- An updated scoping review is needed to understand the treatment patterns of CLL in the real world after 2020, especially fixed-duration BCL2i vs. continuous BTKi. Clinical outcomes with longer follow-up periods and methodological characteristics of primary studies should be studied to inform future RWE studies with rigorous design.

OBJECTIVE

- To summarize treatment patterns, effectiveness, and adverse events of current CLL treatments in real-world clinical practices.
- To describe methodological characteristics of RWE studies on CLL treatments.
- To synthesize whether fixed-duration BCL2i-containing regimens are preferred over continuous BTKi regimens in the real-world setting.

METHOD

Step 1: Searching RWE Studies on CLL in PubMed Database
Search terms: ("chronic lymphocytic leukemia" or "CLL" or "small lymphocytic leukemia" or "SLL") AND ("real-world data" or "real-world evidence" or "electronic health records" or "EHR" or "claims" or "registry")

Step 2: Abstract and Full-text Screening using Rayyan
Inclusion criteria:
- Patients diagnosed with CLL or Small lymphocytic lymphoma (SLL)
- Pharmacotherapies
- Real-world data sources
- Outcomes in effectiveness (e.g., response, survival), adverse events or discontinuation

Exclusion criteria:
- Cost analysis studies
- Population-level analyses

Step 3: Data extraction
Patient characteristics, study characteristics, results

Step 4: Data analysis and synthesis

RESULTS

FIGURE 1: PRISMA

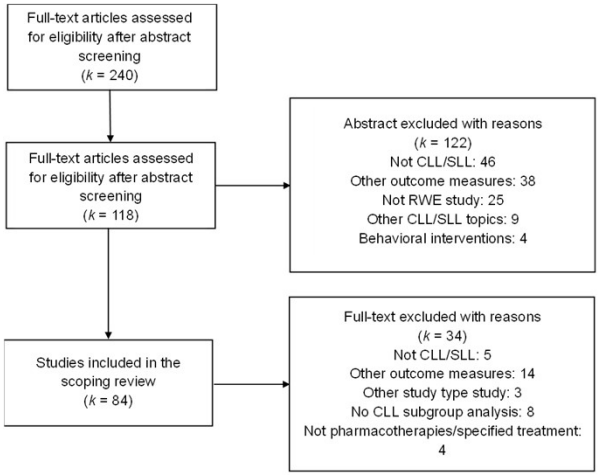

TABLE I: Summary of studies examining effectiveness outcomes

Effectiveness Outcome	Number of Studies
Overall survival	45
Progression-free survival	26
Time to next treatment	23
Overall response rate	12
Complete/partial remission	6
Mortality	3

TABLE II: Summary of studies examining safety outcomes

Safety Outcomes	Number of Studies
Infection	26
Cardiovascular events	22
Bleeding	13
Hypertension	11
Anemia	10
Diarrhea	10
Tumor lysis syndrome	6

RESULTS

- A total of **84** RWE studies on CLL/SLL with **172,085 patients** were included, and the mean age at diagnosis was **70.6 years old**.
- These studies were conducted in North America (e.g., the USA and Canada), Europe (e.g., Germany, Spain, Finland, and Poland), Asia (e.g., Japan and China), and Australia.
- Among the studies, 43 (51.2%) used patient electronic health record data, 20 (23.8%) used claims data, 8 (9.5%) used registry data, and 17 (20.2%) used data sources such as phase IV studies and prospective studies.
- Six studies (7.1%) focused only on newly diagnosed/treatment-naïve CLL/SLL patients, the rest seventy eight studies (92.9%) included all risk types of CLL/SLL including relapsed or refractory CLL/SLL patients.
- Forty-five (53.6%) studies investigated BTKis (especially ibrutinib), 13 (15.5%) investigated BCL2i (i.e., venetoclax-containing regimens), and other treatments included chemoimmunotherapy and anti-CD20 mAb.
- Most studies favored the treatments examined, and five studies on BTKi identified an unmet need for effective CLL/SLL therapies among patients with severe CLL/SLL.

DISCUSSION

- NCCN guidelines (2025) recommend second-generation BTKis and BCL2i as preferred therapies for CLL. However, around half of the RWE studies have focused more on first-generation BTKis, reflecting **the frequent use of ibrutinib in clinical practice worldwide.**
- BTKi and BCL2i are **generally effective treatments and well-tolerated** in newly diagnosed/treatment-naïve and relapsed or refractory CLL patients.
- **Limited number of primary studies were conducted in head-to-head**, and more rigorous designs are needed for future RWE studies.
- **Few studies compare BCL2i to BTKi**, which remains the comparison in effectiveness, safety profiles and patient-reported outcomes unknown between fixed-duration and continuous regimens.

REFERENCES

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