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Anticipating FUTURE EVIDENCE needs in relapsed/refractory chronic lymphocytic leukemia (R/R CLL)

A living evidence analysis for HTA, JCA, and IRA decision-making

BACKGROUND

The treatment landscape of chronic lymphocytic leukemia (CLL) continues to evolve with the introduction of **BCL2-inhibitors** (BCL2i), second-generation **covalent BTK inhibitors** (cBTKi), and **non-covalent BTK inhibitors** (ncBTKi).

Simultaneously, implementation of **EU Joint Clinical Assessment (JCA)** and **Medicare Drug Price Negotiation** under the Inflation Reduction Act (IRA) has increased demand for timely evidence on emerging therapies, patient populations, and treatment pathways.

OBJECTIVES

to characterize the development landscape in relapsed/refractory (R/R) CLL and identify emerging evidence needs relevant to HTA and payer decision-making using the **Oncoscope** Real-Time AI-Assisted Living SLR (**REAL-SLR) database.**

METHODS

Oncoscope REAL-SLR is a **PRISMA-aligned**, continuously updated evidence database organized by tumor type, including CLL. REAL-SLR systematically identifies and structures the evidence from interventional clinical trials, regulatory approvals, clinical guidelines, and HTA reviews with daily updates. Studies are mapped according to clinical stage, treatment pathway, biomarker application, study design, and regulatory/guideline status. Studies evaluating novel therapies with publications from 2022 onward were included.

RESULTS

- As of June 15, 2026, the REAL-SLR included 341 investigational studies, of which 212 (62%) evaluated R/R CLL.
- Thirty-six studies investigated emerging therapies, including BCL2 inhibitors, next-generation BTK inhibitors, BTK degraders, CAR-Ts, and bispecific antibodies.
- Sixty-one percent reported outcomes in patients previously exposed to cBTKi and/or BCL2i, while 19% evaluated del(17p)/TP53-mutated populations.
- Only two studies each evaluated double-class or triple-class exposed populations (BGB-16673, rocbrutinib), and three reported outcomes in patients with BTK mutations (BGB-16673, sonrotoclax, selinexor+ibrutinib).
- Overall and progression-free survival were reported in 33% and 64% of studies, respectively.

KEY TAKEAWAYS

Oncoscope living evidence monitoring DEMONSTRATED that therapeutic innovation in R/R CLL is concentrated in previously treated populations, while evidence remains limited for double-class exposed, triple-class exposed, and biomarker-defined subgroups.

These findings highlight emerging EVIDENCE GAPS that may influence comparator selection, value assessment, and evidence-generation strategies.

Oncoscope REAL-SLR use in LIVING EVIDENCE MONITORING may support identification of evolving treatment pathways and evidence requirements relevant to HTA, JCA, IRA, and payer decision-making.

Figure 1. **Continuously updated PRISMA (REAL-SLR framework) in CLL**
(updated Jun 15, 2026)

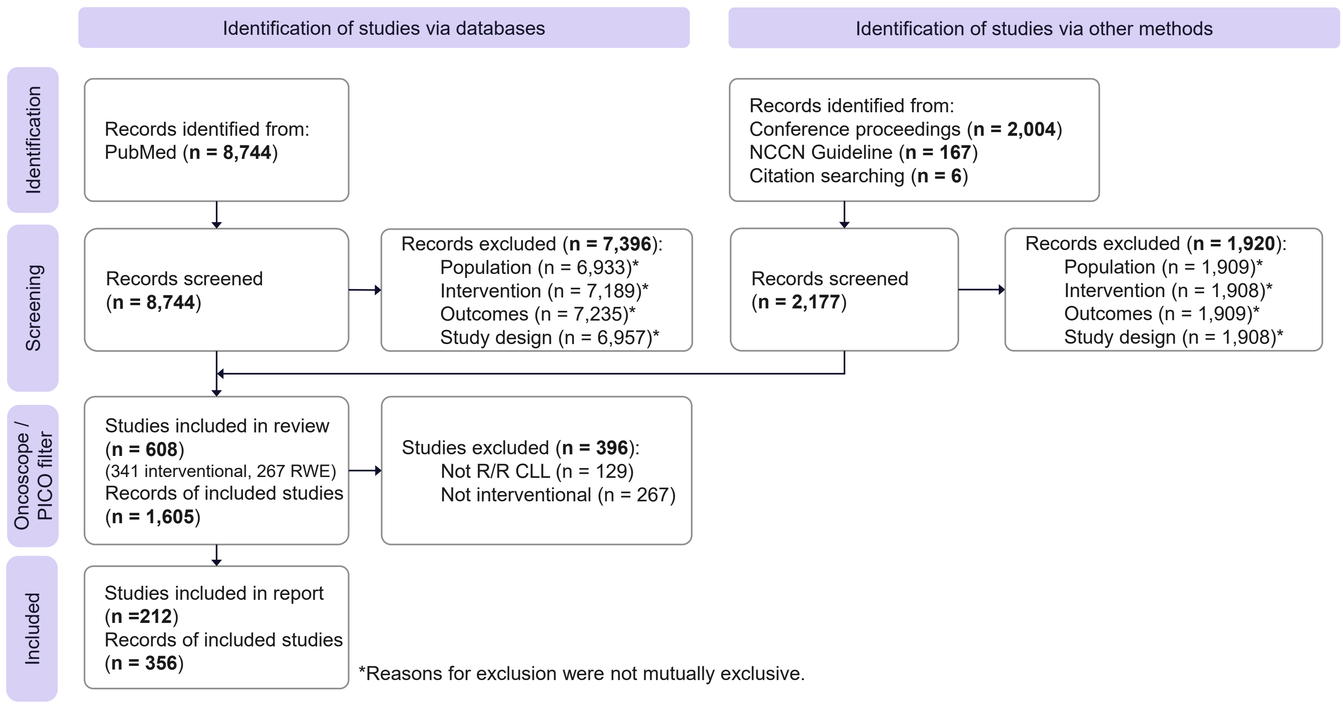


Figure 2. **REAL-SLR evidence capture summary during the study period**

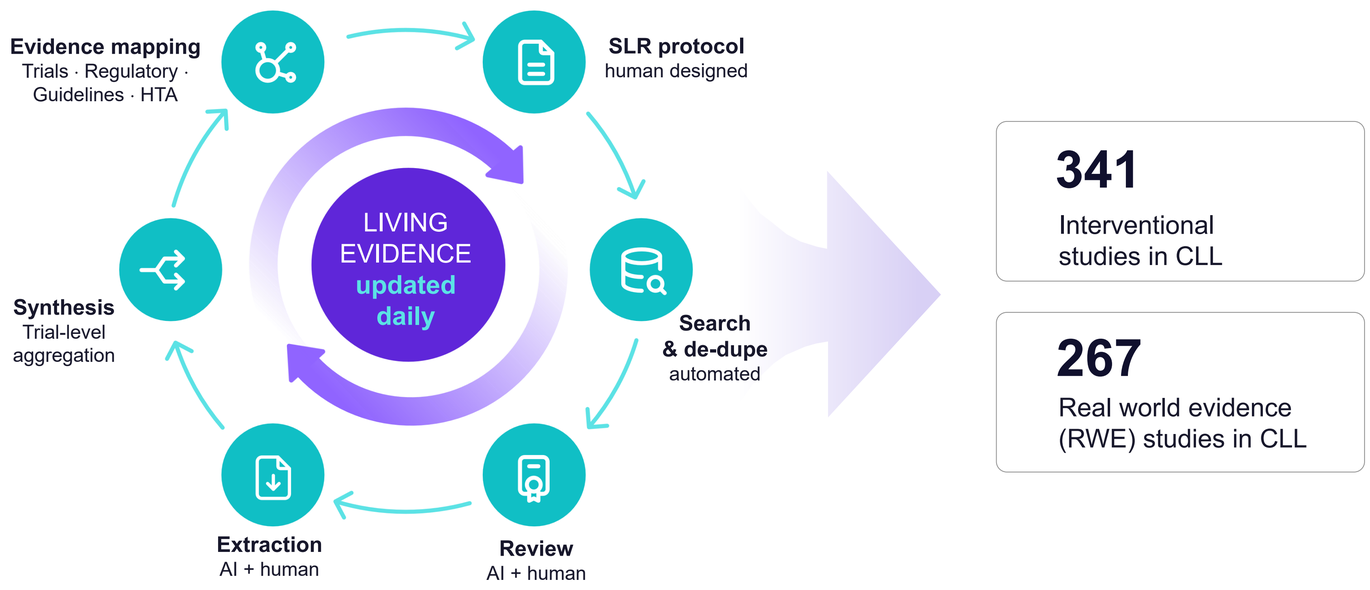
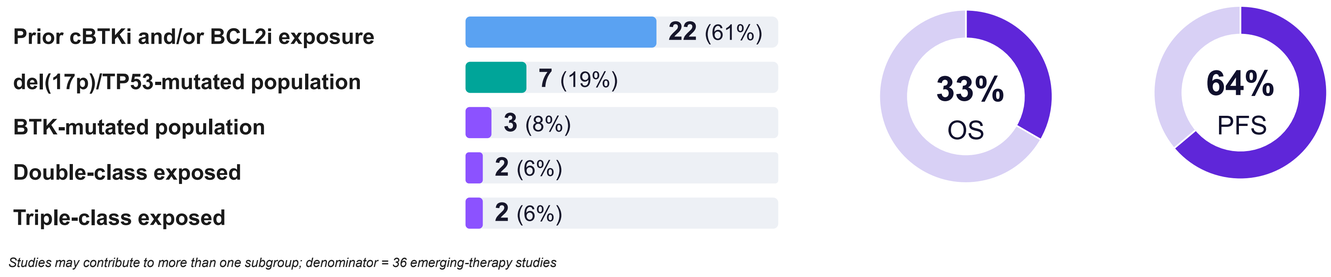


Figure 3. **Living evidence landscape in CLL**
as of Jun 15, 2026



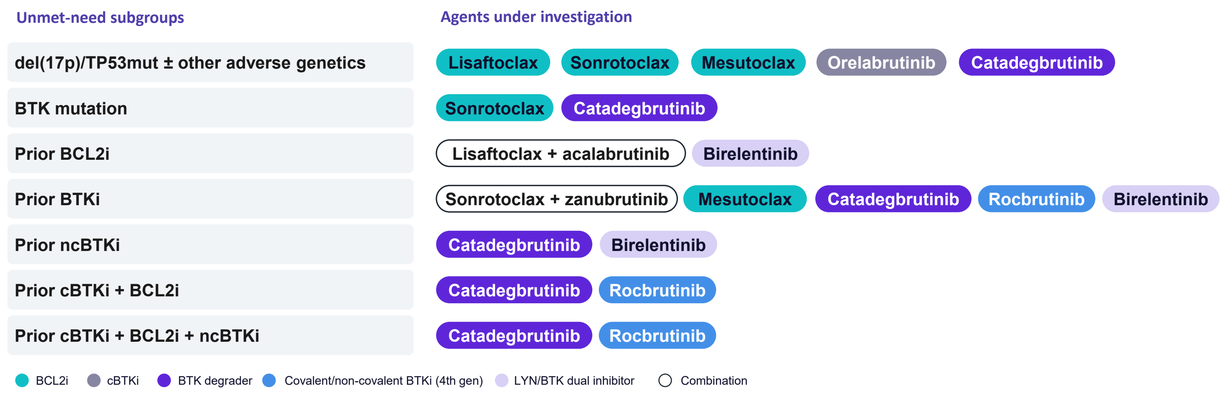
Figure 4. **Emerging-therapy evidence: subgroup representation and survival reporting**



Studies may contribute to more than one subgroup; denominator = 36 emerging-therapy studies

Key evidence gap — Evidence remains limited in sequentially exposed and biomarker-defined populations, highlighting the need for mature comparative survival data.

Figure 5. **CLL/SLL pipeline: new agents by population and unmet-need subgroup**



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ABBREVIATIONS

AR, androgen receptor; **BCL2**, B-cell lymphoma 2; **BTK**, Bruton tyrosine kinase; **BTKi**, Bruton tyrosine kinase inhibitor; **CAR-T**, chimeric antigen receptor T-cell therapy; **cBTKi**, covalent BTK inhibitor; **CLL**, chronic lymphocytic leukemia; **EU**, European Union; **HTA**, health technology assessment; **IRA**, Inflation Reduction Act; **JCA**, Joint Clinical Assessment; **NCCN,** National Comprehensive Cancer Network; **OS**, overall survival; **PFS**, progression-free survival; **PRISMA**, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; **R/R**, relapsed/refractory; **RWE**, real-world evidence; **REAL-SLR**, Real-Time AI-Assisted Living Systematic Literature Review; **SLR,** systematic literature review; **TP53**, tumor protein p53.