Structured Oncology Literature Screening as the Methodological Foundation for EU Joint Clinical Assessment Preparation and Target Trial Emulation Planning

MSR21

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BACKGROUND

Since January 2025, EU Joint Clinical Assessments (JCAs) require comparative evidence for new cancer medicines at marketing authorisation. In oncology, member-state PICO scoping often requests more comparators than randomised evidence covers (1).

At submission, the new medicine has no real-world use: the published literature is the first window into comparator treatment patterns, outcome definitions and real-world data (RWD) capabilities.

Target trial emulation (TTE) can address comparator gaps, but only if eligibility, treatment strategies, outcomes and confounders are understood in advance (3, 4).

JCA PICO scope → **Comparator evidence gap** → **TTE needs prior knowledge of the data**

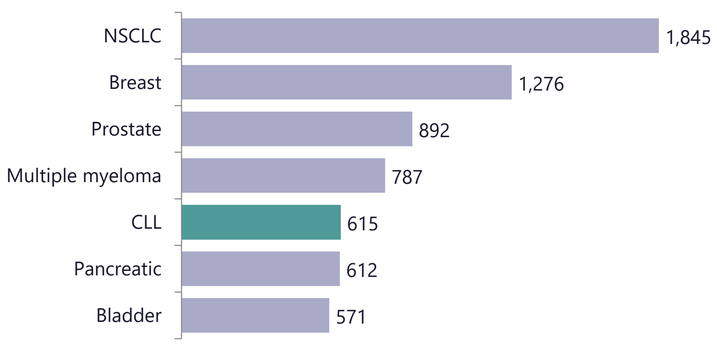
OBJECTIVE

To develop a replicable framework for structured oncology literature screening that identifies the design elements governing TTE validity and the comparator evidence gaps relevant to JCA, illustrated in chronic lymphocytic leukaemia (CLL).

METHODS

Data source: Oncoscope, a daily-updated Real-Time AI-Assisted Systematic Literature Review (REAL-SLR). A multi-model agentic AI system (GPT-4.1, o3, Claude Sonnet 4) emulates Cochrane-compliant screening and extraction, with 100% human quality control (6).

7 cancer libraries · 6,598 studies



CLL RWE library: observational studies (n≥50) from North America, EU, UK and Australia, published 2020 onwards and reporting at least one eligible outcome; PubMed plus ASCO, ASH and EHA abstracts; PROSPERO CRD420261292168 (7). 347 interventional and 268 RWE studies.

Extraction framework: abstract-level data mapped to the seven target trial components (2) and JCA domains.

TTE component	Elements assessed	JCA link
Eligibility	Line of therapy, biomarkers, age, frailty	Population
Treatment strategies	Regimen, continuous vs fixed-duration, sequencing	Intervention / comparator
Assignment	Adjustment method, covariates	Certainty
Follow-up	Time zero, censoring, duration	Interpretability
Outcomes	OS, PFS, TTNT, AEs, HRQoL	All four domains
Causal contrast	ITT- vs per-protocol-type analyses	Estimand
Analysis	Methods, sensitivity analyses	Certainty

Outputs: for each element, the proportion of studies reporting it, as a measure of evidence availability; summarised in a TTF design matrix and JCA readiness scorecard (author-defined thresholds: ≥50%, 20–49%, <20%).

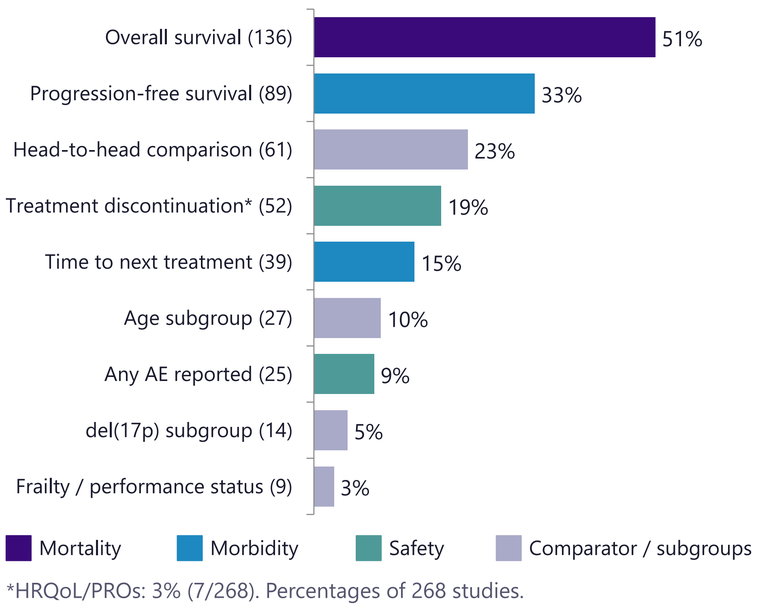
RESULTS

268 RWE studies
in the CLL library, published 2020 onwards

Line: naïve 34% · R/R 18% · mixed 45% · Richter 4%
Region: EU/UK 44% · N America 46% · Australia 2% · Unknown 8%

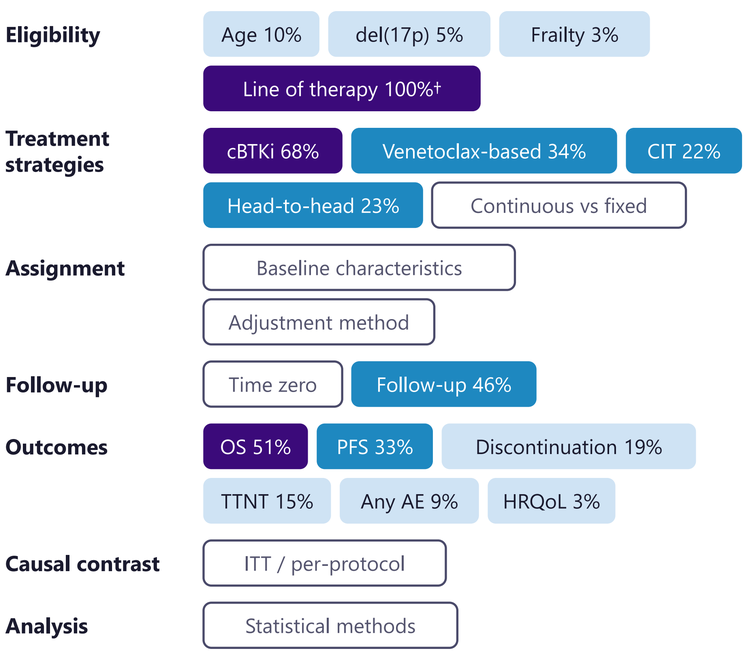
Evidence availability, % of studies

Share of studies reporting each element: the published evidence available, not how complete each study is.



*HRQoL/PROs: 3% (7/268). Percentages of 268 studies.

TTF design matrix



†Inferred from treatment history where not stated.

Finding 1: Survival outcomes dominate.

- OS (51%) and PFS (33%) are the most consistently reported outcomes; TTNT, key for fixed-duration regimens, in only 15%.
- Only 5% (14/268) compare BTKi with venetoclax-based therapy, the key current comparison.
- 45% of studies mix lines of therapy, limiting mapping to line-specific PICOs.

Finding 2: HRQoL, safety and subgroups are sparse.

- HRQoL/PROs are reported in only 3% of studies (7/268); numerical AE data in 9%.
- del(17p) (5%) and frailty (3%), key drivers of treatment choice, are rarely reported.

Finding 3: TE design elements are not extracted.

- Baseline characteristics, confounding adjustment, time zero and analytic approach are not captured at abstract level.
- These define emulation validity and require full-text review.

CONCLUSIONS

Literature screening is the earliest JCA readiness check. It assesses TTE design validity and JCA comparator feasibility before launch, ahead of patient-level data access.

Outcomes are visible; design elements are not. In CLL, survival is well reported, but safety, HRQoL, subgroups and TTE design elements are sparse or not extracted.

The framework scales across indications. The indication-agnostic schema can be applied across Oncoscope's seven cancer libraries as new JCAs arise.

IMPLICATIONS FOR JCA

1. **Pre-scoping:** anticipate likely comparators and subpopulations through PICO mapping.
2. **PICO scoping:** map each PICO to randomised, indirect or RWE-only evidence (5).
3. **Dossier preparation:** specify external comparators and target trials, align outcomes, and contextualise single-arm trials.
4. **Post-JCA:** turn identified gaps into an evidence generation plan for national appraisal.

JCA READINESS SCORECARD

Mortality	Well reported	OS in 51% of studies
Morbidity	Partial	PFS 33%; TTNT 15%
Safety	Sparse	Any AE 9%; discontinuation 19%
HRQoL	Sparse	HRQoL/PROs in 3% of studies

Ratings use author-defined thresholds (≥50% well reported; 20–49% partial; <20% sparse).

LIMITATIONS

Abstract-level extraction understates what full texts report. Searches cover PubMed and three congresses, English only, studies of ≥50 patients. Literature reporting does not establish RWD availability, and the platform complements, not replaces, JCA systematic information retrieval.

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