The True Value of Living Systematic Reviews (LSRs): A Case Report Within Systemic Lupus Erythematosus (SLE)

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Background

- A living systematic review (LSR) is a type of systematic literature review (SLR) that is continually updated to incorporate new, relevant evidence as it becomes available.[1]
- SLRs aim to summarize available evidence for specific health questions; however, traditional SLRs can be quickly outdated.
- LSRs have been proposed to overcome this limitation, particularly within rapidly evolving therapy areas such as systemic lupus erythematosus (SLE).
- The therapeutic goals of SLE previously focused on survival but are moving towards therapy related side effects and organ damage, with growing attention on health-related quality of life and biologics.
- LiveSLR®, an up-to-date Cochrane/NICE-compliant curated SLR library following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards, features an interactive platform to create user-friendly SLRs, ready for analyses and updates, with customizable filters to refine the SLR for specific population, intervention, comparison, outcomes, and study design (PICOS) criteria, or for specific geographic regions allowing for targeted review for local markets.
- With a comprehensive library of evidence, the LiveSLR® SLE database can be kept up to date with monthly congress reviews and artificial intelligence (AI)-driven real-time competitive intelligence tracking.
- Subsequent human-driven full literature review updates can be conducted at any point to allow for up-to-date availability of evidence.
- The rapidity of availability of up-to-date SLRs will be particularly beneficial for Health Economic & Outcome Research and Market Access activities including indirect treatment comparisons, cost-effectiveness modelling, and development of global or local health technology assessment (HTA) dossiers.
- Th LiveSLR® platform supports this need with automatic report generation.

Objectives

- To outline and assess current clinical evidence published within SLE, detailing methods and cadence of LSRs.
- To consider efficiency gains made by utilization of the LiveSLR® platform in the conduct of the LSR.

Methods

- Two literature searches were conducted: an initial search on December 19, 2022, and an update on March 12, 2024.
- Literature searches were conducted in Embase and Medline using LiveSLR®, including a combination of free-text and controlled vocabulary terms specific to each database (e.g., Emtree terms for Embase or Medical Subject Headings in MEDLINE).
- Broad, generalizable inclusion criteria were applied to capture clinical evidence from randomized controlled trials (RCTs) and real-world evidence (RWE), shown in Table 1.
- LiveSLR® filters were predefined based on the disease area and information requirements to promote data customizability.
- Relevant data were manually extracted into predefined tables, with automated SLR reports generated using LiveSLR®.
- The SLRs were conducted based on PRISMA reporting standards,[2] as well as general methodological requirements outlined in the Cochrane Handbook for Systematic Reviews of Interventions,[3] and by key HTA agencies, such as the National Institute for Health and Care Excellence (NICE),[4] Canadian Agency for Drugs and Technologies in Health (CADTH; now replaced by Canada's Drug Agency),[5,6] and Institute for Quality and Efficiency in Health Care (IQWiG).[7]
- Results from the December 2022 and March 2024 searches were uploaded on to the LiveSLR® platform.
- LiveSLR® was used to generate interactive graphics to visually demonstrate the distribution of evidence identified within the SLR.

Methods (cont.)

Table 1. PICOS criteria

PICOS	Inclusion criteria	
Population	Disease: patients diagnosed with SLE Disease severity: moderate to severe SLE patients Phase of therapy: induction or maintenance	
Intervention/ comparator	Belimumab, anifrolumab, obinutuzumab, ianalumab, dapirolizumab pegol, deucravacitinib, litifilimab (BIIB059), brepocitinib (JAK/TYK2 inhibitor)	
Outcomes	- Any efficacy outcomes - Any safety outcomes - Any HRQoL and/or patient-reported outcomes	
Study design	Interventional studies: - RCTs - SLRs, MAICs, and meta-analyses (for cross-checking only)	Real world evidence: - Prospective observational studies - Retrospective studies - Registry analyses - Cross-sectional studies - Database analyses - SLRs and meta-analyses (for cross-checking only)
Timeframe	Time: 2022 to current (FDA approved first targeted therapy in 2011)	
Language	English language	
Other	Failed RCTs for products not proceeding with further development will be rejected	

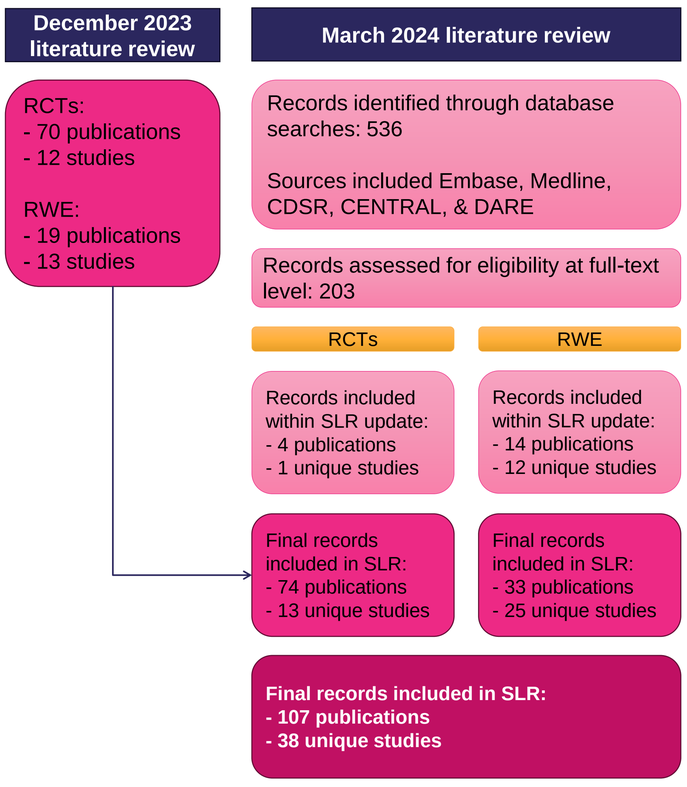
Abbreviations: FDA, food and drug administration; HRQoL, health-related quality of life; JAK, Janus kinase; MAIC, matching-adjusted indirect comparison; PICOS, population, intervention, comparison, outcomes and study design; RCT, randomized controlled trial; SLE, systemic lupus erythematosus; SLR, systematic literature review; TYK2, tyrosine kinase 2.

Results

SLR findings

- The 2022 database searches returned 2,231 records:
  - RCT: 70 publications from 12 unique studies.
  - RWE: 19 publications from 13 unique studies.
- In 2024, 536 new records were captured:
  - RCT: four publications reporting on one study.
  - RWE: 14 publications from 12 unique studies.
- In total, 38 studies were included for data extraction and inclusion within the SLR, comprising 13 unique RCTs and 25 unique RWE studies (Figure 1).
- Belimumab, anifrolumab, dapirolizumab pegol, and deucravacitinib showed promising results in RCTs.
- RCT data showed that the interventions had steroid-sparing activity and were effective in reducing disease activity and severe flares relative to placebo.
- RWE studies supported the belimumab RCT results, but RWE was generally lacking for other treatments.
- Subsequent head-to-head comparisons within RCTs or indirect treatment comparison of the available interventions may provide a stronger indication of the relative effectiveness of the currently available treatment options for people with SLE.

Figure 1. PRISMA flow diagram



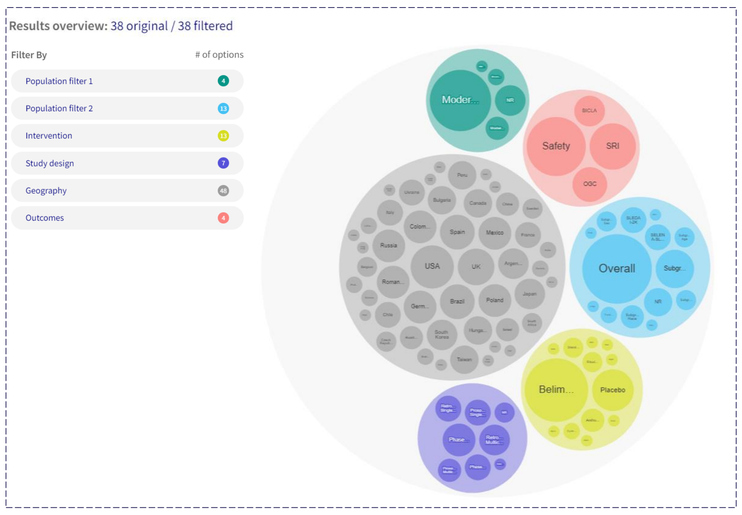
Abbreviations: CDSR, Cochrane Database of Systematic Reviews; CENTRAL, Cochrane Central Register of Controlled Trials; DARE, Database of Abstracts of Reviews of Effects; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, randomized controlled trial; RWE, real world evidence; SLR, systematic literature review.

LiveSLR®

- Figures 2 and 3 present the distribution of evidence by PICOS and geography, respectively.

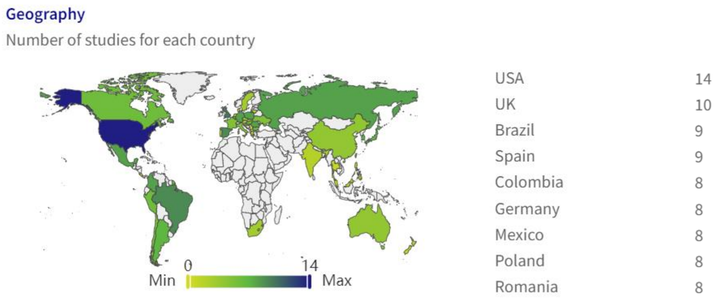
Results (cont.)

Figure 2. LiveSLR® PICOS visualization



Abbreviations: BICLA, British Isles Lupus Assessment Group-based Composite Lupus Assessment; NR, not reported; OCG, oral glucocorticosteroid; PICOS, population, intervention, comparison, outcomes and study design; SRI, SLE Responder Index; UK, United Kingdom; USA, United States of America.

Figure 3. LiveSLR® graphic for geographic distribution of evidence



Abbreviations: UK, United Kingdom; USA, United States of America.

LiveSLR® reporting

- The LiveSLR® platform enabled automatic report generation aligning with HTA requirements.
- The automatically generated reports included:
  - A description of the SLR methods, including data sources and search strategies, study eligibility criteria (including any PICOS customization applied through the LiveSLR® platform), study selection process, and data extraction methods.
  - Updated PRISMA diagrams demonstrating the flow of literature from identification at source to inclusion or exclusion within the SLR.
  - Tables to show a summary of study characteristics, a summary of patient demographics and baseline characteristics, and summaries of efficacy/effectiveness and safety outcome data.
  - A fully formatted citation list of all publications included within the SLR.
- The automated SLE report produced through LiveSLR® contained seven tables presenting combined data from interventional and RWE data (downloaded within ~2 minutes) and 14 tables of outcome data stratified by study design, presenting data independently for interventional and RWE studies (requiring an additional 4 minutes).
- Overall, the ~6-minute report update and generation using the LiveSLR® platform saved ~56 hours versus human-only SLR generation, equating to a 99.8% efficiency improvement.

Conclusions

- An SLR search update reviewing clinical evidence in SLE 16 months after the primary search generated 18 new publications, providing a considerable addition to the available evidence on current therapy options.
- The update provides insight into the appropriate cadence for LSRs and highlights efficiencies gained with LiveSLR®.

References

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Conflict of interest: Ben Mayer, Jessica Agranat, Cristiana Tzonev, Omar Irfan, Sara Lucas, and Victoria Young were employees of Cytel Inc at the time of the study.

Funding Information: This study was funded by Cytel Inc.