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# Chimeric antigen receptor (CAR)-based cellular therapy for lupus nephritis: a systematic review of renal-specific outcomes

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**ADMINISTRATIVE INFORMATION**

**Support -** No support.

**Review Stage at time of this submission -** Formal screening of search results against eligibility criteria.

**Conflicts of interest -** None declared.

**INPLASY registration number:** INPLASY202690095

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 September 2026 and was last updated on 22 September 2026.

## INTRODUCTION

**Review question / Objective** In patients with lupus nephritis (P), what are the renal-specific efficacy and safety outcomes (O) of chimeric antigen receptor (CAR)-based cellular therapy, including autologous and allogeneic CAR-T cells, CAR-NK cells and in vivo CAR-T (I), compared with baseline status or no comparator (C), across randomized trials, non-randomized trials, cohorts, case series and case reports (S)? The primary objective is to characterize complete renal response. Secondary objectives are to describe partial renal response, proteinuria, estimated glomerular filtration rate, dialysis independence, repeat-biopsy histology, serologic and global disease-activity responses, drug-free remission, relapse, B-cell reconstitution and adverse events, and to identify heterogeneity in renal outcome definitions.

**Rationale** Lupus nephritis remains a principal determinant of morbidity, kidney failure and mortality in systemic lupus erythematosus, and a substantial proportion of patients do not achieve durable renal response with sequential immunosuppression and B-cell-directed biologics. CAR-based cellular therapy achieves deep, tissue-level depletion of autoreactive B cells and, in some constructs, plasma cells, and early reports describe drug-free remission in refractory disease. Existing systematic reviews have summarized outcomes at the level of systemic lupus erythematosus, treating the kidney as one organ domain among many. Renal endpoints such as complete renal response, proteinuria, glomerular filtration rate, dialysis independence and histologic response on repeat biopsy behave differently from global disease-activity indices and are defined inconsistently across reports. Overlapping publications from the same centers also risk double-counting patients. A systematic review restricted to renal-specific outcomes, with explicit deduplication of overlapping cohorts, is needed to define what is known about kidney outcomes after CAR-based therapy and to inform the design of controlled trials.

**Condition being studied** Lupus nephritis is immune-complex-mediated glomerulonephritis occurring in systemic lupus erythematosus, classified histologically by the ISN/RPS system (classes I-VI). Proliferative (class III/IV) and membranous (class V) disease carry the highest risk of progressive chronic kidney disease and kidney failure. Standard therapy combines glucocorticoids with mycophenolate, cyclophosphamide, calcineurin inhibitors or biologic agents, yet refractory and relapsing disease remains common.

## METHODS

**Search strategy** Databases: PubMed/MEDLINE, PubMed Central, Europe PMC, Cochrane Library (CENTRAL), and Google Scholar, from inception to the date of the final search, without date limits. Trial registries: ClinicalTrials.gov, Chinese Clinical Trial Registry (ChiCTR), EU Clinical Trials Register and CTIS. Conference proceedings: American College of Rheumatology Convergence, EULAR, American Society of Nephrology Kidney Week, European Renal Association and American Society of Hematology annual meetings. Reference lists of included studies and relevant reviews will be hand-searched.

PubMed strategy:
("Lupus Nephritis"[MeSH] OR "lupus nephritis"[tiab] OR "Lupus Erythematosus, Systemic"[MeSH] OR "systemic lupus erythematosus"[tiab] OR SLE[tiab]) AND ("Receptors, Chimeric Antigen"[MeSH] OR "Immunotherapy, Adoptive"[MeSH] OR "chimeric antigen receptor"[tiab] OR "CAR-T"[tiab] OR "CAR T"[tiab] OR "CAR-NK"[tiab] OR "CAR NK"[tiab] OR "CD19 CAR"[tiab] OR "BCMA CAR"[tiab] OR "cellular therapy"[tiab] OR "in vivo CAR"[tiab])

The strategy will be adapted to the syntax and controlled vocabulary of each source. Full strings and search dates will be reported in the final review.

**Participant or population** Patients of any age and sex with lupus nephritis. Biopsy-confirmed lupus nephritis (any ISN/RPS class) is preferred; reports describing renal involvement of systemic lupus erythematosus without biopsy confirmation will be recorded and analyzed separately. Patients with systemic lupus erythematosus without extractable renal data will be excluded.

**Intervention** Any CAR-based cellular therapy, including autologous CD19 CAR-T; BCMA-directed CAR-T; dual-target, compound or co-infused constructs (e.g., CD19/BCMA, CD20/BCMA, CD19/CD22 bicistronic); allogeneic, gene-edited or induced pluripotent stem cell-derived CAR-T; CAR-NK cells; and in vivo-generated CAR-T. Any lymphodepletion regimen, dose and number of infusions will be eligible.

**Comparator** No comparator is required. Most eligible studies are expected to be single-arm; outcomes will be assessed relative to pre-treatment baseline. Where available, comparisons with standard-of-care immunosuppression or other active therapy will be extracted.

**Study designs to be included** Randomized controlled trials, non-randomized and single-arm trials, prospective and retrospective cohorts, case series, case reports, and conference abstracts reporting extractable renal data. Reviews, editorials and preclinical studies are excluded.

**Eligibility criteria** Inclusion: human studies reporting at least one renal outcome (renal response, proteinuria, eGFR or serum creatinine, dialysis status or kidney histology) in patients with lupus nephritis treated with any CAR-based cellular therapy. Exclusion: reviews, commentaries, preclinical or in vitro studies; SLE reports without extractable renal data; press releases without an accompanying abstract or publication. Overlapping reports from the same center or cohort will be collapsed into single study units, retaining the most complete or most recent report per patient; earlier reports will be used only to supplement follow-up data.

**Information sources** Electronic databases (PubMed/MEDLINE, PubMed Central, Europe PMC, Cochrane Library, Google Scholar); trial registries (ClinicalTrials.gov, ChiCTR, EU CTR/CTIS); conference proceedings (ACR Convergence, EULAR, ASN Kidney Week, ERA, ASH); reference lists of included studies and prior reviews. Corresponding authors will be contacted when patient-level renal data are missing or unclear.

**Main outcome(s)** Complete renal response, as defined by each study, at the latest reported follow-up and at 6 and 12 months where available. Definitions (proteinuria and eGFR thresholds, urinary sediment criteria, timing) will be extracted verbatim to document heterogeneity. Outcomes will be summarized as counts and proportions of evaluable patients.

**Additional outcome(s)** Partial renal response; urine protein-to-creatinine ratio or 24-hour

proteinuria; eGFR and serum creatinine; dialysis dependence and recovery; histologic findings on repeat kidney biopsy; anti-dsDNA and complement (C3/C4); SLEDAI-2K; DORIS remission; Lupus Low Disease Activity State; drug-free remission; relapse; B-cell depletion and reconstitution kinetics; safety, including cytokine release syndrome, immune effector cell-associated neurotoxicity syndrome, infections, hypogammaglobulinemia, cytopenias, hemophagocytic lymphohistiocytosis-like syndromes, thrombotic microangiopathy, podocytopathy and death.

**Data management** Search results will be exported to a reference manager and deduplicated. Two reviewers (M.C. and M.L.) will independently screen titles and abstracts, then full texts, against the eligibility criteria, with disagreements resolved by consensus. Data will be extracted independently by both reviewers into a piloted standardized form capturing study design, country, product and target, cell source, lymphodepletion, dose, biopsy class, baseline and follow-up renal parameters, response definitions, follow-up duration and adverse events. Patient-level data will be extracted where reported. Overlapping cohorts will be mapped and collapsed before patient counting. Reasons for full-text exclusion will be recorded and reported in a PRISMA 2020 flow diagram.

**Quality assessment / Risk of bias analysis** Two reviewers will independently assess risk of bias, resolving disagreements by consensus. Case reports and case series will be appraised with the Joanna Briggs Institute critical appraisal checklists; single-arm trials with the tool of Murad et al. and MINORS; ROBINS-I will be applied to any comparative non-randomized study and RoB 2 to any randomized trial. Certainty of evidence for key renal outcomes will be rated with GRADE.

**Strategy of data synthesis** A structured descriptive synthesis will be performed, reported according to PRISMA 2020. Study characteristics, renal outcomes and safety will be tabulated, with patient-level data where available. A random-effects single-arm proportion meta-analysis of complete renal response (Freeman-Tukey double-arcsine transformation or generalized linear mixed model with logit link; 95% confidence intervals; heterogeneity by I-squared and tau-squared) will be performed only if at least 8 to 10 non-overlapping, biopsy-confirmed lupus nephritis patients sharing a common complete renal response definition can be assembled after deduplication. If this threshold is not met, results will be reported descriptively and the reason for not pooling will be stated.

**Subgroup analysis** If data permit, outcomes will be described separately by CAR target and construct (CD19, BCMA-containing, dual-target), cell source (autologous, allogeneic, CAR-NK, in vivo), ISN/RPS biopsy class, baseline eGFR and dialysis dependence, and pediatric versus adult patients.

**Sensitivity analysis** If a meta-analysis is performed, sensitivity analyses will restrict to peer-reviewed full publications (excluding conference abstracts), to biopsy-confirmed lupus nephritis, and to studies at lower risk of bias, and will test alternative deduplication assumptions for overlapping cohorts.

**Language restriction** No language restrictions will be applied.

**Country(ies) involved** United States.

**Other relevant information** Planned target journal: Clinical Rheumatology. Registered and ongoing trials of CAR-based therapy in lupus nephritis identified in registries will be tabulated separately to describe the pipeline of forthcoming evidence.

**Keywords** lupus nephritis; systemic lupus erythematosus; chimeric antigen receptor; CAR-T; CAR-NK; complete renal response; B cells.

**Dissemination plans** The completed review will be submitted for publication in a peer-reviewed rheumatology journal and may be presented at scientific meetings.

**Contributions of each author**

Author 1 - Maria Carpintero - Performed literature searching, screening, study selection, data extraction and risk-of-bias assessment; contributed to drafting and critical revision of the manuscript.

Author 2 - Marco Ladino - Conceived the review; performed literature searching, screening, study selection, data extraction and risk-of-bias assessment; drafted and critically revised the manuscript; guarantor of the review.