DATA SUPPLEMENT

Appendix A. Search strategies

Table S1. Search strategies for systematic review topics

Search dates: May 2018; updated search June 2020; updated search July 7, 2022; updated search April 23, 2023

The updated searches conducted in 2022 included both lupus nephritis and ANCA and combined all subtopics (antimalarials, immunosuppressive treatments of both proliferative and nonproliferative lupus nephritis)

Database	Search strategy
PubMed	(wegener* OR systemic vasculitis OR ((renal OR kidney*) AND vasculitis) OR rapidly progressive glomeruloneph* OR (glomerular* AND necrosis) OR (glomerular* AND crescent*) OR anti-neutrophil cytoplasmic antibod* OR antineutrophil cytoplasmic antibod* OR (anca AND vasculitis) OR lupus nephritis OR "lupus glomerulonephritis" OR "Lupus Nephritis"[Mesh]) AND ("Random Allocation"[Mesh] OR "Clinical Trial" [Publication Type] OR "Double-Blind Method"[Mesh] OR "Single-Blind Method"[Mesh] OR random* OR "Placebos"[Mesh] OR placebo OR ((clinical OR controlled) AND trial*) OR ((singl* OR doubl* OR trebl* OR tripl*) AND (blind* OR mask*)) OR rct OR crossover OR cross-over OR cross-over OR "treatment switching" OR "Treatment Switching"[Mesh] OR RCT OR "Randomized Controlled Trial" [Publication Type])
Embase	#1 'vasculitis'/exp OR 'vasculitis' #2 renal OR kidney* #3 #1 AND #2 #4 'rapidly progressive glomerulonephritis' #5 glomerular AND necrosis #6 glomerular* AND crescent* #7 cytoplasmic AND antibod* #8 antineutrophil OR 'anti neutrophil' #9 #7 AND #8 #10 'anca associated vasculitis' #11 'wegener granulomatosis' #12 granulomatosis AND polyangiitis #13 systemic #14 #1 AND #13 #15 wegener* #16 #3 OR #4 OR #5 OR #6 OR #9 OR #10 OR #11 OR #12 OR #14 OR #15 #17 'lupus erythematosus nephritis' #18 'lupus nephritis' #19 'lupus glomerulonephritis' #20 #16 OR #17 OR #18 OR #19 #21 'randomized controlled trial' #22 'crossover procedure' #23 'double blind procedure' #24 'double-blind procedure' #25 'single blind procedure' #26 'single-blind procedure' #27 random* #28 factorial*

	#29	crossover OR 'cross over'
	#30	'placebo'
	#31	single* AND blind*
	#32	double* AND blind*
	#33	assign*
	#34	allocat*
	#35	allocat*
	#36	'volunteer'
	#37	#21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36
	#38	#20 AND #37
	#39	#20 AND #37 AND ([article]/lim OR [article in press]/lim) AND [2020-2022]/py
Cochrane CENTRAL	#1	(wegener*):ti,ab,kw OR (systemic vasculitis):ti,ab,kw OR ((renal or kidney*) and vasculitis):ti,ab,kw OR (rapidly progressing glomeruloneph*):ti,ab,kw OR ("glomerular" and (necrosis or crescent*)):ti,ab,kw (Word variations have been searched)
	#2	((anti-neutrophil or antineutrophil) and cytoplasmic antibod*):ti,ab,kw OR (ANCA associated vasculitis):ti,ab,kw OR (ANCA-associated vasculitis):ti,ab,kw OR (lupus nephritis OR lupus glomerulonephritis):ti,ab,kw (Word variations have been searched)
	#3	#1 OR #2 with Cochrane Library publication date from Jan 2020 to present, in Cochrane Reviews, Trials

Appendix B. Concurrence with Institute of Medicine (IOM) standards for guideline development

Table S2. Guideline development checklist–IOM standards for development of trustworthy clinical practice guidelines (1)

IOM Standard	Description	Addressed in KDIGO 2023 Lupus Nephritis guideline
Establishing transparency	Clear description on the process of guideline development.	See *Methods for Guideline Development*
Management of conflicts of interests	Disclosure of a comprehensive conflict of interests of the Work Group against a set-criteria and a clear strategy to manage conflicts of interests	See *Work Group Financial Disclosures*
Guideline group composition and guideline development	Appropriate clinical and methodological expertise in the Work Group The processes of guideline development are transparent and allow for involvement of all Work Group Members	For guideline group composition – see *Work Group Membership* For guideline development process see *Methods for Guideline Development*
Establishing evidence foundations for rating strength of recommendations	Rationale is provided for the rating the strength of the recommendation and the transparency for the rating the quality of the evidence.	See *Methods for Guideline Development*
Articulation of recommendations	Clear and standardized wording of recommendations	All recommendations were written to standards of GRADE and were actionable statements. Please see *Methods for Guideline Development*
External review	An external review of relevant experts and stakeholders was conducted. All comments received from external review are considered for finalization of the guideline.	An external public review was undertaken in April 2023.
Updating	An update for the guidelines is planned, with a provisional timeframe provided.	The KDIGO clinical practice guideline will be updated. However, no set timeframe has been provided.

Table S3. Adapted systematic review reporting standards checklist–IOM standards for systematic reviews (2)

Appropriate IOM systematic review standards*	Addressed in Addressed in KDIGO 2023 Lupus Nephritis guideline
Methods	
Include a research protocol with appropriate eligibility criteria (PICO format)	See *Table 2 clinical question and systematic review topics in PICO format*
Include a search strategy	See *Appendix A*
Include a study selection and data extraction process	See guideline development process see *Methods for Guideline Development – Literature searching and article selection, data extraction*
Methods on critical appraisal	See *Methods for Guideline Development – Critical appraisal of studies*
Methods of synthesize of the evidence	See *Methods for Guideline Development – Evidence synthesis and meta-analysis*
Results	
Study selection processes	See *Methods for Guideline Development – Figure 15 – Search yield and study flow diagram*
Appraisal of individual studies quality	The summary of findings tables in *Appendix C & D* provide an assessment of risk of bias for all studies in a comparison between intervention and comparator.
Meta-analysis results	See *Appendix C & D* for summary of findings tables for meta-analysis results for all critical and important outcomes
Table and figures	See *Appendix C & D* for summary of findings tables

References

1. Institute of Medicine Committee on Standards for Developing Trustworthy Clinical Practice Guidelines. Clinical practice guidelines we can trust. Graham R, Mancher M, editors. National Academies Press Washington, DC; 2011.
2. Institute of Medicine Committee on Standards for Systematic Reviews of Comparative Effectiveness R. In: Eden J, Levit L, Berg A, Morton S, editors. Finding What Works in Health Care: Standards for Systematic Reviews. Washington (DC): National Academies Press (US) Copyright 2011 by the National Academy of Sciences. All rights reserved; 2011.

Appendix C. Data supplement - summary of findings (SoF) tables cited in the guideline text

Table S4.
Population: Patients with lupus nephritis
Intervention: Antimalarials
Comparator: Standard of care

Outcome Timeframe	**Study results and measurements**	**Evidence summary**	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Based on data from 697 patients in 2 studies Follow up 10 years (mean)	In a Spanish cohort study (Siso 2008), antimalarial use before diagnosis of lupus nephritis may decrease mortality (P=0.017) in a univariate model (OR 0.13, 95% CI 0.02, 0.96). However, this was presented as statistically significant (2% vs. 11%, P=0.029). In a multivariable cox regression analysis, antimalarial use before diagnosis of lupus nephritis was a statistically significant variable for development of end-stage kidney disease (HR 0.29, 95% CI 0.026, 1.009, P=0.05). In a Chinese retrospective single study (Zheng 2012), patients with lupus nephritis treated with hydroxychloroquine compared to no hydroxychloroquine treatment may decrease mortality in a cox proportional regression model (HR, 0.197, 95% CI 0.047, 0.820).	**Very Low** Due to serious risk of bias[1]	We are uncertain whether antimalarials decrease mortality.
Kidney failure	Based on data from 206 patients in 1 study Follow up 148 months (mean)	In a Spanish cohort study (Siso 2008), antimalarial use before diagnosis of lupus nephritis had little or no difference on end-stage kidney disease (OR 0.14, 95% CI 0.02, 1.10). However, this was presented as statistically significant (2% vs. 11%, P=0.029). In a multivariable cox regression analysis, antimalarial use before diagnosis of lupus nephritis was a statistically significant variable for development of end-stage kidney disease (HR 0.29, 95% CI 0.026, 1.009, P=0.05).	**Very Low** Due to serious imprecision[2]	We are uncertain whether antimalarials increase or decrease kidney failure
≥50% GFR loss or kidney failure	Based on data from 203 patients in 1 study Follow up 10 years	In multi-ethnic LUMINA US cohort (Pons-Estel 2009), patients with lupus nephritis and no kidney damage treated with hydroxychloroquine compared to no hydroxychloroquine treatment may reduce ≥50% GFR loss or end-stage kidney disease (HR 0.29, 95% CI 0.13, 0.68) after adjusting for confounders.	**Low** Due to serious risk of bias, Upgraded due to Large magnitude of effect[3]	Antimalarials may decrease ≥50% GFR loss and kidney failure

Outcome Timeframe	**Study results and measurements**	**Evidence summary**	**Certainty of the evidence**	**Plain text summary**
Infection	Based on data from 7319 patients in 2 studies	Feldman 2015, a retrospective registry (Medicaid Analytic extract (MAX) of 33,565 patients with SLE, showed that compared to no use, hydroxychloroquine in patients with lupus nephritis (n=7113) lupus nephritis may protect against serious infection (HR 0.73, 95% CI 0.68, 0.77). Patients with lupus nephritis under Medicaid are generally of lower socioeconomic status, and at high risk of infections. Therefore, this finding may not be generalizable to the broad lupus nephritis population. One single-center Spanish cohort study (Siso 2008), found that patients with biopsy-proven lupus nephritis prescribed with hydroxychloroquine before diagnosis of lupus nephritis compared to no prescription of hydroxychloroquine had less infections (OR 0.30, 95% CI 0.12, 0.75). This remained significant in a multivariate model adjusted for age, gender and length of follow-up.	**Low** Due to serious indirectness, Upgraded due to Large magnitude of effect[4]	Antimalarials may decrease infections.
Malignancy	Based on data from 206 patients in 1 study Follow up 148 months (mean)	It is uncertain if antimalarial use has an effect on malignancy. This is based on one single-center Spanish cohort study (Siso 2008) that had patients with biopsy-proven lupus nephritis prescribed with hydroxychloroquine before diagnosis of lupus nephritis compared to no prescription of hydroxychloroquine (OR 0.23, 95% 0.01 to 4.30, univariant model)	**Very Low** Due to serious imprecision[5]	We are uncertain whether antimalarials increase or decrease malignancy.
Complete remission	Based on data from 89 patients in 2 studies Follow up within 16 months	In the Hopkins lupus cohort (Kasitanon 2006), patients with membranous lupus nephritis and initially treated with mycophenolate mofetil and receive hydroxychloroquine are more likely to achieve complete remission compared to those who did not receive hydroxychloroquine (P=0.036) (OR 6.13, 95% CI 1.17, 32.10). In the retrospective and prospective single-center cohort study (Mejia-Vilet 2016), patients with pure membranous lupus nephritis treated with azathioprine, intravenous cyclophosphamide or mycophenolate mofetil plus glucocorticoids, after adjusting for age, serum creatinine and 24hr UPCR, adjunctive antimalarial therapy was independently associated with higher complete remission rates (HR 2.46, 1.08, 5.64, p = 0.032). However, in this study there may be some confounding factors evident.	**Low** Due to serious risk of bias, Due to serious imprecision, Upgraded due to Very large magnitude of effect[6]	Antimalarials may increase complete remission
Serum creatinine	Based on data from 206 patients in 1 study Follow up 148 months	From a Spanish cohort (Siso 2008) patients ever treated with an antimalarial before diagnosis of lupus nephritis compared to no antimalarial treatment may have little or no difference on serum creatinine >2 mg/dl (OR 0.81, 95% CI 0.34, 1.94) and serum creatinine >4 mg/dl (OR 0.15, 95% CI 0.02, 1.19).	**Very Low** Due to serious imprecision[7]	We are uncertain whether antimalarials increase or decrease serum creatinine

Outcome Timeframe	**Study results and measurements**	**Evidence summary**	**Certainty of the evidence**	**Plain text summary**
	(mean)			
Ischemic heart disease	Based on data from 206 patients in 1 study Follow up 148 months (mean)	One single-center Spanish cohort study (Siso 2008), found that patients with biopsy-proven lupus nephritis prescribed with hydroxychloroquine before diagnosis of lupus nephritis compared to no prescription of hydroxychloroquine may have had little or no effect on similar ischemic heart disease (OR 1.93, 95% CI 0.41, 9.09).	**Low** Observational data	Antimalarials may have little to no effect on ischemic heart disease
Stroke	Based on data from 206 patients in 1 study Follow up 148 months (mean)	One single-center Spanish cohort study (Siso 2008), found that patients with biopsy-proven lupus nephritis prescribed with hydroxychloroquine before diagnosis of lupus nephritis compared to no prescription of hydroxychloroquine may have had little or no effect on stroke (OR 1.44, 95% CI 0.46, 4.55).	**Low** Observational data	Antimalarials may have little to no effect on stroke
eGFR ≤60 ml/min/1.73 m^2	Based on data from 256 patients in 1 study Follow up 8.5 ± 6.1 years (mean)	In an Israeli retrospective cohort single-center study (Pokroy-Shapira 2014) on patients with lupus nephritis (not all cases were biopsy proven). The study found that hydroxychloroquine compared no hydroxychloroquine treatment, may decrease chronic kidney disease progression (GFR ≤ 60 ml/min/1.73 m^2) (p=0.02, HR 0.4, 95% CI 0.2, 0.9).	**Very Low** Due to serious indirectness, Due to serious risk of bias, Due to serious imprecision[8]	We are uncertain whether antimalarials increase or decrease eGFR ≤60 ml/min/1.73 m^2.

1. **Risk of bias: Serious.** Potential confounders not examined.
2. **Imprecision: Serious.** Only data from one study, Low number of patients in treatment cohort.
3. **Risk of bias: Serious.** due to differences between the patients treated with hydroxychloroquine compared to those not treated with hydroxychloroquine; **Upgrade: Large magnitude of effect.**
4. **Indirectness: Serious.** Differences between the population of interest and those studied may result in data not being representative of the LN population. The patients in Feldman 2015, were recruited from Medicaid Analytic extract (MAX) which may have different characteristics to those in the general lupus nephritis population.; **Upgrade: Large magnitude of effect.**
5. **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
6. **Risk of bias: Serious.** due to study not adjusting for potential confounders and selection bias concerns, with patients lost to follow-up and changing mycophenolate mofetil therapy because of treatment failure; **Imprecision: Serious.** Low number of patients, **Upgrade: Very large magnitude of effect.**
7. **Imprecision: Serious.** Only data from one study, Wide confidence intervals.
8. **Risk of bias: Serious.** due to confounding because of lack of adjustment for biopsy-proven nephritis in the treatment cohorts; **Indirectness: Serious.** Differences between the population of interest and those studied as lupus nephritis was determined by the ACR classification criteria not kidney biopsy; **Imprecision: Serious.** Low number of patients in the never treated with hydroxychloroquine cohort, Only data from one study.

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Table S5.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Intravenous cyclophosphamide
Comparator: Induction: Glucocorticoids alone

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Glucocorticoids alone	Intravenous cyclophosphamide	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: 0.98 (95% CI: 0.53 - 1.82) Based on data from 226 patients in 5 studies[1] Mean follow up 42 months	**170** per 1000	**167** per 1000 Difference: **3 fewer per 1000** (95% CI: 80 fewer - 139 more)	**Low** Due to serious imprecision, Due to serious risk of bias[2]	Intravenous cyclophosphamide may have little or no difference on all-cause mortality
Kidney failure	Relative risk: 0.63 (95% CI: 0.39 - 1.03) Based on data from 278 patients in 5 studies[3] Mean follow up 65 months	**243** per 1000	**153** per 1000 Difference: **90 fewer per 1000** (95% CI: 148 fewer - 7 more)	**Moderate** Due to serious risk of bias[4]	Intravenous cyclophosphamide probably has little or no difference on kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 0.87 (95% CI: 0.5 - 1.51) Based on data from 291 patients in 6 studies[5] Mean follow up 55 months	**150** per 1000	**131** per 1000 Difference: **19 fewer per 1000** (95% CI: 75 fewer - 76 more)	**Moderate** Due to serious risk of bias[6]	Intravenous cyclophosphamide probably has little or no difference on infection
Malignancy	Relative risk: 0.82 (95% CI: 0.07 - 9.9) Based on data from 117 patients in 2 studies[7] Mean follow up 102 months	**26** per 1000	**21** per 1000 Difference: **5 fewer per 1000** (95% CI: 24 fewer - 231 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether intravenous cyclophosphamide increases or decreases malignancy
Glucocorticoid-related adverse events	(95% CI: -)	Difference:			No studies were found that looked at glucocorticoid-related adverse events
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission

Outcome	Study results and measurements Timeframe	Absolute effect estimates Glucocorticoids alone	 Intravenous cyclophosphamide	Certainty of the evidence	Plain text summary
Complete remission of proteinuria	Relative risk: 2.63 (95% CI: 0.13 - 54.64) Based on data from 13 patients in 1 study[9] Follow up 2.5 months	**0** per 1000	**143** per 1000 Difference: **143 more per 1000** (95% CI: 116 fewer – 402 more)	**Very low** Due to serious risk of bias, Due to serious indirectness, Due to very serious imprecision[10]	We are uncertain whether intravenous cyclophosphamide increases or decreases complete remission of proteinuria
Kidney relapse	Relative risk: 0.23 (95% CI: 0.08 - 0.62) Based on data from 84 patients in 2 studies[11] Mean follow up 54 months	**438** per 1000	**101** per 1000 Difference: **337 fewer per 1000** (95% CI: 403 fewer - 166 fewer)	**Moderate** Due to serious risk of bias[12]	Intravenous cyclophosphamide probably decreases kidney relapse
Doubling serum creatinine	Relative risk: 0.59 (95% CI: 0.4 - 0.88) Based on data from 228 patients in 4 studies[13] Mean follow up 65 months	**395** per 1000	**233** per 1000 Difference: **162 fewer per 1000** (95% CI: 237 fewer - 47 fewer)	**Moderate** Due to serious risk of bias[14]	Intravenous cyclophosphamide probably decreases doubling serum creatinine
Stable kidney function[13]	Relative risk: 1.2 (95% CI: 1.0 - 1.45) Based on data from 278 patients in 5 studies[14] Mean follow up 65 months	**589** per 1000	**707** per 1000 Difference: **118 more per 1000** (95% CI: 0 fewer - 265 more)	**Moderate** Due to serious risk of bias[15]	Cyclophosphamide plus glucocorticoids probably increases stable kidney function
Ovarian failure	Relative risk: 2.18 (95% CI: 1.1 - 4.34) Based on data from 147 patients in 3 studies[16] Mean follow up 88 months	**188** per 1000	**410** per 1000 Difference: **222 more per 1000** (95% CI: 19 more - 628 more)	**Low** Due to serious imprecision, Due to serious risk of bias[17]	Intravenous cyclophosphamide may increase ovarian failure
Annual GFR loss	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss
Creatinine clearance		**65.4** ml/min	**76.2** ml/min	**Very low**	We are uncertain whether intravenous

Outcome	Study results and measurements Timeframe	Absolute effect estimates Glucocorticoids alone	 Intravenous cyclophosphamide	Certainty of the evidence	Plain text summary
	Based on data from 63 patients in 2 studies[17] Mean follow up 54 months	Difference: **6.6 higher** (95% CI: 5.3 lower - 18.5 higher)		Due to serious risk of bias, Due to very serious inconsistency, Due to serious imprecision[18]	cyclophosphamide increases or decreases creatinine clearance

1. Systematic review [538] with included studies: [466], [490], [510], [509], [517] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Serious.** Wide confidence intervals.
3. Systematic review [538] with included studies: [517], [466], [490], [509], [471] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.**
5. Systematic review [538] with included studies: [510], [471], [517], [509], [490], [466] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.**
7. Systematic review [538] with included studies: [466], [471] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, due to few events.
9. Primary study [510] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Indirectness: Serious.** The outcome time frame in studies were insufficient; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients and few events.
11. Systematic review [538] with included studies: [517], [490] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.**
13. (<20% serum creatinine worsening)
14. Systematic review [540] with included studies: [468], [511], [519], [473], [492] **Baseline/comparator:** Control arm of reference used for intervention.
15. **Risk of bias: Serious.**
16. Systematic review [538] with included studies: [471], [466], [509], [490] **Baseline/comparator:** Control arm of reference used for intervention.
17. **Risk of bias: Serious.**
18. Systematic review [538] with included studies: [471], [466], [490] **Baseline/comparator:** Control arm of reference used for intervention.
19. **Risk of bias: Serious. Imprecision: Serious.** Wide confidence intervals, Low number of patients.
20. Systematic review [538] with included studies: [510], [517] **Baseline/comparator:** Control arm of reference used for intervention.
21. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Inconsistency: Very Serious.** The magnitude of statistical heterogeneity was high, with I^2:73 %., Point estimates vary widely; **Imprecision: Serious.** Wide confidence intervals.

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Table S6.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: High-dose cyclophosphamide
Comparator: Induction: Low-dose cyclophosphamide

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Low-dose cyclophosphamide	**Absolute effect estimates** High-dose cyclophosphamide	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: 0.97 (95% CI: 0.14 - 6.56) Based on data from 121 patients in 2 studies[1] Follow up 12 months	**32** per 1000	**31** per 1000 Difference: **1 fewer per 1000** (95% CI: 28 fewer - 178 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether high-dose cyclophosphamide increases or decreases mortality
Kidney failure	Relative risk: 0.49 (95% CI: 0.05 - 5.2) Based on data from 135 patients in 2 studies[3] Mean follow up 27 months	**31** per 1000	**15** per 1000 Difference: **16 fewer per 1000** (95% CI: 29 fewer - 130 more)	**Moderate** Due to serious imprecision[4]	High-dose cyclophosphamide probably has little or no difference on kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.44 (95% CI: 0.83 - 2.49) Based on data from 327 patients in 4 studies[5] Mean follow up 22 months	**159** per 1000	**229** per 1000 Difference: **70 more per 1000** (95% CI: 27 fewer - 237 more)	**Moderate** Due to serious imprecision[6]	High dose cyclophosphamide probably has little or no difference on infection
Malignancy	Relative risk: 1.44 (95% CI: 0.09 - 23.31) Based on data from 206 patients in 2 studies[7] Follow up 8.4 years	**11** per 1000	**16** per 1000 Difference: **5 more per 1000** (95% CI: 10 fewer - 245 more)	**Low** Due to serious inconsistency, Due to serious imprecision[8]	High-dose cyclophosphamide may have little or no difference on malignancy
Complete remission	Relative risk: 1.09 (95% CI: 0.63 - 1.86) Based on data from 267 patients in 3 studies[9] Mean follow up 16 months	**393** per 1000	**428** per 1000 Difference: **35 more per 1000** (95% CI: 145 fewer - 338 more)	**Moderate** Due to serious imprecision[10]	High-dose cyclophosphamide probably has little or no difference on complete remission

Outcome	Study results and measurements Timeframe	Absolute effect estimates Low-dose cyclophosphamide	 High-dose cyclophosphamide	Certainty of the evidence	Plain text summary
Doubling of serum creatinine	Relative risk: 0.33 (95% CI: 0.04 - 3.02) Based on data from 135 patients in 2 studies[11] Mean follow up 27 months	**47** per 1000	**16** per 1000 Difference: **31 fewer per 1000** (95% CI: 45 fewer - 95 more)	**Low** Due to serious risk of bias, Due to serious imprecision[12]	High-dose cyclophosphamide may have little or no difference on doubling of serum creatinine
Annual GFR loss	(95% CI: -)	Difference:			No studies were found that looked at annual loss of GFR
Creatinine clearance	Based on data from 117 patients in 1 study[13] Follow up 24 months	**67.7** ml/min	**55.1** ml/min Difference: **12.6 lower** (95% CI: 23.6 lower - 1.6 lower)	**Very low** Due to serious risk of bias, Due to very serious imprecision[14]	We are uncertain whether high-dose cyclophosphamide increases or decreases creatinine clearance

1. Systematic review [538] with included studies: [518], [508] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Very Serious.** Wide confidence intervals, due to few events.
3. Systematic review [538] with included studies: [494], [508] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Serious.** Wide confidence intervals.
5. Systematic review [538] with included studies: [519], [494], [518], [508] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Serious.** Wide confidence intervals, due to few events.
7. Systematic review [538] with included studies: [519], [494] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Inconsistency: Serious. Imprecision: Serious.** Wide confidence intervals, due to few events.
9. Systematic review [538] with included studies: [518], [494], [519] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Imprecision: Serious.** Wide confidence intervals.
11. Systematic review [538] with included studies: [494], [508] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Serious.** Wide confidence intervals, due to few events.
13. Systematic review [538] with included studies: [519] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious. Imprecision: Very Serious.** Wide confidence intervals, only data from one study.

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Table S7.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Mycophenolate mofetil
Comparator: Induction: Intravenous cyclophosphamide

Outcome	Study results and measurements Timeframe	Absolute effect estimates Intravenous cyclophosphamide	 Mycophenolate mofetil	Certainty of the evidence	Plain text summary
All-cause mortality	Relative risk: 1.12 (95% CI: 0.61 - 2.06) Based on data from 826 patients in 8 studies[1] Mean follow up 6 months	**48** per 1000	**54** per 1000 Difference: **6 more per 1000** (95% CI: 19 fewer - 51 more)	**Very low** Due to serious indirectness, Due to very serious imprecision[2]	We are uncertain whether mycophenolate mofetil increases or decreases mortality
Kidney failure	Relative risk: 0.71 (95% CI: 0.27 - 1.84) Based on data from 231 patients in 3 studies[3] Mean follow up 6 months	**85** per 1000	**60** per 1000 Difference: **25 fewer per 1000** (95% CI: 62 fewer - 71 more)	**Very low** Due to serious imprecision, Due to serious indirectness, Due to serious risk of bias[4]	We are uncertain whether mycophenolate mofetil increases or decreases kidney failure.
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.02 (95% CI: 0.67 - 1.54) Based on data from 699 patients in 6 studies[5] Mean follow up 6 months	**107** per 1000	**116** per 1000 Difference: **2 more per 1000** (95% CI: 38 fewer - 62 more)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Mycophenolate mofetil may have little or no difference on infection
Malignancy	Relative risk: 0.65 (95% CI: 0.11 - 3.86) Based on data from 364 patients in 1 study[7] Follow up 6 months	**17** per 1000	**11** per 1000 Difference: **6 fewer per 1000** (95% CI: 15 fewer - 49 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether mycophenolate mofetil increases or decreases malignancy
Alopecia	Relative risk: 0.29 (95% CI: 0.19 - 0.46) Based on data from 622 patients in 3 studies[9] Mean follow up 6 months	**239** per 1000	**69** per 1000 Difference: **170 fewer per 1000** (95% CI: 194 fewer - 129 fewer)	**Moderate** Due to serious imprecision[10]	Mycophenolate mofetil probably improves alopecia
Ovarian failure	Relative risk: 0.36 (95% CI: 0.06 - 2.18) Based on data from 539 patients in 3 studies[11] Mean follow up 6 months	**41** per 1000	**15** per 1000 Difference: **26 fewer per 1000** (95% CI: 39 fewer - 48 more)	**Very low** Due to very serious imprecision, Due to serious risk of bias, Due to serious inconsistency[12]	We are uncertain whether mycophenolate mofetil increases or decreases ovarian failure

Outcome	Study results and measurements Timeframe	Absolute effect estimates Intravenous cyclophosphamide	 Mycophenolate mofetil	Certainty of the evidence	Plain text summary
Diarrhea	Relative risk: 2.42 (95% CI: 1.64 - 3.58) Based on data from 609 patients in 4 studies[13] Mean follow up 6 months	**100** per 1000	**242** per 1000 Difference: **142 more per 1000** (95% CI: 64 more - 258 more)	**Moderate** Due to serious imprecision[14]	Mycophenolate mofetil probably increases diarrhea
Glucocorticoid-related adverse events	(95% CI: -)	Difference:			No studies were found that looked at glucocorticoid-related adverse events
Complete kidney remission	Relative risk: 1.17 (95% CI: 0.97 - 1.42) Based on data from 868 patients in 9 studies[15] Mean follow up 6 months	**222** per 1000	**260** per 1000 Difference: **38 more per 1000** (95% CI: 7 fewer - 93 more)	**Moderate** Due to serious risk of bias[16]	Mycophenolate mofetil probably has little or no difference on complete kidney remission
Annual GFR loss	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [538] with included studies: [488], [525], [521], [465], [523], [500], [481], [524] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Indirectness: Serious.** The outcome time frame in studies were insufficient; **Imprecision: Very Serious.** Wide confidence intervals, due to small number of events.
3. Systematic review with included studies: [488], [481], [525] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Study limitations; **Indirectness: Serious.** Total number of events small; **Imprecision: Serious.** Risk estimate includes null effect and estimate consistent with both appreciable benefit and harm.
5. Systematic review [538] with included studies: [488], [481], [465], [525], [521], [500] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Study limitations; **Imprecision: Serious.** Total number of events small, risk estimate includes null effect and estimate consistent with both appreciable benefit and harm.
7. Systematic review [538] with included studies: [465] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** due to pharmaceutical affiliated authors involved in data analysis and authorship; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
9. Systematic review [548] with included studies: [488], [465], [523] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Imprecision: Serious.** Due to total number of events small.
11. Systematic review [538] with included studies: [488], [465], [523] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Study limitations; **Inconsistency: Serious.** Point estimates vary widely; **Imprecision: Very Serious.** Total number of events small, risk estimate includes null effect and estimate consistent with both appreciable benefit and harm.
13. Systematic review [538] with included studies: [521], [465], [488], [481] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Imprecision: Serious.** due to Total number of events small.
15. Systematic review [538] with included studies: [524], [488], [481], [465], [525], [500], [523], [526], [521] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Study limitations.

References

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Table S8.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Mycophenolate mofetil plus tacrolimus
Comparator: Induction: Intravenous cyclophosphamide

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Intravenous cyclophosphamide	**Absolute effect estimates** Mycophenolate mofetil plus tacrolimus	**Certainty of evidence**	**Plain text summary**
All-cause mortality	No events Based on data from 455 patients in 3 studies[1] Follow up (range) 6-17 months	**0** per 1000	**0** per 1000 Difference: **0 more per 1000** (95% CI 9 fewer – 9 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether mycophenolate mofetil plus tacrolimus increases or decreases mortality
Kidney failure	No events Based on data from 53 patients in 1 study[3] Follow up 17 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI 71 fewer – 71 more)	**Very low** Due to very serious imprecision[4]	We are uncertain whether mycophenolate mofetil plus tacrolimus increases or decreases kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection, major	Relative risk: 1.33 (95% CI 0.25 - 7.14) Based on data from 455 patients in 3 studies[5] Follow up (range) 6-17 months	**35** per 1000	**48** per 1000 Difference: **12 more per 1000** (95% CI 26 fewer – 215 more)	**Very low** Due to very serious imprecision[6]	We are uncertain whether mycophenolate mofetil plus tacrolimus increases or decreases infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Serious adverse events	Relative risk: 2.21 (95% CI 0.88 - 5.53) Based on data from 458 patients in 3 studies[7] Follow up (range) 6-17 months	**26** per 1000	**61** per 1000 Difference: **32 more per 1000** (95% CI 3 fewer – 119 more)	**Low** Due to serious risk of bias Due to serious imprecision[8]	Selection of mycophenolate mofetil plus tacrolimus or cyclophosphamide may have little or no difference on serious adverse events

Outcome	Study results and measurements Timeframe	Absolute effect estimates Intravenous cyclophosphamide	 Mycophenolate mofetil plus tacrolimus	Certainty of evidence	Plain text summary
Adverse events leading to discontinuation	Relative risk: 1.67 (95% CI 0.47 – 6.01) Based on data from 458 patients in 3 studies[9] Follow up (range) 6-17 months	**26** per 1000	**52** per 1000 Difference: **18 more per 1000** (95% CI 14 fewer – 131 more)	**Very low** Due to very serious imprecision[10]	We are uncertain whether mycophenolate mofetil plus tacrolimus increases or decreases discontinuation due to adverse events
Complete remission	Relative risk: 1.98 (95% CI 1.48 - 2.66) Based on data from 455 patients in 3 studies[11] Follow up (range) 6-17 months	**243** per 1000	**537** per 1000 **Difference: 239 more per 1000** (95% CI 116 more – 404 more)	**Low** Due to serious risk of bias[12]	Mycophenolate mofetil plus tacrolimus may increase complete kidney remission
Relapse	(95% CI: -)	Difference:			No studies were found that looked at relapse
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Based on 3 Studies [468], [502], [550]
2. **Imprecision: Very serious.** Wide confidence intervals
3. Based on 1 Study [550]
4. **Imprecision: Very serious.** One study with no events in either arm
5. Based on 3 studies [468], [502], [550]
6. **Imprecision: Very serious.** Wide confidence intervals
7. Based on 3 studies [468], [502], [550] but one study had 0 events [550]
8. **Risk of bias: Serious. Imprecision: Serious.** Wide confidence intervals.
9. Based on 3 studies [468], [502], [550]
10. **Imprecision: Very serious.** Wide confidence intervals
11. Based on 3 studies [468], [502], [550]
12. **Risk of bias: Serious.**

References

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Table S9.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Voclosporin (with mycophenolate mofetil and rapidly tapered steroids)
Comparator: Induction: Placebo (with mycophenolate mofetil and rapidly tapered steroids)

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Placebo	Voclosporin	**Certainty of evidence**	**Plain text summary**
All-cause mortality	Relative risk: 1.43 (95% CI 0.03 - 65.22) Based on data from 533 patients in 2 studies[1] Follow up 12 months	**22** per 1000	**27** per 1000 Difference: **9 more per 1000** (95% CI 21 fewer – 1000 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether voclosporin increases or decreases all-cause mortality.
Kidney failure	Relative risk: 1.00 (95% CI 0.06 - 15.86) Based on data from 356 patients in 1 study[3] Follow up 12 months	**6** per 1000	**6** per 1000 Difference: **0 more per 1000** (95% CI 16 fewer – 16 more)	**Very low** Due to very serious imprecision[4]	We are uncertain whether voclosporin increases or decreases kidney failure.
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.07 (95% CI 0.65 - 1.76) Based on data from 533 patients in 2 studies[5] Follow up 12 months	**101** per 1000	**108** per 1000 Difference: **7 more per 1000** (95% CI 36 fewer – 76 more more)	**Low** Due to serious imprecision[6]	Voclosporin may have little or no difference on serious infections.
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Serious adverse events	Relative risk: 1.26 (95% CI 0.71 - 2.25) Based on data from 533 patients in 2 studies[7] Follow up 12 months	**195** per 1000	**231** per 1000 Difference: **51 more per 1000** (95% CI 57 fewer – 244 more)	**Low** Due to serious imprecision[8]	Voclosporin may have little or no difference on serious adverse events.
Adverse events leading to discontinuation	Relative risk: 1.11 (95% CI 0.50 - 2.49) Based on data from 533 patients in 2 studies[9] Follow up 12 months	**131** per 1000	**139** per 1000 Difference: **14 more per 1000** (95% CI 66 fewer – 195 more)	**Very low** Due to very serious imprecision[10]	We are uncertain whether voclosporin increases or decreases discontinuation due to adverse events
Complete remission	Relative risk: 1.91 (95% CI 1.47 - 2.47) Based on data from 534 patients in 2 studies[11] Follow up 12 months	**229** per 1000	**443** per 1000 Difference: **208 more per 1000** (95% CI 108 more – 337 more)	**High**[12]	Voclosporin increases complete remissions

Outcome	Study results and measurements Timeframe	Absolute effect estimates Placebo Voclosporin	Certainty of evidence	Plain text summary
Complete remission Pure Class V	Relative risk 2.7 (95% CI 0.8 - 9.7) Based on data from 25 patients in 1 study[13] Follow-up 12 months	Difference: Insufficient data to calculate	**Low** Due to serious imprecision[14]	Voclosporin may increase complete remissions among patients with pure Class V LN[15]
Relapse	(95% CI: -)	Difference:		No studies were found that looked at relapse
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:		No studies were found that looked at annual GFR loss

1. Based on 2 studies [549], [551], [552]
2. **Imprecision: Very serious.** Wide confidence intervals
3. Based on 1 study [549], [551]
4. **Imprecision: Very serious.** Single study with very wide confidence intervals
5. Based on 2 studies [549], [551], [552]
6. **Imprecision: Serious.** Wide confidence intervals
7. Based on 2 studies [549], [551], [552]
8. **Imprecision: Serious.** Wide confidence intervals
9. Based on 2 studies [549], [551], [552]
10. **Imprecision: Very serious.** Wide confidence intervals
11. Based on 2 studies [549], [551], [552]
12. **Risk of bias: Low. Consistent**. **Effect**: large and significant.
13. Based on 1 study [549], [551
14. **Imprecision: Serious.** Single study.
15. Effect size consistent with overall finding in non-pure Class V, and other subgroups.

References

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Table S10.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: CNI-included triple therapy (tacrolimus or voclosporin + mycophenolate mofetil + glucocorticoids)
Comparator: Induction: Standard of care (cyclophosphamide or mycophenolate mofetil + glucocorticoids)

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Standard of care	CNI triple therapy	**Certainty of evidence**	**Plain text summary**
All-cause mortality	Relative risk: 1.43 (95% CI 0.03 - 65.2) Based on data from 988 patients in 5 studies[1] Follow up ~2-17 months (range)	**5** per 1000	**4** per 1000 Difference: **2 more per 1000** (95% CI 3 fewer– 231 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether CNI increases or decreases mortality compared with standard of care
Kidney failure	Relative risk: 1.00 (95% CI 0.06 - 15.9) Based on data from 409 patients in 2 studies[3] Follow up 13 and 17 months	**1** per 1000	**1** per 1000 Difference: **0 more per 1000** (95% CI 1 fewer– 15 more)	**Very low** Due to very serious imprecision[4]	We are uncertain whether CNI increases or decreases kidney failure compared with standard of care
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection (pneumonia)	Relative risk: 1.51 (95% CI 0.66 - 3.47) Based on data from 991 patients in 5 studies[5] Follow up (range) ~2-17 months	**24** per 1000	**42** per 1000 Difference: **12 more per 1000** (95% CI 8 fewer– 59 more)	**Low** Due to serious risk of bias Due to serious imprecision[6]	CNI may have little or no difference on complete remission compared with standard of care
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Serious adverse events	Relative risk: 1.43 (95% CI 0.85 - 2.40) Based on data from 991 patients in 5 studies[7] Follow up (range) ~2-17 months	**95** per 1000	**135** per 1000 Difference: **41 more per 1000** (95% CI 14 fewer– 133 more)	**Very low** Due to serious risk of bias Due to serious indirectness[8]	We are uncertain whether CNI increases or decreases serious adverse events compared with standard of care
Adverse events leading to discontinuation	Relative risk: 1.13 (95% CI 0.45 - 2.80) Based on data from 814 patients in 4 studies[9] Follow up (range) ~2-17 months	**64** per 1000	**71** per 1000 Difference: **8 more per 1000** (95% CI 33 fewer– 108 more)	**Very low** Due to very serious imprecision[10]	We are uncertain whether CNI increases or decreases adverse events leading to discontinuation compared with standard of care

Outcome	Study results and measurements Timeframe	Absolute effect estimates Standard of care	 CNI triple therapy	Certainty of evidence	Plain text summary
Complete remission	Relative risk: 1.93 (95% CI 1.60 - 2.32) Based on data from 989 patients in 5 studies[11] Follow up (range) ~2-17 months	**234** per 1000	**461** per 1000 Difference: **217 more per 1000** (95% CI 141 more– 309 more)	**Moderate** Due to serious risk of bias Due to indirectness Upgraded for strong effect[12]	CNI probably increases complete remission compared with standard of care
Relapse	(95% CI: -)	Difference:			No studies were found that looked at relapse
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Based on five studies [468], [502], [550], [551], [552]
2. **Imprecision: Serious.** Wide confidence intervals.
3. Based on two studies [550], [552], but one study had 0 events [550]
4. **Imprecision: Serious**. Wide confidence intervals.
5. Based on five studies [468]. [502], [550], [551], [552]
6. **Risk of bias: Serious. Imprecision: Serious.** Wide confidence intervals
7. Based on five studies [468]. [502], [550], [551], [552]
8. **Risk of bias: Serious. Directness: Serious**. Variable comparisons and outcome definitions.
9. Based on four studies [468], [502], [550], [552]
10. **Imprecision: Very serious.** Wide confidence intervals
11. Based on five studies [468]. [502], [550], [551], [552]
12. **Risk of bias: Serious. Indirectness: Serious.** Variable comparisons. Upgraded for **Strong Effect**.

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Table S11.
Population: Patients with proliferative lupus nephritis (Class III/IV) or pure Class V lupus nephritis
Intervention: Induction: Belimumab
Comparator: Induction: Placebo

Outcome	Study results and measurements Timeframe	Absolute effect estimates Placebo	 Belimumab	Certainty of evidence	Plain text summary
All-cause mortality	Relative risk: 1.2 (95% CI 0.37 - 3.88) Based on data from 491 patients in 2 studies[1] Follow up 24 months	**13** per 1000	**16** per 1000 Difference: **3 more per 1000** (95% CI 8 fewer – 37 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether belimumab increases or decreases all-cause mortality
Kidney failure	Relative risk: 0.65 (95% CI 0.08 - 5.12) Based on data from 491 patients in 2 studies[3] Follow up 24 months	**1** per 1000	**0** per 1000 Difference: **0 more per 1000** (95% CI 1 fewer – 5 more)	**Very low** Due to very serious imprecision[4]	We are uncertain whether belimumab increases or decreases kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 0.74 (95% CI 0.36 - 1.51) Based on data from 491 patients in 2 studies[5] Follow up 24 months	**156** per 1000	**124** per 1000 Difference: **41 fewer per 1000** (95% CI 100 fewer – 80 more)	**Low** Due to serious imprecision[6]	We are uncertain whether belimumab increases or decreases all-cause mortality
Malignancy	Relative risk: 7.0 (95% CI 0.36 - 134.74) Based on data from 448 patients in 1 study[7] Follow up 26 months	**0** per 1000	**13** per 1000 Difference: **13 more per 1000** (95% CI 4 fewer – 31 more)	**Low** Due to very serious imprecision[8]	There were too few who experienced the kidney failure, to determine whether belimumab made a difference
Serious adverse events	Relative risk: 0.66 (95% CI 0.31 - 1.41) Based on data from 491 patients in 2 studies[9] Follow up 24 months	**313** per 1000	**249** per 1000 Difference: **107 fewer per 1000** (95% CI 216 fewer – 127 more)	**Low** Due to risk of bias Due to some inconsistency Due to serious imprecision[10]	Belimumab may have little or no difference on serious adverse events.
Adverse events leading to discontinuation	Relative risk: 1.00 (95% CI 0.62 - 1.61) Based on data from 491 patients in 2 studies[11] Follow up 24 months	**115** per 1000	**115** per 1000 Difference: **0 fewer per 1000** (95% CI 43 fewer – 70 more)	**Low** Due to serious imprecision[12]	Belimumab may have little or no difference on discontinuation due to adverse events.
Complete remission	Relative risk: 1.51 (95% CI 1.09 - 2.07) Based on data from 491 patients in 2 studies[13] Follow up 24 months	**191** per 1000	**291** per 1000 Difference: **97 more per 1000** (95% CI 18 more – 205 more)	**Moderate** Due to some risk of bias[14]	Belimumab probably increases complete kidney response

Outcome	Study results and measurements Timeframe	Absolute effect estimates Placebo Belimumab	Certainty of evidence	Plain text summary
Complete remission Pure Class V	Relative risk: 1.09 (95% CI 0.68 - 1.76) Data based on 72 patients in 1 study[15] Follow-up 24 months	Difference: Insufficient data to calculate	**Low** Sparse data[16]	Belimumab may have little or no difference on complete kidney response in patients with pure Class V LN
Relapse	Relative risk: 0.55 (95% CI 0.36 - 0.84) Based on data from 446 patients in 1 study[17] Follow up 24 months	**229** per 1000 **126** per 1000 Difference: **103 fewer per 1000** (95% CI 173 fewer – 33 fewer)	**Low** Sparse data[18]	Belimumab may decrease complete relapse
Relapse Pure Class V	Relative risk: 0.48 (95% CI 0.19 - 1.23) Data based on 72 patients in 1 study[19] Follow-up 24 months	Difference: Insufficient data to calculate	**Low** Sparse data[20]	Belimumab may decrease complete relapse in patients with pure Class V LN[21]
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:		No studies were found that looked at annual GFR loss

1. Based on two studies [544], [553], [554] but one study had 0 events [554]
2. **Imprecision: Very serious** Wide confidence intervals
3. Based on two studies [544], [553], [554]
4. **Imprecision: Very serious** Wide confidence intervals
5. Based on two studies [544], [553], [554]
6. **Imprecision: Serious** Wide confidence intervals
7. Based on one study [544], [553]
8. **Imprecision: Very serious** Single study
9. Based on two studies [544], [553], [554]
10. **Risk of bias: Serious. Imprecision: Serious** Wide confidence intervals. **Inconsistency: Serious**
11. Based on two studies [544], [553], [554]
12. **Imprecision: Serious** Wide confidence intervals
13. Based on two studies [544], [553], [554]
14. **Risk of bias. Moderate**
15. Based on one study [544], [553]
16. **Imprecision: Serious** sparse data. **Other:** Reported data and reported odds ratio did not align, but same conclusion either way.
17. Based on one study [544], [553]
18. **Imprecision: Very serious** sparse data/single study
19. Based on one study [544], [553]
20. **Imprecision: Very serious** sparse data/single study
21. Effect size consistent with overall finding in non-pure Class V, and other subgroups.

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Table S12.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Reduced-dose oral glucocorticoid
Comparator: Induction: Standard-dose oral glucocorticoid

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Standard dose	**Absolute effect estimates** Reduced dose	**Certainty of evidence**	**Plain text summary**
All-cause mortality	Relative risk: 4.83 (95% CI 0.59 - 39.77) Based on data from 113 patients in 2 studies[1] Follow up 6 months	**69** per 1000	**0** per 1000 Difference: **69 fewer per 1000** (95% CI 134 fewer – 4 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether reduced dose oral glucocorticoid increases or decreases mortality
Kidney failure	(95% CI: -)		Difference:		No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)		Difference:		No studies were found that looked at ≥50% loss of GFR
Infection - Major infections	Relative risk: 0.19 (95% CI 0.03 - 1.01) Based on data from 133 patients in 3 studies[3] Follow up 6 months	**100** per 1000	**7** per 1000 Difference: **81 fewer per 1000** (95% CI 97 fewer – 1 more)	**Low** Due to serious risk of bias[4]	Reduced dose corticosteroids may decrease major infection
Infection - Herpes zoster	Relative risk: 0.31 (95% CI 0.07 - 1.45) Based on data from 133 patients in 3 studies[5] Follow up 6 months and 24 months	**165** per 1000	**6** per 1000 Difference: **113 fewer per 1000** (95% CI 154 fewer – 74 more)	**Moderate** Due to serious risk of bias Due to serious imprecision[6]	Reduced dose glucocorticoid may have little or no difference on herpes zoster
Malignancy	(95% CI: -)		Difference:		No studies were found that looked at malignancy
Serious adverse events	Based on data from 27 patients in 1 study[7] Follow up 6 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI 135 fewer – 135 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether reduced-dose oral glucocorticoid increases or decreases serious adverse events
Adverse events leading to discontinuation	(95% CI: -)		Difference:		No studies were found that looked at adverse events leading to discontinuation

Outcome	Study results and measurements Timeframe	Absolute effect estimates Standard dose	 Reduced dose	Certainty of evidence	Plain text summary
Complete remission	Relative risk: 0.85 (95% CI 0.60 - 1.19) Based on data from 133 patients in 3 studies[9] Follow up 6-24 months (range)	**342** per 1000	**280** per 1000 Difference: **53 fewer per 1000** (95% CI 136 fewer – 64 more)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Reduced dose glucocorticoid may have little or no difference on complete remission
Relapse	Relative risk: 0.42 (95% CI 0.02 - 9.84) Based on data from 81 patients in 1 study[11] Follow up 6 months	**36** per 1000	**0** per 1000 Difference: **36 fewer per 1000** (95% CI 136 fewer – 66 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[12]	We are uncertain whether reduced-dose oral glucocorticoid increases or decreases relapse
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Based on two studies [528], [555]
2. **Risk of bias: Serious. Imprecision: Very serious.** Wide confidence intervals
3. Based on three studies [528], [555], [556] but one study had 0 events [555].
4. **Risk of Bias: Serious**. **Imprecision: Serious** Wide confidence intervals. **Directness:** Variable definitions of major infection
5. Based on three studies [528], [555], [556]
6. **Risk of bias: Serious. Imprecision: Serious** Wide confidence intervals
7. Based on one study [555]
8. **Risk of bias: Very Serious. Imprecision: Very Serious** Single study. Wide confidence intervals
9. Based on three studies [528], [555], [556]
10. **Risk of bias: Serious. Imprecision: Serious** Wide confidence intervals
11. Based on one study [528]
12. **Risk of bias: Serious. Imprecision: Very Serious** Wide confidence intervals

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Table S13.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Intravenous cyclophosphamide
Comparator: Induction: Oral cyclophosphamide

Outcome	Study results and measurements Timeframe	Absolute effect estimates Oral CYC	Absolute effect estimates Intravenous CYC	Certainty of the evidence	Plain text summary
All-cause mortality	Relative risk: 0.8 (95% CI: 0.2 - 3.24) Based on data from 67 patients in 2 studies[1] Mean follow up 5.5 years	**235** per 1000	**188** per 1000 Difference: **47 fewer per 1000** (95% CI: 188 fewer - 526 more)	**Low** Due to very serious imprecision[2]	Intravenous cyclophosphamide may have little or no difference on all-cause mortality
Kidney failure	Relative risk: 0.23 (95% CI: 0.04 - 1.28) Based on data from 67 patients in 2 studies[3] Mean follow up 5.5 years	**176** per 1000	**40** per 1000 Difference: **136 fewer per 1000** (95% CI: 169 fewer - 49 more)	**Low** Due to very serious imprecision[4]	Intravenous cyclophosphamide may have little or no difference on kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Malignancy	Relative risk: 1.43 (95% CI: 0.41 - 4.96) Based on data from 67 patients in 2 studies[5] Mean follow up 5.5 years	**88** per 1000	**126** per 1000 Difference: **38 more per 1000** (95% CI: 52 fewer - 348 more)	**Low** Due to very serious imprecision[6]	Intravenous cyclophosphamide may have little or no difference on malignancy
Infection	Relative risk: 1.16 (95% CI: 0.47 - 2.9) Based on data from 67 patients in 2 studies[7] Mean follow up 5.5 years	**206** per 1000	**239** per 1000 Difference: **33 more per 1000** (95% CI: 109 fewer - 391 more)	**Low** Due to very serious imprecision[8]	Intravenous cyclophosphamide may have little or no difference on infection
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Doubling of serum creatinine	Relative risk: 0.67 (95% CI: 0.23 - 1.98) Based on data from 67 patients in 2 studies[9] Mean follow up 5.5 years	**176** per 1000	**118** per 1000 Difference: **58 fewer per 1000** (95% CI: 136 fewer - 172 more)	**Low** Due to very serious imprecision[10]	Intravenous cyclophosphamide may have little or no difference on doubling serum creatinine

Outcome	Study results and measurements Timeframe	Absolute effect estimates Oral CYC	 Intravenous CYC	Certainty of the evidence	Plain text summary
Ovarian failure	Relative risk: 0.7 (95% CI: 0.37 - 1.3) Based on data from 56 patients in 2 studies[11] Mean follow up 5.5 years	**308** per 1000	**216** per 1000 Difference: **92 fewer per 1000** (95% CI: 194 fewer - 92 more)	**Low** Due to very serious imprecision[12]	Intravenous cyclophosphamide may have little or no difference on ovarian failure
Annual GFR loss	(95% CI: -)		Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [538] with included studies: [466], [514] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients.
3. Systematic review [538] with included studies: [514], [466] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients.
5. Systematic review [538] with included studies: [466], [514] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients and few events.
7. Systematic review [538] with included studies: [514], [466] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients and few events.
9. Systematic review [538] with included studies: [466], [514] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients and few events.
11. Systematic review [538] with included studies: [466], [514] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients and few events.

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Table S14.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Mycophenolate mofetil
Comparator: Induction: Tacrolimus

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Tacrolimus	Mycophenolate mofetil	**Certainty of evidence**	**Plain text summary**
All-cause mortality	Relative risk: 1.22 (95% CI 0.59, 2.49) Based on data from 273 patients in 3 studies[1] Follow up range 6-118 months	**84** per 1000	**102** per 1000 Difference: **18 more per 1000** (95% CI 34 fewer – 125 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether mycophenolate mofetil increases or decreases mortality
Kidney failure	Relative risk: 1.22 (95% CI 0.51, 2.91) Based on data from 150 patients in 1 study[3] Follow up 30 months	**108** per 1000	**132** per 1000 Difference: **23 more per 1000** (95% CI 80 fewer – 127 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether mycophenolate mofetil increases or decreases kidney failure
Kidney failure CKD G4-G5	Relative risk: 0.97 (95% CI 0.50, 1.90) Based on data from 150 patients in 1 study[5] Follow up 118 months	**189** per 1000	**184** per 1000 Difference: **5 fewer per 1000** (95% CI 130 fewer – 120 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether mycophenolate mofetil increases or decreases kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 2.14 (95% CI 0.93, 4.92) Based on data from 190 patients in 2 studies[7] Mean follow up 18 months	**158** per 1000	**74** per 1000 Difference: **84 more per 1000** (95% CI 5 fewer – 290 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether mycophenolate mofetil increases or decreases infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Serious adverse events or discontinuations due to adverse events	(95% CI: -)	Difference:			No studies were found that looked at serious adverse events
Complete remission	Relative risk: 1.02 (95% CI 0.83 - 1.26) Based on data from 273 patients in 3 studies[9] Mean follow up 16 months	**559** per 1000	**548** per 1000 Difference: **11 more per 1000** (95% CI 93 fewer – 142 more)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Mycophenolate mofetil may have little or no difference on complete remission

Outcome	Study results and measurements Timeframe	Absolute effect estimates Tacrolimus	 Mycophenolate mofetil	Certainty of evidence	Plain text summary
Relapse	Relative risk: 0.67 (95% CI 0.48 - 0.93) Based on data from 150 patients in 1 study[11] Follow up 30 months	**608** per 1000	**408** per 1000 Difference: **200 fewer per 1000** (95% CI 357 fewer – 43 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[12]	Mycophenolate mofetil may decrease kidney relapse
Renal flare	Relative risk: 1.27 (95% CI 0.80 - 2.01) Based on data from 150 patients in 1 study[13] Follow up 118 months	**289** per 1000	**368** per 1000 Difference: **79 more per 1000** (95% CI 70 fewer – 228 more)	**Low** Due to serious risk of bias, Due to serious imprecision[14]	Mycophenolate mofetil may have little or no difference on nephritic flare
Renal flare Pure Class V	Relative risk: NR Based on data from 28 patients in 1 study[15] Follow up >132 months	Cumulative rates (approximate) ~70%	~55% Difference: Insufficient data to calculate	**Very low** Due to very serious imprecision[16]	We are uncertain whether mycophenolate mofetil increases or decreases renal flare in patients with Class V LN
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Based on three studies [499], [502], [524], [557]
2. **Risk of bias: Serious. Imprecision: Very serious.** Wide confidence intervals
3. Based on one study [524], [557]
4. **Risk of bias: Serious. Imprecision: Very serious.** Single study
5. Based on one study [524], [557]
6. **Risk of bias: Serious. Imprecision: Very serious.** Single study
7. Based on two studies [502], [524], [557]
8. **Risk of bias: Serious. Imprecision: Very serious.** Wide confidence intervals
9. Based on three studies [499], [502], [524], [557]
10. **Risk of bias: Serious. Imprecision: Serious.** Wide confidence intervals
11. Based on one study [524], [557]
12. **Risk of bias: Serious. Imprecision: Serious.** Single study
13. Based on one study [524], [557]
14. **Risk of bias: Serious. Imprecision: Serious.** Single study
15. Based on one study [524], [557]
16. **Imprecision: Very serious.** Single study

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Table S15.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Tacrolimus (with methylprednisolone ± mycophenolate mofetil)
Comparator: Induction: Cyclophosphamide (with methylprednisolone ± mycophenolate mofetil)

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Cyclo-phosphamide	Tacrolimus	**Certainty of evidence**	**Plain text summary**
All-cause mortality	Relative risk: 0.90 (95% CI 0.06 - 14.3) Based on data from 299 patients in 1 study[1] Follow up 6 months	**7** per 1000	**6** per 1000 Difference: **1 fewer per 1000** (95% CI 19 fewer – 18 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether tacrolimus increases or decreases all-cause mortality compared with cyclophosphamide
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 0.55 (95% CI 0.29 - 1.03) Based on data from 299 patients in 1 study[3] Follow up 6 months	**162** per 1000	**89** per 1000 Difference: **73 fewer per 1000** (95% CI 148 fewer – 2 more)	**Low** Due to very serious risk of bias Due to imprecision[4]	Tacrolimus may decrease infections compared with cyclophosphamide
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Serious adverse events	Relative risk: 0.81 (95% CI 0.52 - 1.27) Based on data from 613 patients in 3 studies[5] Follow up 6-27 months	**70** per 1000	**67** per 1000 Difference: **13 fewer per 1000** (95% CI 33 fewer – 19 more)	**Low** Due to very serious risk of bias Due to serious imprecision[6]	Tacrolimus may have little or no difference on serious adverse events compared with cyclophosphamide
Adverse events leading to discontinuation	Relative risk: 0.75 (95% CI 0.48 - 1.16) Based on data from 299 patients in 1 study[7] Follow up 6 months	**246** per 1000	**185** per 1000 Difference: **62 more per 1000** (95% CI 155 fewer – 32 more)	**Low** Due to very serious risk of bias Due to serious imprecision[8]	Tacrolimus may have little or no difference on discontinuation due to adverse events compared with cyclophosphamide

Outcome	Study results and measurements Timeframe	Absolute effect estimates Cyclo-phosphamide	Tacrolimus	Certainty of evidence	Plain text summary
Complete remission	Relative risk: 1.23 (95% CI 1.03 - 1.48) Based on data from 613 patients in 3 studies[9] Follow up 6-27 months	**402** per 1000	**497** per 1000 Difference: **93 more per 1000** (95% CI 10 more – 193 more)	**Low** Due to very serious risk of bias[10]	Tacrolimus may increase complete remission compared with cyclophosphamide
Complete remission Pure Class V	Relative risk: 2.21 (95% CI 0.67 - 7.26) Based on data from 37 patients in 1 study[11] Follow up 6 months	Difference: Insufficient data to calculate		**Very low** Due to very serious risk of bias[12]	We are uncertain whether tacrolimus increases or decreases all-cause mortality compared with cyclophosphamide in patients with pure Class V LN
Relapse	(95% CI: -)	Difference:			No studies were found that looked at relapse
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Based on one study [560]
2. **Risk of bias: Very serious. Imprecision: Serious.** Wide confidence intervals
3. Based on one study [560]
4. **Risk of bias: Very serious. Imprecision: Serious.** Sparse data/single study
5. Based on three studies [558], [559], [560], but one study had 0 events [558].
6. **Risk of bias: Very serious. Imprecision: Serious.** Wide confidence intervals
7. Based on one study [560]
8. **Risk of bias: Very serious. Imprecision: Serious.** Wide confidence intervals
9. Based on three studies [558], [559], [560]
10. **Risk of bias: Very serious.**
11. Based on one study [560]
12. **Risk of bias: Very serious. Imprecision: Serious** Data from a single study

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Table S16.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Cyclophosphamide
Comparator: Induction: Azathioprine

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** **Azathioprine** **Cyclophosphamide**	**Certainty of the evidence**	**Plain text summary**
All cause-mortality 5 years	Relative risk: 1.39 (95% CI: 0.25 - 7.77) Based on data from 146 patients in 2 studies[1] Follow up 12.5 years	**107** per 1000 **149** per 1000 Difference: **42 more per 1000** (95% CI: 80 fewer - 724 more)	**Very low** Due to serious inconsistency, Due to very serious imprecision[2]	We are uncertain whether cyclophosphamide increases or decreases all-cause mortality
Kidney failure	Relative risk: 0.4 (95% CI: 0.15 - 1.07) Based on data from 144 patients in 2 studies[3] Mean follow up 21 months	**125** per 1000 **50** per 1000 Difference: **75 fewer per 1000** (95% CI: 106 fewer - 9 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Cyclophosphamide may have little or no difference on kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:		No studies were found that looked at ≥50% loss of GFR
Malignancy	Relative risk: 0.59 (95% CI: 0.13 - 2.63) Based on data from 144 patients in 2 studies[5] Mean follow up 21 months	**54** per 1000 **32** per 1000 Difference: **22 fewer per 1000** (95% CI: 47 fewer - 88 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether cyclophosphamide increases or decreases malignancy
Infection	Relative risk: 1.25 (95% CI: 0.27 - 5.86) Based on data from 57 patients in 1 study[7] Follow up 18 months	**105** per 1000 **131** per 1000 Difference: **26 more per 1000** (95% CI: 77 fewer - 510 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether cyclophosphamide increases or decreases infection
Complete remission	(95% CI: -)	Difference:		No studies were found that looked at complete remission
Doubling of serum creatinine	Relative risk: 0.48 (95% CI: 0.24 - 0.95) Based on data from 144 patients in 2 studies[9] Mean follow up 21 months	**250** per 1000 **120** per 1000 Difference: **130 fewer per 1000** (95% CI: 190 fewer - 13 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Cyclophosphamide may decrease doubling of serum creatinine slightly
	Relative risk: 2.03 (95% CI: 0.64 - 6.46)	**143** per 1000 **290** per 1000	**Very low**	We are uncertain whether

Outcome	Study results and measurements Timeframe	Absolute effect estimates Azathioprine Cyclophosphamide	Certainty of the evidence	Plain text summary
Complete remission in proteinuria	Based on data from 59 patients in 1 study[11] Follow up 22 months	Difference: **147 more per 1000** (95% CI: 51 fewer - 781 more)	Due to serious risk of bias, Due to very serious imprecision[12]	cyclophosphamide increases or decreases complete remission in proteinuria
Ovarian failure	Relative risk: 2.11 (95% CI: 0.59 - 7.53) Based on data from 126 patients in 2 studies[13] Mean follow up 21 months	**91** per 1000 **192** per 1000 Difference: **101 more per 1000** (95% CI: 37 fewer - 594 more)	**Low** Due to very serious imprecision[14]	Cyclophosphamide may make little or no difference to ovarian failure
Annual GFR loss 3 years	(95% CI: -)	Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [538] with included studies: [491], [177] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Inconsistency: Serious.** The magnitude of statistical heterogeneity was substantial, with I^2:67; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients and events.
3. Systematic review [538] with included studies: [466], [491] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias and pooling of participants across multiple trials; **Imprecision: Serious.** Low number of patients and few events.
5. Systematic review [538] with included studies: [466], [491] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious. Imprecision: Very Serious.** Wide confidence intervals, Low number of patients and few events.
7. Primary study [466] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias and pooling of participants across trials; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients and few events.
9. Systematic review with included studies: [491], [466] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious. Imprecision: Serious.** Low number of patients and few events.
11. Primary study [177] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients and few events.
13. Systematic review [538] with included studies: [491], [466] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients and few events.

References

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Table S17.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Plasma exchange plus immunosuppression
Comparator: Induction: Immunosuppression alone

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Immunosuppression	Plasma exchange + immunosuppression	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: 1.62 (95% CI: 0.64 - 4.09) Based on data from 125 patients in 2 studies[1] Mean follow up 18.5 months	**92** per 1000	**149** per 1000 Difference: **57 more per 1000** (95% CI: 33 fewer - 284 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Plasma exchange plus immunosuppression may have little or no difference on all-cause mortality
Kidney failure	Relative risk: 1.24 (95% CI: 0.6 - 2.57) Based on data from 143 patients in 3 studies[3] Mean follow up 20 months	**149** per 1000	**185** per 1000 Difference: **36 more per 1000** (95% CI: 60 fewer - 234 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Plasma exchange plus immunosuppression may have little or no difference on kidney failure
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 0.69 (95% CI: 0.35 - 1.37) Based on data from 125 patients in 2 studies[5] Mean follow up 18.5 months	**246** per 1000	**170** per 1000 Difference: **76 fewer per 1000** (95% CI: 160 fewer - 91 more)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Plasma exchange plus immunosuppression may have little or no difference on infection
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Stable kidney function[7]	Relative risk: 1.1 (95% CI: 0.94 - 1.3) Based on data from 75 patients in 3 studies[8] Mean follow up 20 months	**780** per 1000	**858** per 1000 Difference: **78 more per 1000** (95% CI: 47 fewer - 234 more)	**Low** Due to serious risk of bias, Due to serious imprecision[9]	Plasma exchange plus immunosuppression may have little or no difference on stable kidney function

Outcome	Study results and measurements Timeframe	Absolute effect estimates Immunosuppression	 Plasma exchange + immunosuppression	Certainty of the evidence	Plain text summary
Annual loss of GFR 3 years	(95% CI: -)	Difference:			No studies were found that looked at annual loss of GFR
Creatinine clearance	Based on data from 12 patients in 1 study[10] Mean follow up 19 months	**66** ml/min	**92** ml/min Difference: **26 higher** (95% CI: 17.6 lower - 69.6 higher)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[11]	We are uncertain whether plasma exchange plus immunosuppression increases or decreases creatinine clearance

1. Systematic review [538] with included studies: [498], [475] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Trials stopping earlier than scheduled, resulting in potential for overestimating benefits, Selective outcome reporting; **Imprecision: Serious.** Low number of patients and few events, Wide confidence intervals.
3. Systematic review [538] with included studies: [475], [498], [512] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Selective outcome reporting, Trials stopping earlier than scheduled, resulting in potential for overestimating benefits; **Imprecision: Serious.** Wide confidence intervals, Only data from one study, Low number of patients.
5. Systematic review [538] with included studies: [475], [498] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Selective outcome reporting, Trials stopping earlier than scheduled, resulting in potential for overestimating benefits; **Imprecision: Serious.** Wide confidence intervals, Low number of patients.
7. (<20% worsening in serum creatinine)
8. Systematic review [538] with included studies: [475], [479], [512] **Baseline/comparator:** Control arm of reference used for intervention.
9. **Risk of bias: Serious.** Selective outcome reporting, Trials stopping earlier than scheduled, resulting in potential for overestimating benefits; **Imprecision: Serious.** Low number of patients.
10. Primary study [474] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients.

References

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Table S18.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Sirukumab plus other immunosuppressive agent
Comparator: Induction: Placebo plus other immunosuppressive agent

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Placebo	Sirukumab	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk (95% CI: -) Based on data from 25 patients in 1 study[1] Follow up 11 months	**0** per 1000	per 1000 Difference: **fewer per 1000** (95% CI: 0 fewer - fewer)	**Very low** Due to very serious risk of bias, Due to serious imprecision[2]	There were too few who experienced all-cause mortality to determine whether sirukumab plus other immunosuppressive agent made a difference
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 0.93 (95% CI: 0.66 - 1.32) Based on data from 25 patients in 1 study[3] Follow up 11 months	**1000** per 1000	**930** per 1000 Difference: **70 fewer per 1000** (95% CI: 340 fewer - 320 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether sirukumab plus other immunosuppressive agent increases or decreases infection
Malignancy	Relative risk (95% CI: -) Based on data from 25 patients in 1 study[5] Follow up 11 months	**0** per 1000	per 1000 Difference: **fewer per 1000**	**Very low** Due to very serious risk of bias, Due to serious imprecision[6]	There were too few who experienced the malignancy to determine whether sirukumab plus other immunosuppressive agent made a difference
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Diarrhea	Relative risk: 1.59 (95% CI: 0.1 - 26.15) Based on data from 25 patients in 1 study[7] Follow up 11 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI: 0 fewer - 0 fewer)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[8]	There were too few who experienced diarrhea to determine whether induction: sirukumab plus other immunosuppressive agent made a difference

Annual GFR loss	(95% CI: -)	Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [538] with included studies: [527] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, due to authors with affiliations to the pharmaceutical sponsor and differences between groups at baseline; **Imprecision: Serious.** Only data from one study, Wide confidence intervals, Only data from one study, Low number of patients.
3. Systematic review [538] with included studies: [527] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, due to authors with affiliations to the pharmaceutical sponsor and differences between groups at baseline; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients.
5. Systematic review [538] with included studies: [527] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Very Serious.** unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, due to authors with affiliations to the pharmaceutical sponsor and differences between groups at baseline; **Imprecision: Serious.** Only data from one study, Low number of patients.
7. Systematic review [538] with included studies: [527] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Very Serious.** unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias, due to authors with affiliations to the pharmaceutical sponsor and differences between groups at baseline; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients, due to few events.

References

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Table 19.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Laquinimod plus other immunosuppressive agent
Comparator: Induction: Placebo plus other immunosuppressive agent

Outcome	Study results and measurements Timeframe	Absolute effect estimates Placebo	 Laquinimod	Certainty of the evidence	Plain text summary
All cause-mortality	Relative risk: 1.5 (95% CI: 0.06 - 34.79) Based on data from 46 patients in 1 study[1] Follow up 6 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI: 0 fewer - 0 fewer)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	There were too few who experienced all-cause mortality to determine whether laquinimod plus other immunosuppressive agent made a difference
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	Relative risk: 1.55 (95% CI: 0.7 - 3.42) Based on data from 46 patients in 1 study[3] Follow up 6 months	**333** per 1000	**516** per 1000 Difference: **183 more per 1000** (95% CI: 100 fewer - 806 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether laquinimod compared with an immunosuppressive agent increases or decreases complete remission
Annual GFR loss	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Primary study [495] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients and few events.
3. Systematic review [538] with included studies: [495] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients.

References

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Table S20.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Rituximab plus mycophenolate mofetil
Comparator: Induction: Placebo plus mycophenolate mofetil

Outcome	Study results and measurements Timeframe	Absolute effect estimates Placebo	Absolute effect estimates Rituximab	Certainty of the evidence	Plain text summary
All-cause mortality	Relative risk: 5.0 (95% CI: 0.24 - 102.35) Based on data from 144 patients in 1 study[1] Follow up 12 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI: 0 fewer - 0 fewer)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether rituximab plus mycophenolate mofetil increases or decreases mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.0 (95% CI: 0.48 - 2.08) Based on data from 144 patients in 1 study[3] Follow up 12 months	**167** per 1000	**167** per 1000 Difference: **0 fewer per 1000** (95% CI: 87 fewer - 180 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether rituximab plus mycophenolate mofetil increases or decreases infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	Relative risk: 0.86 (95% CI: 0.51 - 1.45) Based on data from 144 patients in 1 study[5] Follow up 12 months	**306** per 1000	**263** per 1000 Difference: **43 fewer per 1000** (95% CI: 150 fewer - 138 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether rituximab plus mycophenolate mofetil increases or decreases complete remission
Stable kidney function	Relative risk: 1.24 (95% CI: 0.9 - 1.71) Based on data from 144 patients in 1 study[7] Follow up 12 months	**458** per 1000	**568** per 1000 Difference: **110 more per 1000** (95% CI: 46 fewer - 325 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether rituximab plus mycophenolate mofetil increases or decreases complete stable kidney function
Annual GFR loss	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Primary study [507] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** due to authors with pharmaceutical affiliations include in the authorship; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.

3. Primary study [507] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** due to authors with pharmaceutical affiliations include in the authorship; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
5. Primary study [507] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Due to authors with pharmaceutical affiliations include in the authorship; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Wide confidence intervals, Only data from one study, Low number of patients.
7. Primary study [507] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Due to authors with pharmaceutical affiliations include in the authorship; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.

References

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Table S21.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Rituximab plus cyclophosphamide
Comparator: Induction: Rituximab

Outcome	Study results and measurements Timeframe	Absolute effect estimates Rituximab	 Rituximab plus cyclophosphamide	Certainty of the evidence	Plain text summary
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
Infection	Relative risk: 0.9 (95% CI: 0.07 - 12.38) Based on data from 19 patients in 1 study[1] Follow up 48 weeks	**111** per 1000	**100** per 1000 Difference: **11 fewer per 1000** (95% CI: 103 fewer - 1263 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether rituximab plus cyclophosphamide increases or decreases infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Complete remission	Relative risk: 0.9 (95% CI: 0.16 - 5.13) Based on data from 19 patients in 1 study[3] Follow up 48 weeks	**222** per 1000	**200** per 1000 Difference: **22 fewer per 1000** (95% CI: 186 fewer - 917 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether rituximab plus cyclophosphamide increases or decreases complete remission
Annual GFR loss	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Primary study [499] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients and few events.
3. Primary study [499] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients and few events.

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Table S22.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Abatacept plus other immunosuppressive agent
Comparator: Induction: Placebo plus other immunosuppressive agent

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Placebo	Abatacept	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: 0.29 (95% CI: 0.1 - 0.91) Based on data from 432 patients in 2 studies[1] Mean follow up 12 months	**48** per 1000	**14** per 1000 Difference: **34 fewer per 1000** (95% CI: 43 fewer - 4 fewer)	**Very low** Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision[2]	We are uncertain whether abatacept plus other immunosuppressive agent increases or decreases mortality
Kidney failure	Relative risk: 0.84 (95% CI: 0.21 - 3.45) Based on data from 298 patients in 1 study[3] Follow up 12 months	**30** per 1000	**25** per 1000 Difference: **5 fewer per 1000** (95% CI: 24 fewer - 74 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether abatacept plus other immunosuppressive agent increases or decreases kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.29 (95% CI: 0.81 - 2.04) Based on data from 432 patients in 2 studies[5] Mean follow up 12 months	**131** per 1000	**169** per 1000 Difference: **38 more per 1000** (95% CI: 25 fewer - 136 more)	**Very low** Due to serious risk of bias, Due to serious indirectness, Due to serious imprecision[6]	We are uncertain whether abatacept plus other immunosuppressive agent increases or decreases infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	Relative risk: 1.13 (95% CI: 0.74 - 1.71) Based on data from 432 patients in 2 studies[7] Mean follow up 12 months	**173** per 1000	**195** per 1000 Difference: **22 more per 1000** (95% CI: 45 fewer - 123 more)	**Very low** Due to serious risk of bias, Due to serious indirectness, Due to very serious imprecision[8]	We are uncertain whether abatacept plus other immunosuppressive agent increases or decreases complete remission
Kidney relapse	Relative risk: 1.03 (95% CI: 0.22 - 4.92) Based on data from 134 patients in 1 study[9] Follow up 24 and 52 weeks	**44** per 1000	**45** per 1000 Difference: **1 more per 1000** (95% CI: 34 fewer - 172 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[10]	We are uncertain whether abatacept plus other immunosuppressive agent increases or decreases kidney relapse
Annual GFR loss	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [538] with included studies: [464], [485] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** due to authors with affiliations to the pharmaceutical sponsor; **Indirectness: Serious.** Differences between the intervention/comparator of interest and those studied, Differences between the outcomes of interest and those reported (e.g., short-term/surrogate, not patient-important); **Imprecision: Serious.** Low number of patients and few events, Wide confidence intervals, Low number of patients.
3. Primary study [485] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Due to authors with affiliations to the pharmaceutical sponsor; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients and events.
5. Systematic review [538] with included studies: [464], [485] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Due to authors with affiliations to the pharmaceutical sponsor; **Indirectness: Serious.** Differences between the intervention/comparator of interest and those studied; **Imprecision: Serious.** Low number of patients and few events.
7. Systematic review [538] with included studies: [464], [485] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Due to authors with affiliations to the pharmaceutical sponsor; **Indirectness: Serious.** Differences between the outcomes of interest and those reported (e.g., short-term/surrogate, not patient-important); **Imprecision: Very Serious.** Wide confidence intervals, Low number of events, Wide confidence intervals, Only data from one study, Low number of patients.
9. Systematic review with included studies: [464] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Due to authors with affiliations to the pharmaceutical sponsor; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients and few events.

References

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Table S23.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Ocrelizumab plus other immunosuppressive agent
Comparator: Induction: Placebo plus other immunosuppressive agent

Outcome	Study results and measurements Timeframe	Absolute effect estimates Placebo	Ocrelizumab	Certainty of the evidence	Plain text summary
All-cause mortality	Relative risk: 0.66 (95% CI: 0.23 - 1.85) Based on data from 379 patients in 1 study[1] Follow up 11 months	**48** per 1000	**32** per 1000 Difference: **16 fewer per 1000** (95% CI: 37 fewer - 41 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether ocrelizumab plus immunosuppressive agent increases or decreases mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.14 (95% CI: 0.95 - 1.36) Based on data from 378 patients in 1 study[3] Follow up 11 months	**560** per 1000	**638** per 1000 Difference: **78 more per 1000** (95% CI: 28 fewer - 202 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Ocrelizumab plus other immunosuppressive agent may have little or no difference on infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	Relative risk: 1.07 (95% CI: 0.74 - 1.56) Based on data from 223 patients in 1 study[5] Follow up 11 months	**347** per 1000	**371** per 1000 Difference: **24 more per 1000** (95% CI: 90 fewer - 194 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether ocrelizumab plus immunosuppressive agent increases or decreases complete remission
Annual GFR loss	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Primary study [505] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, and unclear concealment of allocation during randomization process, resulting in potential for selection bias, due to authors with affiliations to the pharmaceutical sponsor; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Wide confidence intervals, Only data from one study.
3. Primary study [505] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, and unclear concealment of allocation during randomization process, resulting in potential for selection bias, due to authors with affiliations to the pharmaceutical sponsor; **Imprecision: Serious.** Only data from one study.
5. Primary study [505] **Baseline/comparator:** Control arm of reference used for intervention.

6. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, and unclear concealment of allocation during randomization process, resulting in potential for selection bias, due to authors with affiliations to the pharmaceutical sponsor; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.

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Table S24.
Population: Patients with proliferative lupus nephritis
Intervention: Maintenance: Azathioprine
Comparator: Maintenance: Mycophenolate mofetil

Outcome	Study results and measurements Timeframe	Absolute effect estimates Mycophenolate mofetil	Absolute effect estimates Azathioprine	Certainty of the evidence	Plain text summary
All-cause mortality	Relative risk: 1.15 (95% CI: 0.34 - 3.87) Based on data from 451 patients in 4 studies[1] Mean follow up 49 months	**22** per 1000	**25** per 1000 Difference: **3 more per 1000** (95% CI: 15 fewer - 63 more)	**Very low** Due to serious indirectness, Due to very serious imprecision[2]	We are uncertain whether azathioprine increases or decreases all-cause mortality
Kidney failure	Relative risk: 1.7 (95% CI: 0.52 - 5.54) Based on data from 452 patients in 4 studies[3] Mean follow up 49 months	**17** per 1000	**29** per 1000 Difference: **12 more per 1000** (95% CI: 8 fewer - 77 more)	**Very low** Due to serious indirectness, Due to very serious imprecision[4]	We are uncertain whether azathioprine increases or decreases kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Malignancy	Relative risk: 4.04 (95% CI: 0.45 - 36.07) Based on data from 370 patients in 3 studies[5] Mean follow up 54 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI: 0 fewer - 0 fewer)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether azathioprine increases or decreases malignancy
Infection	Relative risk: 1.08 (95% CI: 0.6 - 1.96) Based on data from 412 patients in 3 studies[7] Mean follow up 42 months	**91** per 1000	**98** per 1000 Difference: **7 more per 1000** (95% CI: 36 fewer - 87 more)	**Low** Due to very serious imprecision[8]	Azathioprine may have little or no difference on infection
Kidney relapse	Relative risk: 1.75 (95% CI: 1.2 - 2.55) Based on data from 452 patients in 4 studies[9] Mean follow up 49 months	**152** per 1000	**266** per 1000 Difference: **114 more per 1000** (95% CI: 30 more - 236 more)	**Moderate** Due to serious imprecision[10]	Azathioprine probably increases kidney relapse
Doubling serum creatinine	Relative risk: 2.19 (95% CI: 1.03 - 4.66) Based on data from 452 patients in 4 studies[11] Mean follow up 49 months	**39** per 1000	**85** per 1000 Difference: **46 more per 1000** (95% CI: 1 more - 143 more)	**Moderate** Due to serious imprecision[12]	Azathioprine probably increases doubling serum creatinine
Ovarian failure	Relative risk: 0.77 (95% CI: 0.17 - 3.42)	**45** per 1000	**35** per 1000	**Very low**	We are uncertain whether

Outcome	Study results and measurements Timeframe	Absolute effect estimates Mycophenolate mofetil / Azathioprine	Certainty of the evidence	Plain text summary
	Based on data from 177 patients in 2 studies[13] Mean follow up 45 months	Difference: **10 fewer per 1000** (95% CI: 37 fewer - 109 more)	Due to very serious imprecision, Due to serious risk of bias[14]	azathioprine increases or decreases ovarian failure
Leukopenia	Relative risk: 5.61 (95% CI: 1.68 - 18.72) Based on data from 412 patients in 3 studies[15] Follow up 42 months (mean)	**10** per 1000 / **56** per 1000 Difference: **46 more per 1000** (95% CI: 7 more - 177 more)	**Moderate** Due to serious risk of bias[16]	In maintenance therapy, azathioprine probably increases leukopenia
Annual GFR loss	(95% CI: -)	Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [538] with included studies: [496], [531], [465], [530] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Indirectness: Serious.** The outcome time frame in studies were insufficient; **Imprecision: Very Serious.** Wide confidence intervals and few events.
3. Systematic review [538] with included studies: [496], [531], [465], [530] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Indirectness: Serious.** The outcome time frame in studies were insufficient; **Imprecision: Very Serious.** Wide confidence intervals and few events.
5. Systematic review [538] with included studies: [530], [531], [465] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, due to few events.
7. Systematic review [538] with included studies: [496], [531], [465] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Imprecision: Very Serious.** Wide confidence intervals, due to few events.
9. Systematic review [538] with included studies: [465], [530], [531], [496] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Imprecision: Serious.** due to few events.
11. Systematic review [538] with included studies: [496], [531], [465], [530] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Imprecision: Serious.** due to few events.
13. Systematic review [538] with included studies: [531], [496] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients and few events.
15. Systematic review [538] with included studies: [531], [465], [496] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.**

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Table S25.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Long duration (18 months) cyclophosphamide
Comparator: Induction: Short duration (6 months) cyclophosphamide

Outcome	Study results and measurements Timeframe	Absolute effect estimates Short duration Long duration	Certainty of the evidence	Plain text summary
All-cause mortality	(95% CI: -)	Difference:		No studies were found that looked at all-cause mortality
Kidney failure	Relative risk: 0.4 (95% CI: 0.09 - 1.83) Based on data from 40 patients in 1 study[1] Follow up 10 years	**250** per 1000 **100** per 1000 Difference: **150 fewer per 1000** (95% CI: 227 fewer - 208 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether long duration cyclophosphamide increases or decreases kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:		No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.0 (95% CI: 0.07 - 14.9) Based on data from 40 patients in 1 study[3] Follow up 10 years	**50** per 1000 **50** per 1000 Difference: **0 fewer per 1000** (95% CI: 46 fewer - 695 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether long duration cyclophosphamide increases or decreases infection
Malignancy	Relative risk: 3.0 (95% CI: 0.13 - 69.52) Based on data from 40 patients in 1 study[5] Follow up 10 years	**0** per 1000 **0** per 1000 Difference: **0 fewer per 1000** (95% CI: 0 fewer - 0 fewer)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether long duration cyclophosphamide increases or decreases malignancy
Complete remission	(95% CI: -)	Difference:		No studies were found that looked at complete remission
Doubling of serum creatinine	Relative risk: 0.43 (95% CI: 0.13 - 1.43) Based on data from 40 patients in 1 study[7] Follow up 10 years	**350** per 1000 **151** per 1000 Difference: **199 fewer per 1000** (95% CI: 305 fewer - 150 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether long duration cyclophosphamide increases or decreases doubling serum creatinine
Stable kidney function (<20% worsening in serum creatinine)	Relative risk: 1.31 (95% CI: 0.9 - 1.89) Based on data from 40 patients in 1 study[9] Follow up 10 years	**650** per 1000 **851** per 1000 Difference: **201 more per 1000** (95% CI: 65 fewer - 578 more)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Long duration cyclophosphamide probably has little or no difference on stable kidney function (<20% worsening in serum creatinine)
Ovarian failure	Relative risk: 2.05 (95% CI: 0.6 - 7.02)	**188** per 1000 **385** per 1000	**Very low**	We are uncertain whether long duration

Outcome	Study results and measurements Timeframe	Absolute effect estimates Short duration Long duration	Certainty of the evidence	Plain text summary
	Based on data from 29 patients in 1 study[11] Follow up 10 years	Difference: **197 more per 1000** (95% CI: 75.0 fewer - 1132.0 more)	Due to serious risk of bias, Due to very serious imprecision[12]	cyclophosphamide increases or decreases ovarian failure
Annual loss of GFR	(95% CI: -)	Difference:		No studies were found that looked at annual loss of GFR

1. Systematic review [540] with included studies: [473] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
3. Systematic review [540] with included studies: [473] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
5. Systematic review [540] with included studies: [473] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study
7. Systematic review [540] with included studies: [473] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
9. Systematic review [540] with included studies: [473] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Wide confidence intervals, Low number of patients
11. Systematic review [540] with included studies: [473] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

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Table S26.
Population: Patients with proliferative lupus nephritis
Intervention: Maintenance: Azathioprine
Comparator: Maintenance: Cyclophosphamide

Outcome	Study results and measurements Timeframe	Absolute effect estimates Cyclophosphamide Azathioprine	Certainty of the evidence	Plain text summary
All-cause mortality	Relative risk: 0.12 (95% CI: 0.01 - 2.03) Based on data from 39 patients in 1 study[1] Follow up 72 months	**200** per 1000 **24** per 1000 Difference: **176 fewer per 1000** (95% CI: 198 fewer - 206 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether azathioprine increases or decreases all-cause mortality
≥50% loss of GFR	(95% CI: -)	Difference:		No studies were found that looked at ≥50% loss of GFR
Malignancy	(95% CI: -)	Difference:		No studies were found that looked at malignancy
Infection	(95% CI: -)	Difference:		No studies were found that looked at infection
Doubling serum creatinine	Relative risk: 0.79 (95% CI: 0.34 - 1.85) Based on data from 39 patients in 1 study[3] Follow up 72 months	**400** per 1000 **316** per 1000 Difference: **84 fewer per 1000** (95% CI: 264 fewer - 340 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether azathioprine increases or decreases doubling serum creatinine
Kidney relapse	Relative risk: 0.79 (95% CI: 0.34 - 1.85) Based on data from 39 patients in 1 study[5] Follow up 72 months	**400** per 1000 **316** per 1000 Difference: **84 fewer per 1000** (95% CI: 264 fewer - 340 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether azathioprine increases or decreases kidney relapse
Kidney failure	Relative risk: 0.35 (95% CI: 0.04 - 3.09) Based on data from 39 patients in 1 study[7] Follow up 72 months	**150** per 1000 **52** per 1000 Difference: **98 fewer per 1000** (95% CI: 144 fewer - 313 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether azathioprine increases or decreases kidney failure
Annual GFR loss	(95% CI: -)	Difference:		No studies were found that looked at annual GFR loss

Outcome	Study results and measurements Timeframe	Absolute effect estimates Cyclophosphamide	 Azathioprine	Certainty of the evidence	Plain text summary
Creatinine clearance	Based on data from 38 patients in 1 study[9] Follow up 1 year	ml/min Difference: **15.7 lower** (95% CI: 23.7 lower - 7.7 lower)	ml/min	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Azathioprine may decrease creatinine clearance

1. Systematic review [538] with included studies: [530] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients.
3. Systematic review [538] with included studies: [530] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients.
5. Systematic review [538] with included studies: [530] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients.
7. Systematic review [538] with included studies: [530] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients.
9. Systematic review [538] with included studies: [530] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study, Low number of patients.

References

[530] Contreras G, Pardo V, Leclercq B, Lenz O, Tozman E, O'Nan P, Roth D. Sequential therapies for proliferative lupus nephritis. The New England Journal of Medicine 2004;350(10):971-980

Table S27.
Population: Patients with proliferative lupus nephritis
Intervention: Maintenance: Immunosuppressive therapy (IST) (mycophenolate mofetil or azathioprine) continuation
Comparator: Maintenance: IST (mycophenolate mofetil or azathioprine) taper

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** IST taper	IST continuation	**Certainty of evidence**	**Plain text summary**
All-cause mortality	Based on data from 96 patients in 1 study[1] Follow up 24 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI 40 fewer – 40 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether maintenance IST continuation increases or decreases all-cause mortality
Kidney failure	Based on data from 96 patients in 1 study[3] Follow up 24 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI 40 fewer – 40 more)	**Very low** Due to very serious imprecision[4]	We are uncertain whether maintenance IST continuation increases or decreases kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.36 (95% CI 0.77 - 2.38) Based on data from 96 patients in 1 study[5] Follow up 24 months	**292** per 1000	**396** per 1000 Difference: **104 more per 1000** (95% CI 85 fewer – 293 more)	**Low** Some risk of bias Sparse data[6]	Maintenance IST continuation may have little or no difference on discontinuation due to adverse events.
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Adverse events, serious	Relative risk: 0.33 (95% CI 0.04, 3.09) Based on data from 96 patients in 1 study[7] Follow up 24 months	**63** per 1000	**21** per 1000 Difference: **42 fewer per 1000** (95% CI 121 fewer – 38 more)	**Very low** Due to very serious imprecision[8]	We are uncertain whether maintenance IST continuation increases or decreases serious adverse events
Adverse events leading to discontinuation	Based on data from 96 patients in 1 study[9] Follow up 24 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI 40 fewer – 40 more)	**Very low** Due to very serious imprecision[10]	We are uncertain whether maintenance IST continuation increases or decreases discontinuation due to adverse events
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission

Outcome	Study results and measurements Timeframe	Absolute effect estimates IST taper	 IST continuation	Certainty of evidence	Plain text summary
Relapse	Relative risk: 0.46 (95% CI 0.18, 1.19) P=0.11 Based on data from 96 patients in 1 study[11] Follow up 24 months	**273** per 1000	**125** per 1000 Difference: **148 fewer per 1000** (95% CI 315 fewer – 19 more)	**Low** Due to serious imprecision Some risk of bias Sparse data[12]	Maintenance IST continuation may decrease risk of relapse.
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Based on one study [561]
2. **Imprecision: Very Serious.** Single study
3. Based on one study [561]
4. **Imprecision: Very Serious.** Single study
5. Based on one study [561]
6. **Risk of bias: Serious.** Some RoB; **Imprecision: Serious.** Sparse data/single study
7. Based on one study [561]
8. **Imprecision: Very Serious.** Single study
9. Based on one study [561]
10. **Imprecision: Very Serious.** Single study
11. Based on one study [561] "Non-inferiority not demonstrated"
12. **Risk of bias: Serious.** Some RoB; **Imprecision: Serious.** Sparse data/single study

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Table S28.
Population: Patients with proliferative lupus nephritis
Intervention: Maintenance: Leflunomide
Comparator: Maintenance: Azathioprine

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Azathioprine Leflunomide	**Certainty of evidence**	**Plain text summary**
All-cause mortality	No events Based on data from 215 patients in 1 study[1] Follow up 36 months	**0** per 1000 **0** per 1000 **Difference: 0 fewer per 1000** (95% CI 18 fewer – 18 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether azathioprine increases or decreases all-cause mortality compared with leflunomide
Kidney failure	No events Based on data from 215 patients in 1 study[3] Follow up 36 months	**0** per 1000 **0** per 1000 **Difference: 0 fewer per 1000** (95% CI 18 fewer – 18 more)	**Very low** Due to very serious imprecision[4]	We are uncertain whether azathioprine increases or decreases kidney failure compared with leflunomide
≥50% loss of GFR	(95% CI: -)	Difference:		No studies were found that looked at ≥50% loss of GFR
Infection, severe	No events Based on data from 215 patients in 1 study[5] Follow up 36 months	**0** per 1000 **0** per 1000 **Difference: 0 fewer per 1000** (95% CI 18 fewer – 18 more)	**Very low** Due to very serious imprecision[6]	We are uncertain whether azathioprine increases or decreases severe infection compared with leflunomide
Malignancy	No events Based on data from 215 patients in 1 study[7] Follow up 36 months	**0** per 1000 **0** per 1000 **Difference: 0 fewer per 1000** (95% CI 18 fewer – 18 more)	**Very low** Due to very serious imprecision[8]	We are uncertain whether azathioprine increases or decreases malignancy compared with leflunomide
Adverse events, serious	No events Based on data from 215 patients in 1 study[9] Follow up 36 months	**0** per 1000 **0** per 1000 **Difference: 0 fewer per 1000** (95% CI 18 fewer – 18 more)	**Very low** Due to very serious imprecision[10]	We are uncertain whether azathioprine increases or decreases serious adverse events compared with leflunomide

Outcome	Study results and measurements Timeframe	Absolute effect estimates Azathioprine Leflunomide	Certainty of evidence	Plain text summary
Adverse events leading to discontinuation	Relative risk: 0.40 (95% CI: 0.08 - 2.00) Based on data from 215 patients in 1 study[11] Follow up 36 months	**19** per 1000 **47** per 1000 **Difference: 28 fewer per 1000** (95% CI 76 fewer – 19 more)	**Very low** Due to very serious imprecision[12]	We are uncertain whether azathioprine increases or decreases discontinuation due to adverse events compared with leflunomide
Complete remission	(95% CI: -)	Difference:		No studies were found that looked at complete remission
Relapse	(95% CI: -)	Difference:		No studies were found that looked at relapse
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:		No studies were found that looked at annual GFR loss

1. One study [562]
2. **Imprecision: Very serious.** Single study
3. One study [562]
4. **Imprecision: Very serious.** Single study
5. One study [562]
6. **Imprecision: Very serious.** Single study
7. One study [562]
8. **Imprecision: Very serious.** Single study
9. One study [562]
10. **Imprecision: Very serious.** Single study
11. One study [562]
12. **Imprecision: Very serious.** Single study

References

[562] Fu, Q.; Wu, C.; Dai, M.; Wang, S.; Xu, J.; Dai, L.; Li, Z.; He, L.; Zhu, X.; Sun, L.; Lu, L.; Bao, C.. Leflunomide versus azathioprine for maintenance therapy of lupus nephritis: a prospective, multicentre, randomised trial and long-term follow-up. Ann Rheum Dis 2022;81(11):1549-1555. [PubMed: 35788493]

Appendix D. Data supplement - Additional SoF tables developed as part of the evidence review

Table S29.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Calcineurin inhibitors
Comparator: Induction: Cyclophosphamide

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Induction: cyclophosphamide	**Absolute effect estimates** Induction: Calcineurin inhibitors	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: 0.41 (95% CI: 0.06 - 2.69) Based on data from 153 patients in 3 studies[1] Follow up 5 years	**40** per 1000	**16** per 1000 Difference: **24 fewer per 1000** (95% CI: 38 fewer - 68 more)	**Very low** Due to serious indirectness, Due to very serious imprecision[2]	We are uncertain whether calcineurin inhibitors increases or decreases all-cause mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 0.73 (95% CI: 0.33 - 1.63) Based on data from 138 patients in 3 studies[3] Mean follow up 7 months	**212** per 1000	**155** per 1000 Difference: **57 fewer per 1000** (95% CI: 142 fewer - 134 more)	**Very low** Due to serious indirectness, Due to very serious imprecision[4]	We are uncertain whether calcineurin inhibitors increases or decreases infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	Relative risk: 1.35 (95% CI: 0.94 - 1.93) Based on data from 178 patients in 4 studies[5] Mean follow up 6.75 months	**333** per 1000	**450** per 1000 Difference: **117 more per 1000** (95% CI: 20 fewer - 310 more)	**Low** Due to serious indirectness, Due to serious imprecision[6]	Calcineurin inhibitors may have little or no difference on complete remission
Annual GFR loss 1 year	Based on data from 38 patients in 1 study[7] Follow up 12 months	ml/min/year	ml/min/year Difference: **19.6 higher** (95% CI: 10.0 higher - 29.2 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Calcineurin inhibitors may increase annual GFR loss

1. Systematic review [540] with included studies: [475], [517], [502] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Indirectness: Serious.** Differences between the intervention/comparator of interest and those studied; **Imprecision: Very Serious.** Wide confidence intervals, due to few events
3. Systematic review [540] with included studies: [495], [475], [502] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Indirectness: Serious.** Differences between the intervention/comparator of interest and those studied; **Imprecision: Very Serious.** Wide confidence intervals, due to few events
5. Systematic review [540] with included studies: [517], [502], [475], [495] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Indirectness: Serious.** Differences between the intervention/comparator of interest and those studied; **Imprecision: Serious.**
7. Primary study [486] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients

References

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Table S30.
Population: Patients with nonproliferative lupus nephritis (Class V)
Intervention: Induction: Intravenous cyclophosphamide
Comparator: Induction: Cyclosporine

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Cyclosporine	Intravenous cyclophosphamide	**Certainty of the evidence**	**Plain text summary**
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 0.78 (95% CI: 0.34 - 1.77) Based on data from 27 patients in 1 study[1] Follow up 12 months	**533** per 1000	**416** per 1000 Difference: **117 fewer per 1000** (95% CI: 352 fewer - 410 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether intravenous cyclophosphamide improves or worsen major infection
Malignancy	Relative risk: 0.41 (95% CI: 0.02 - 9.25) Based on data from 27 patients in 1 study[3] Follow up 12 months	**67** per 1000	**27** per 1000 Difference: **40 fewer per 1000** (95% CI: 66 fewer - 553 more)	**Very low** Due to very serious risk of bias, Due to serious indirectness, Due to very serious imprecision[4]	We are uncertain whether intravenous cyclophosphamide improves or worsen malignancy
Complete remission	Relative risk: 1.39 (95% CI: 0.86 - 2.25) Based on data from 27 patients in 1 study[5] Follow up 12 Months	**600** per 1000	**834** per 1000 Difference: **234 more per 1000** (95% CI: 84 fewer - 750 more)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Intravenous cyclophosphamide may have little or no difference on complete remission
Doubling of serum creatinine	Relative risk: 1.25 (95% CI: 0.09 - 17.98) Based on data from 27 patients in 1 study[7]	**67** per 1000	**84** per 1000 Difference: **17 more per 1000** (95% CI: 61 fewer - 1138 more)	**Very low** Due to very serious imprecision, Due to serious risk of bias, Due to very serious risk of bias[8]	We are uncertain whether intravenous cyclophosphamide improves or worsen major infection
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality

Outcome	Study results and measurements Timeframe	Absolute effect estimates Cyclosporine	 Intravenous cyclophosphamide	Certainty of the evidence	Plain text summary
Annual GFR loss	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Primary study [455] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** After randomization 7 patients were not randomly assigned to CsA; they were only assigned to receive either Prednisone or Intravenous cyclophosphamide, which could result in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Indirectness: No serious.** The outcome time frame in studies were insufficient; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients, Wide confidence intervals
3. Primary study [455] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** After randomization 7 patients were not randomly assigned to CsA; they were only assigned to receive either Prednisone or Intravenous cyclophosphamide, which could result in potential for selection bias; **Indirectness: Serious.** The outcome time frame in studies were insufficient; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study
5. Systematic review [540] with included studies: [455] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** After randomization 7 patients were not randomly assigned to CsA; they were only assigned to receive either Prednisone or Intravenous cyclophosphamide, which could result in potential for selection bias; **Imprecision: Serious.** Low number of patients, only data from one study
7. Systematic review [540] with included studies: [455] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Very Serious.** After randomization 7 patients were not randomly assigned to CsA; they were only assigned to receive either Prednisone or Intravenous cyclophosphamide, which could result in potential for selection bias; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study

References

[455] Austin HA, Illei GG, Braun MJ, Balow JE. Randomized, controlled trial of prednisone, cyclophosphamide, and cyclosporine in lupus membranous nephropathy. Journal of the American Society of Nephrology: JASN 2009;20(4):901-11

Table S31.
Population: Children with proliferative lupus nephritis
Intervention: Induction: Intravenous glucocorticoids
Comparator: Induction: Oral glucocorticoids

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Oral glucocorticoids	**Absolute effect estimates** Intravenous glucocorticoids	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk (95% CI: -) Based on data from 22 patients in 1 study[1] Follow up 59 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI: 16 fewer - 22 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	There were too few who experienced the mortality to determine whether intravenous glucocorticoids made a difference
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Kidney relapse	Relative risk: 0.95 (95% CI: 0.44 - 2.04) Based on data from 22 patients in 1 study[3] Follow up 59 months	**600** per 1000	**570** per 1000 Difference: **30 fewer per 1000** (95% CI: 336 fewer - 624 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether intravenous or oral glucocorticoids increases or decreases kidney relapse
Annual GFR loss		Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [540] with included studies: [531] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious. Imprecision: Very Serious.** Only data from one study, Low number of patients and no events

3. Systematic review [540] with included studies: [531] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious. Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients and few events

References

[531] Barron KS, Person DA, Brewer EJ, Beale MG, Robson AM. Pulse methylprednisolone therapy in diffuse proliferative lupus nephritis. The Journal of Pediatrics 1982;101(1):137-141

Table S32.
Population: Patients with nonproliferative lupus nephritis (Class V)
Intervention: Induction: Cyclosporine
Comparator: Induction: Prednisone

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Prednisone Cyclosporine	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:		No studies were found that looked at all-cause mortality
Kidney failure	(95% CI: -)	Difference:		No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:		No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.56 (95% CI: 0.53 - 4.57) Based on data from 27 patients in 1 study[1] Follow up 12 months	**267** per 1000 **417** per 1000 Difference: **150 more per 1000** (95% CI: 125 fewer - 953 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether cyclosporine improves or worsen major infection
Malignancy	Relative risk: 0.0 (95% CI: 0.0 - 0.0) Based on data from 27 patients in 1 study[3] Follow up 12 months	**0** per 1000 **0** per 1000 Difference: **0 fewer per 1000** (95% CI: 0 fewer - 0 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	There were too few who experienced the malignancy to determine whether cyclosporine made a difference
Doubling of serum creatinine	Relative risk: 0.63 (95% CI: 0.06 - 6.09) Based on data from 27 patients in 1 study[5] Follow up 12 months	**133** per 1000 **84** per 1000 Difference: **49 fewer per 1000** (95% CI: 125 fewer - 677 more)	**Very low** Due to very serious imprecision, Due to very serious risk of bias, Due to serious risk of bias[6]	We are uncertain whether cyclosporine improves or worsen double
Complete remission	Relative risk: 3.13 (95% CI: 1.3 - 7.51) Based on data from 27 patients in 1 study[7] Follow up 12 months	**267** per 1000 **836** per 1000 Difference: **569 more per 1000** (95% CI: 80 more - 1738 more)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Cyclosporine may improve complete remission

Outcome	Study results and measurements Timeframe	Absolute effect estimates Prednisone Cyclosporine	Certainty of the evidence	Plain text summary
Annual GFR loss		Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [540] with included studies: [455] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** After randomization 7 patients were not randomly assigned to CsA; they were only assigned to receive either Prednisone or Intravenous cyclophosphamide, which could result in potential for selection bias. Unclear of blinding of outcome assessors, resulting in potential for detection bias in assessment of infections.; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study
3. Systematic review [540] with included studies: [455] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** After randomization 7 patients were not randomly assigned to CsA; they were only assigned to receive either Prednisone or Intravenous cyclophosphamide, which could result in potential for selection bias; **Indirectness: No serious.** The outcome time frame in studies were insufficient; **Imprecision: Serious.** Low number of patients, only data from one study
5. Systematic review [540] with included studies: [455] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** After randomization 7 patients were not randomly assigned to CsA; they were only assigned to receive either Prednisone or Intravenous cyclophosphamide, which could result in potential for selection bias; **Imprecision: Very Serious.** Low number of patients, Wide confidence intervals, Only data from one study
7. Systematic review [540] with included studies: [455] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** After randomization 7 patients were not randomly assigned to CsA; they were only assigned to receive either Prednisone or Intravenous cyclophosphamide, which could result in potential for selection bias; **Indirectness: No serious.** The outcome time frame in studies were insufficient; **Imprecision: Serious.** Wide confidence intervals above the null, Low number of patients, Only data from one study, Low number of patients, Only data from one study

References

[455] Austin HA, Illei GG, Braun MJ, Balow JE. Randomized, controlled trial of prednisone, cyclophosphamide, and cyclosporine in lupus membranous nephropathy. Journal of the American Society of Nephrology: JASN 2009;20(4):901-11

Table S33.
Population: Patients with nonproliferative lupus nephritis (Class V)
Intervention: Induction: Intravenous cyclophosphamide
Comparator: Induction: Prednisone

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Prednisone	Intravenous cyclophosphamide	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
Infection	Relative risk: 2.0 (95% CI: 0.76 - 5.24) Based on data from 30 patients in 1 study[1] Follow up 12 months	**267** per 1000	**534** per 1000 Difference: **267 more per 1000** (95% CI: 64 fewer - 1132 more)	**Very low** Due to very serious imprecision, Due to serious risk of bias[2]	We are uncertain whether intravenous cyclophosphamide improves or worsen infection
Malignancy	Relative risk: 3.0 (95% CI: 0.13 - 68.26) Based on data from 30 patients in 1 study[3] Follow up 12 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI: 0 fewer - 0 fewer)	**Very low** Due to very serious imprecision, Due to serious indirectness[4]	We are uncertain whether intravenous cyclophosphamide increases or decreases malignancy
Complete remission	Relative risk: 2.25 (95% CI: 0.88 - 5.73) Based on data from 30 patients in 1 study[5] Follow up 12 months	**267** per 1000	**601** per 1000 Difference: **334 more per 1000** (95% CI: 32 fewer - 1263 more)	**Low** Due to very serious imprecision[6]	Intravenous cyclophosphamide may have little or no difference on complete remission
Doubling of serum creatinine	Relative risk: 0.5 (95% CI: 0.05 - 4.94) Based on data from 30 patients in 1 study[7]	**133** per 1000	**67** per 1000 Difference: **67 fewer per 1000** (95% CI: 126 fewer - 524 more)	**Low** Due to very serious imprecision[8]	Intravenous cyclophosphamide may have little or no difference on doubling serum creatinine

Outcome	Study results and measurements Timeframe Follow up 12 months	Absolute effect estimates Prednisone	Intravenous cyclophosphamide	Certainty of the evidence	Plain text summary
Annual GFR loss		Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [540] with included studies: [455] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias of infection. **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study
3. Systematic review [540] with included studies: [455] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Indirectness: Serious.** The outcome time frame in studies were insufficient; **Imprecision: Very Serious.** Only data from one study, Wide confidence intervals, Low number of patients
5. Systematic review [540] with included studies: [455] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study
7. Systematic review [540] with included studies: [455] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study

References

[455] Austin HA, Illei GG, Braun MJ, Balow JE. Randomized, controlled trial of prednisone, cyclophosphamide, and cyclosporine in lupus membranous nephropathy. Journal of the American Society of Nephrology: JASN 2009;20(4):901-11

Table S34.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Azathioprine plus glucocorticoids
Comparator: Induction: Glucocorticoids alone

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Glucocorticoids alone	**Absolute effect estimates** Azathioprine plus glucocorticoids	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: 0.6 (95% CI: 0.36 - 0.99) Based on data from 78 patients in 3 studies[1] Follow up 4 years (mean)	**571** per 1000	**343** per 1000 Difference: **228 fewer per 1000** (95% CI: 365 fewer - 6 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Azathioprine plus glucocorticoids may decrease mortality slightly
Kidney failure	Relative risk: 0.66 (95% CI: 0.17 - 2.55) Based on data from 54 patients in 2 studies[3] Follow up 5 years (mean)	**409** per 1000	**270** per 1000 Difference: **139 fewer per 1000** (95% CI: 339 fewer - 634 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether azathioprine plus glucocorticoids increases or decreases kidney failure
≥50% loss of GFR	(95% CI: -)		Difference:		No studies were found that looked at ≥50% loss of GFR
Infection	(95% CI: -)		Difference:		No studies were found that looked at infection
Malignancy	Relative risk: 2.0 (95% CI: 0.11 - 37.22) Based on data from 26 patients in 1 study[5] Follow up 120 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI: 0 fewer - 0 fewer)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	There were too few who experienced malignancy to determine whether azathioprine plus glucocorticoids made a difference
Complete remission of proteinuria	Relative risk: 0.95 (95% CI: 0.54 - 1.69) Based on data from 37 patients in 2 studies[7] Follow up 3 years (mean)	**421** per 1000	**400** per 1000 Difference: **21 fewer per 1000** (95% CI: 194 fewer - 290 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether azathioprine plus glucocorticoids increases or decreases complete remission of proteinuria
Doubling of serum creatinine	Relative risk: 0.98 (95% CI: 0.36 - 2.68) Based on data from 26 patients in 1 study[9] Follow up 7 years	**429** per 1000	**420** per 1000 Difference: **9 fewer per 1000** (95% CI: 275 fewer - 721 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[10]	We are uncertain whether azathioprine plus glucocorticoids increases or decreases doubling serum creatinine

Outcome	Study results and measurements Timeframe	Absolute effect estimates Glucocorticoids alone	 Azathioprine plus glucocorticoids	Certainty of the evidence	Plain text summary
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Kidney relapse	Relative risk: 0.78 (95% CI: 0.22 - 2.74) Based on data from 16 patients in 1 study[11] Follow up 120 months	**429** per 1000	**335** per 1000 Difference: **94 fewer per 1000** (95% CI: 335 fewer - 746 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[12]	We are uncertain whether azathioprine plus glucocorticoids increases or decreases kidney relapse
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss
Creatinine clearance	Based on data from 24 patients in 1 study[13] Follow up 24 months	**97** ml/min	**102** ml/min Difference: **5 higher** (95% CI: 3.1 lower - 13.1 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[14]	We are uncertain whether azathioprine plus glucocorticoids increases or decreases creatinine clearance

1. Systematic review [540] with included studies: [468], [494], [474] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious. Imprecision: Serious.** Wide confidence intervals, Low number of patients and few events
3. Systematic review [540] with included studies: [468], [474] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious. Imprecision: Very Serious.** Wide confidence intervals, Low number of patients
5. Primary study [468] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious. Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients and few events
7. Systematic review [540] with included studies: [494], [480] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious. Imprecision: Very Serious.** Wide confidence intervals, Low number of patients
9. Primary study [468] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious. Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
11. Primary study [480] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious. Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients and few numbers
13. Primary study [494] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[468] Austin Ha RD, Klippel JH, Balow JE, le Riche NG, Steinberg AD, Plotz PH, et al. Therapy of lupus nephritis. Controlled trial of prednisone and cytotoxic drugs. New England Journal of Medicine 1986;314(10):614-619
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Table S35.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Mycophenolate mofetil
Comparator: Induction: Oral cyclophosphamide

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Oral cyclophosphamide	Mycophenolate mofetil	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: 0.19 (95% CI: 0.01 - 3.76) Based on data from 62 patients in 1 study[1] Median follow up 63 months	**67** per 1000	**13** per 1000 Difference: **54 fewer per 1000** (95% CI: 66 fewer - 185 more)	**Very low** Due to very serious imprecision, Due to serious risk of bias[2]	We are uncertain whether mycophenolate mofetil increases or decreases mortality
Kidney failure	Relative risk: 0.19 (95% CI: 0.01 - 3.76) Based on data from 62 patients in 1 study[3] Median follow up 63 months	**67** per 1000	**13** per 1000 Difference: **54 fewer per 1000** (95% CI: 66 fewer - 185 more)	**Very low** Due to very serious imprecision, Due to serious risk of bias[4]	We are uncertain whether mycophenolate mofetil increases or decreases kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Ovarian failure	Relative risk: 0.10 (95% CI: 0.01 - 0.73) Based on data from 53 patients in 1 study[5] Median follow up 63 months	**360** per 1000	**36** per 1000 Difference: **324 fewer per 1000** (95% CI: 525 fewer - 124 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Mycophenolate mofetil may decrease ovarian failure
Complete remission in proteinuria	Relative risk: 0.98 (95% CI: 0.74 - 1.3) Based on data from 62 patients in 1 study[7] Median follow up 63 months	**767** per 1000	**752** per 1000 Difference: **15 fewer per 1000** (95% CI: 199 fewer - 230 more)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Mycophenolate mofetil may have little or no difference on complete remission in proteinuria

Outcome	Study results and measurements Timeframe	Absolute effect estimates Oral cyclophosphamide	 Mycophenolate mofetil	Certainty of the evidence	Plain text summary
Leukopenia	Relative risk: 0.06 (95% CI: 0.0 - 0.92) Based on data from 62 patients in 1 study[9] Follow up 63 months (median)	**267** per 1000	**16** per 1000 Difference: **251 fewer per 1000** (95% CI: 267 fewer - 21 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Mycophenolate mofetil may decrease leukopenia
Alopecia	Relative risk: 0.05 (95% CI: 0.0 - 0.81) Based on data from 62 patients in 1 study[11] Follow up 63 months (median)	**300** per 1000	**15** per 1000 Difference: **285 fewer per 1000** (95% CI: 300 fewer - 57 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[12]	Mycophenolate mofetil may decrease alopecia
Infection	Relative risk: 0.21 (95% CI: 0.05 - 0.89) Based on data from 62 patients in 1 study[13] Follow up 63 months	**300** per 1000	**63** per 1000 Difference: **237 fewer per 1000** (95% CI: 285 fewer - 33 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[14]	Mycophenolate mofetil may decrease infection
Annual GFR loss	(95% CI: -)	Difference:			No studies comparing mycophenolate mofetil were found that looked at annual GFR loss

1. Systematic review [540] with included studies: [522] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious. Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
3. Systematic review [540] with included studies: [522] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious. Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
5. Systematic review [540] with included studies: [522] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious. Imprecision: Serious.** Only data from one study, Low number of patients and few events
7. Systematic review [540] with included studies: [522] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious. Imprecision: Serious.** Only data from one study, Low number of patients and few events
9. Systematic review [540] with included studies: [522] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious. Imprecision: Serious.** Only data from one study, Low number of patients and few events
11. Primary study [522] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious. Imprecision: Serious.** Only data from one study, Low number of patients and few events
13. Systematic review [540] with included studies: [522] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious. Imprecision: Serious.** Only data from one study, Low number of patients

References

[522] Chan TM, Li FK, Tang CS, Wong RW, Fang GX, Ji YL, Lau CS, Wong AK, Tong MK, Chan KW, Lai KN. Efficacy of mycophenolate mofetil in patients with diffuse proliferative lupus nephritis. Hong Kong-Guangzhou Nephrology Study Group. The New England Journal of Medicine 2000;343(16):1156-1162

Table S36.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Mycophenolate mofetil plus intravenous cyclophosphamide
Comparator: Induction: Intravenous cyclophosphamide

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Intravenous cyclophosphamide	**Absolute effect estimates** MMF plus intravenous cyclophosphamide	**Certainty of the evidence**	**Plain text summary**
All cause-mortality	Relative risk: 0.95 (95% CI: 0.06 - 14.72) Based on data from 82 patients in 1 study[1] Follow up 6 months	**25** per 1000	**24** per 1000 Difference: **1 fewer per 1000** (95% CI: 24 fewer - 343 more)	**Very low** Due to serious indirectness, Due to very serious imprecision[2]	We are uncertain whether MMF plus intravenous cyclophosphamide increases or decreases mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 0.37 (95% CI: 0.14 - 0.93) Based on data from 82 patients in 1 study[3] Follow up 6 months	**325** per 1000	**120** per 1000 Difference: **205 fewer per 1000** (95% CI: 279 fewer - 23 fewer)	**Low** Due to serious imprecision, Due to serious indirectness[4]	MMF plus intravenous cyclophosphamide may decrease infection
Complete remission	Relative risk: 1.22 (95% CI: 0.78 - 1.89) Based on data from 82 patients in 1 study[5] Follow up 6 months	**450** per 1000	**549** per 1000 Difference: **99 more per 1000** (95% CI: 99 fewer - 400 more)	**Low** Due to serious imprecision, Due to serious indirectness[6]	MMF plus intravenous cyclophosphamide may have little or no difference on complete remission
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Annual GFR loss	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Primary study [513] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Indirectness: Serious.** The outcome time frame in studies were insufficient; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients and few events
3. Primary study [513] **Baseline/comparator:** Control arm of reference used for intervention.

4. **Indirectness: Serious.** Differences between the outcomes of interest and those reported (e.g., short-term/surrogate, not patient-important); **Imprecision: Serious.** Only data from one study, Low number of patients and few events
5. Primary study [513] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Indirectness: Serious.** The outcome time frame in studies were insufficient; **Imprecision: Serious.**

References

[513] Sun J., Zhang H., Ji Y., Gui M., Yi B., Wang J., et al. Efficacy and safety of cyclophosphamide combined with mycophenolate mofetil for induction treatment of class IV lupus nephritis. International Journal of Clinical and Experimental Medicine 2015;8(11):21572-22157

Table S37.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Cyclophosphamide plus azathioprine plus glucocorticoids
Comparator: Induction: Glucocorticoids alone

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Glucocorticoids alone	CYC plus AZA plus glucocorticoid	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: 0.53 (95% CI: 0.17 - 1.68) Based on data from 29 patients in 1 study[1] Follow up 84 months	**429** per 1000	**227** per 1000 Difference: **202 fewer per 1000** (95% CI: 356 fewer - 292 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether CYC plus AZA plus glucocorticoids increases or decreases mortality
Kidney failure	Relative risk: 0.21 (95% CI: 0.04 - 1.02) Based on data from 29 patients in 1 study[3] Follow up 84 months	**429** per 1000	**90** per 1000 Difference: **339 fewer per 1000** (95% CI: 412 fewer - 9 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	CYC plus AZA plus glucocorticoid may have little or no difference on kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Infection	Relative risk: 0.48 (95% CI: 0.1 - 2.3) Based on data from 29 patients in 1 studies[5] Follow up 84 months	**286** per 1000	**137** per 1000 Difference: **149 fewer per 1000** (95% CI: 257 fewer - 372 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether CYC plus AZA plus glucocorticoids increases or decreases infection
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Doubling serum creatinine	Relative risk: 0.16 (95% CI: 0.04 - 0.69) Based on data from 29 patients in 1 study[7]	**571** per 1000	**91** per 1000 Difference: **480 fewer per 1000** (95% CI: 548 fewer - 177 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	CYC plus AZA plus glucocorticoids may decrease doubling serum creatinine

Outcome	Study results and measurements Timeframe	Absolute effect estimates		Certainty of the evidence	Plain text summary
		Glucocorticoids alone	CYC plus AZA plus glucocorticoid		
	Follow up 84 months				
Annual GFR loss	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [540] with included studies: [468] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias and pooling of participants; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
3. Systematic review [540] with included studies: [468] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias and pooling of participants; **Imprecision: Serious.** Low number of patients, Only data from one study, Low number of patients
5. Systematic review [540] with included studies: [468] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias and pooling of participants; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients and few events
7. Systematic review [540] with included studies: [468] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, unclear concealment of allocation during randomization process, resulting in potential for selection bias and pooling of participants; **Imprecision: Serious.** Only data from one study, Low number of patients

References

[468] Austin Ha RD, Klippel JH, Balow JE, le Riche NG, Steinberg AD, Plotz PH, et al. Therapy of lupus nephritis. Controlled trial of prednisone and cytotoxic drugs. New England Journal of Medicine 1986;314(10):614-619

Table S38.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Cyclosporine plus glucocorticoids
Comparator: Induction: Glucocorticoids alone

Outcome	Study results and measurements Timeframe	Absolute effect estimates		Certainty of the evidence	Plain text summary
		Glucocorticoids alone	Cyclosporine plus glucocorticoids		
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Annual GFR loss	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss
Creatinine clearance	Based on data from 10 patients in 1 study[1] Follow up 12 months	**123.8** ml/min	**81.3** ml/min	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether cyclosporine plus glucocorticoids increases or decreases creatinine clearance
		Difference: **42.5 lower** (95% CI: 85.0 lower - 0 higher)			

1. Systematic review [540] with included studies: [469] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study

References

[469] Balletta M., Sabella D., Magri P., Sepe V., Stanziale P., Di Luccio R., et al. Cyclosporin plus steroids versus steroids alone in the treatment of lupus nephritis. Contributions to Nephrology 1992;99 129-130

Table S39.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Misoprostol plus glucocorticoids
Comparator: Induction: Glucocorticoids alone

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Glucocorticoids alone	Misoprostol plus glucocorticoids	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Doubling of serum creatinine	No events Based on data from 14 patients in 1 study[1] Follow up 18 months	**0** per 1000	**0** per 1000 Difference: **0 more per 1000** (95% CI: 24 more – 0 fewer)	**Low** Due to very serious imprecision[2]	There were too few who experienced the doubling of serum creatinine to determine whether misoprostol plus glucocorticoids made a difference
Annual GFR loss		Difference:			No studies were found that looked at annual GFR loss

1. Primary study [518] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients and no events

References

[518] Belmont HM, Kitsis E, Skovron ML, Buyon J, McCullagh E, Abramson S. Misoprostol and Prednisone Treatment of Lupus Nephritis. American journal of therapeutics 1995;2(12):928-932

Table S40.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Plasma exchange
Comparator: Induction: Immunosuppression

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Immunosuppression	Plasma exchange	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Kidney failure	Relative risk: 0.24 (95% CI: 0.01 - 4.44) Based on data from 20 patients in 1 study[1] Follow up 6.5 months	**182** per 1000	**44** per 1000 Difference: **138 fewer per 1000** (95% CI: 180 fewer - 626 more)	**Very low** Due to serious risk of bias, Due to serious indirectness, Due to very serious imprecision[2]	We are uncertain whether plasma exchange increases or decreases kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 0.4 (95% CI: 0.02 - 8.78) Based on data from 20 patients in 1 study[3] Follow up 6.5 months (mean)	**91** per 1000	**36** per 1000 Difference: **55 fewer per 1000** (95% CI: 89 fewer - 708 more)	**Very low** Due to serious risk of bias, Due to serious indirectness, Due to very serious imprecision[4]	We are uncertain whether plasma exchange increases or decreases infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Annual loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at annual loss of GFR
Creatinine clearance	Based on data from 20 patients in 1 study[5] Follow up 6.5 months (mean)	**39.7** ml/min	**55.0** ml/min Difference: **15.3 higher** (95% CI: 5.4 lower - 36.0 higher)	**Very low** Due to serious risk of bias, Due to serious indirectness, Due to very serious imprecision[6]	We are uncertain whether plasma exchange increases or decreases creatinine clearance

1. Systematic review [540] with included studies: [479] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Selective outcome reporting, due to pooling interventions in the cytotoxic group; **Indirectness: Serious.** Differences between the intervention/comparator of interest and those studied; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
3. Systematic review [540] with included studies: [479] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Selective outcome reporting, due to pooling interventions in the cytotoxic arm; **Indirectness: Serious.** Differences between the intervention/comparator of interest and those studied; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
5. Systematic review [540] with included studies: [479] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Selective outcome reporting, due to pooling interventions in the cytotoxic arm; **Indirectness: Serious.** Differences between the intervention/comparator of interest and those studied; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[479] Derksen RH, Hene RJ, Kallenberg CG, Valentijn RM, Kater L. Prospective multicentre trial on the short- term effects of plasma exchange versus cytotoxic drugs in corticosteroid-resistant lupus nephritis. Netherlands Journal of Medicine 1988;33(3-4):168-177

Table S41.
Population: Patients with proliferative lupus nephritis
Intervention: Maintenance: Azathioprine
Comparator: Maintenance: Cyclosporine

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Cyclosporine Azathioprine	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk (95% CI: -) Based on data from 69 patients in 1 study[1] Follow up 24 months	**0** per 1000 **0** per 1000 Difference: **0 more per 1000** (95% CI: 5 fewer - 6 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[2]	There were too few who experienced all-cause mortality to determine whether azathioprine for maintenance therapy made a difference
Kidney failure	Relative risk (95% CI: -) Based on data from 69 patients in 1 study[3] Follow up 24 months	**0** per 1000 **0** per 1000 Difference: **0 more per 1000** (95% CI: 5 fewer - 6 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[4]	There were too few who experienced kidney failure to determine whether azathioprine for maintenance therapy made a difference
≥50% loss of GFR	(95% CI: -)	Difference:		No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 2.18 (95% CI: 1.01 - 4.73) Based on data from 69 patients in 1 study[5] Follow up 24 months	**194** per 1000 **423** per 1000 Difference: **229 more per 1000** (95% CI: 2 more - 724 more)	**Very low** Due to very serious risk of bias, Due to serious imprecision[6]	We are uncertain whether azathioprine in maintenance therapy increases or decreases infection
Malignancy	(95% CI: -)	Difference:		No studies were found that looked at malignancy
Kidney relapse	Relative risk: 1.25 (95% CI: 0.51 - 3.06) Based on data from 69 patients in 1 study[7] Mean follow up 24 months	**194** per 1000 **243** per 1000 Difference: **49 more per 1000** (95% CI: 95 fewer - 400 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether azathioprine in maintenance therapy improves or worsen kidney relapse
Gastrointestinal disturbance	Relative risk: 0.3 (95% CI: 0.09 - 0.97) Based on data from 69 patients in 1 study[9] Follow up 24 months	**306** per 1000 **92** per 1000 Difference: **214 fewer per 1000** (95% CI: 278 fewer - 9 fewer)	**Very low** Due to very serious risk of bias, Due to serious imprecision[10]	We are uncertain whether azathioprine in maintenance therapy improves or worsen gastrointestinal disturbance

Outcome	Study results and measurements Timeframe	Absolute effect estimates Cyclosporine Azathioprine	Certainty of the evidence	Plain text summary
Annual loss of GFR	(95% CI: -)	Difference:		No studies were found that looked at annual loss of GFR

1. Systematic review [540] with included studies: [534] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, due to pharmaceutical sponsor involved in authorship; **Imprecision: Very Serious.** Only data from one study, Low number of patients and no events
3. Systematic review [540] with included studies: [534] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, due to pharmaceutical sponsor involved in authorship; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
5. Systematic review [540] with included studies: [534] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Very Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, due to pharmaceutical sponsor involved in authorship; **Imprecision: Serious.** Wide confidence intervals, only data from one study
7. Systematic review [540] with included studies: [534] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Very Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, due to pharmaceutical sponsor involved in authorship; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
9. Systematic review [540] with included studies: [534] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Very Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, due to pharmaceutical sponsor involved in authorship; **Imprecision: Serious.** Only data from one study, Low number of patients

References

[534] Moroni G, Doria A, Mosca M, Alberighi ODC, Ferraccioli G, Todesco S, Manno C, Altieri P, Ferrara R, Greco S, Ponticelli C. A randomized pilot trial comparing cyclosporine and azathioprine for maintenance therapy in diffuse lupus nephritis over four years. Clinical Journal of the American Society of Nephrology: CJASN 2006;1(5):925-932

Table S42.
Population: Patients with proliferative lupus nephritis
Intervention: Maintenance: Azathioprine
Comparator: Maintenance: Tacrolimus

Outcome	Study results and measurements Timeframe	Absolute effect estimates Tacrolimus Azathioprine	Certainty of the evidence	Plain text summary
All-cause mortality	(95% CI: -)	Difference:		No studies were found that looked at all-cause mortality
≥50% loss of GFR	(95% CI: -)	Difference:		No studies were found that looked at ≥50% loss of GFR
Kidney failure	(95% CI: -)	Difference:		No studies were found that looked at kidney failure
Infection	Relative risk: 1.26 (95% CI: 0.3 - 5.22) Based on data from 70 patients in 1 study[1]	**88** per 1000 **111** per 1000 Difference: **23 more per 1000** (95% CI: 62 fewer - 371 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether azathioprine in maintenance therapy increases or decreases infection
Malignancy	(95% CI: -)	Difference:		No studies were found that looked at malignancy
Kidney relapse	Relative risk: 6.62 (95% CI: 0.35 - 123.63) Based on data from 70 patients in 1 study[3] Follow up 6 months	**0** per 1000 **0** per 1000 Difference: **0 fewer per 1000** (95% CI: 0 fewer - 0 fewer)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether azathioprine in maintenance therapy increases or decreases kidney relapse
Annual loss of GFR	(95% CI: -)	Difference:		No studies were found that looked at annual loss of GFR

1. Systematic review [540] with included studies: [535] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
3. Systematic review [540] with included studies: [535] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients, due to a low number of events

References

[535] Chen W, Liu Q, Chen W, Tang X, Fu P, Liu F, Liao Y, Yang Z, Zhang J, Chen J, Lou T, Fu J, Kong Y, Liu Z, Li Z, Yu X. Outcomes of maintenance therapy with tacrolimus versus azathioprine for active lupus nephritis: a multicenter randomized clinical trial. Lupus 2012;21(9):944-952

Table S43.
Population: Patients with proliferative lupus nephritis
Intervention: Maintenance: Prednisone withdrawal
Comparator: Maintenance: Prednisone continuation

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Prednisone continuation	Prednisone withdrawal	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 0.57 (95% CI: 0.06 - 5.03) Based on data from 15 patients in 1 study[1] Follow up 36 months	**250** per 1000	**142** per 1000 Difference: **108 fewer per 1000** (95% CI: 235 fewer - 1008 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether prednisone withdrawal in maintenance therapy increases or decreases infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Kidney relapse	Relative risk: 0.38 (95% CI: 0.05 - 2.88) Based on data from 15 patients in 1 study[3] Follow up 36 months	**375** per 1000	**142** per 1000 Difference: **233 fewer per 1000** (95% CI: 356 fewer - 705 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether prednisone withdrawal in maintenance therapy increases or decreases kidney relapse
Nonrenal relapse	Relative risk: 0.38 (95% CI: 0.02 - 7.96) Based on data from 15 patients in 1 study[5] Follow up 36 months	**125** per 1000	**47** per 1000 Difference: **78 fewer per 1000** (95% CI: 123 fewer - 870 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether prednisone withdrawal in maintenance therapy increases or decreases nonrenal relapse
Annual GFR loss	(95% CI: -)				

Outcome	Study results and measurements Timeframe	Absolute effect estimates Prednisone continuation	 Prednisone withdrawal	Certainty of the evidence	Plain text summary
		Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [540] with included studies: [488] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Selective outcome reporting, due to pilot study; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
3. Systematic review [540] with included studies: [488] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Selective outcome reporting, due to pilot study; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
5. Systematic review [540] with included studies: [488] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Selective outcome reporting, due to pilot study; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[488] Galbraith L., Manns B., Hemmelgarn B., Walsh M. The Steroids In the Maintenance of remission of Proliferative Lupus nephritis (SIMPL) pilot trial. Canadian Journal of Kidney Health & Disease 2014;1 30-30

Table S44.
Population: Patients with proliferative lupus nephritis
Intervention: Maintenance: Intravenous immunoglobulin
Comparator: Maintenance: Intravenous cyclophosphamide

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Intravenous cyclophosphamide	Intravenous immunoglobulin	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Kidney relapse	(95% CI: -)	Difference:			No studies were found that looked at kidney relapse
Annual GFR loss	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss
Creatinine clearance	Based on data from 13 patients in 1 study[1] Follow up 18 months	**87.0** ml/min	**89.2** ml/min Difference: **2.2 higher** (95% CI: 37.9 lower - 42.3 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether intravenous immunoglobulin in maintenance therapy increases or decreases creatinine clearance

1. Systematic review [540] with included studies: [472] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious. Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References
[472] Boletis JN, Ioannidis JP, Boki KA, Moutsopoulos HM. Intravenous immunoglobulin compared with cyclophosphamide for proliferative lupus nephritis. Lancet 1999;354(9178):569-570

[531] Barron KS, Person DA, Brewer EJ, Beale MG, Robson AM. Pulse methylprednisolone therapy in diffuse proliferative lupus nephritis. The Journal of Pediatrics 1982;101(1):137-141

Table S45.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Anifrolumab 900 mg or 300 mg
Comparator: Induction: Placebo

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Placebo	Anifrolumab	**Certainty of evidence**	**Plain text summary**
All-cause mortality	Relative risk: 1.55 (95% CI 0.06 - 37.3) Based on data from 145 patients in 1 study[1] Follow up 12 months	**0** per 1000	**10** per 1000 Difference: **10 more per 1000** (95% CI 27 fewer – 47 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether anifrolumab increases or decreases all-cause mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Opportunistic infection	Relative risk: 0.51 (95% CI 0.03 - 7.99) Based on data from 145 patients in 1 study[3] Follow up 12 months	**20** per 1000	**10** per 1000 Difference: **10 fewer per 1000** (95% CI 54 fewer – 35 more)	**Very low** Due to very serious imprecision[4]	We are uncertain whether anifrolumab increases or opportunistic infections
Malignancy	Relative risk: 1.55 (95% CI 0.06 - 37.3) Based on data from 145 patients in 1 study[5] Follow up 12 months	**0** per 1000	**10** per 1000 Difference: **10 more per 1000** (95% CI 27 fewer – 47 more)	**Very low** Due to very serious imprecision[6]	We are uncertain whether anifrolumab increases or decreases malignancy
Adverse events, serious	Relative risk: 1.21 (95% CI 0.57 - 2.57) Based on data from 145 patients in 1 study[7] Follow up 12 months	**163** per 1000	**198** per 1000 Difference: **35 more per 1000** (95% CI 96 fewer – 165 more)	**Very low** Due to serious imprecision Sparse data[8]	We are uncertain whether anifrolumab increases or decreases serious adverse events

Outcome	Study results and measurements Timeframe	Absolute effect estimates Placebo	 Anifrolumab	Certainty of evidence	Plain text summary
Adverse events leading to discontinuation	Relative risk: 0.94 (95% CI 0.37 - 2.38) Based on data from 145 patients in 1 study[9] Follow up 12 months	**122** per 1000	**115** per 1000 Difference: **7 fewer per 1000** (95% CI 120 fewer – 104 more)	**Very low** Due to very serious imprecision[10]	We are uncertain whether anifrolumab increases or decreases discontinuation due to adverse events
Complete remission	Relative risk: 1.00 (95% CI 0.58 - 1.70) Based on data from 145 patients in 1 study[11] Follow up 12 months	**311** per 1000	**310** per 1000 Difference: **1 fewer per 1000** (95% CI 167 fewer – 166 more)	**Low** Due to serious imprecision Sparse data[12]	We are uncertain whether anifrolumab increases or decreases complete remission
Relapse	(95% CI: -)	Difference:			No studies were found that looked at annual relapse
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. One study [563]
2. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
3. One study [563]
4. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
5. One study [563]
6. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
7. One study [563]
8. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
9. One study [563]
10. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
11. One study [563]
12. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study

References

[563] Jayne, D.; Rovin, B.; Mysler, E. F.; Furie, R. A.; Houssiau, F. A.; Trasieva, T.; Knagenhjelm, J.; Schwetje, E.; Chia, Y. L.; Tummala, R.; Lindholm, C.. Phase II randomised trial of type I interferon inhibitor anifrolumab in patients with active lupus nephritis. Ann Rheum Dis 2022;81(4):496-506. [PubMed: 35144924]

Table S46.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Anifrolumab 900 mg
Comparator: Induction: Anifrolumab 300 mg

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** Anifrolumab 300	Anifrolumab 900	**Certainty of evidence**	**Plain text summary**
All-cause mortality	Relative risk: 0.29 (95% CI 0.01 - 7.06) Based on data from 96 patients in 1 study[1] Follow up 12 months	**22** per 1000	**0** per 1000 Difference: **22 fewer per 1000** (95% CI 80 fewer – 36 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether anifrolumab 900 mg vs. 300 mg increases or decreases all-cause mortality
Kidney failure	(95% CI: -)		Difference:		No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)		Difference:		No studies were found that looked at ≥50% loss of GFR
Opportunistic infection	Relative risk: 0.29 (95% CI 0.01 - 7.06) Based on data from 96 patients in 1 study[3] Follow up 12 months	**22** per 1000	**0** per 1000 Difference: **22 fewer per 1000** (95% CI 80 fewer – 36 more)	**Very low** Due to very serious imprecision[4]	We are uncertain whether anifrolumab 900 mg vs. 300 mg increases or decreases opportunistic infection
Malignancy	Relative risk: 2.65 (95% CI 0.11, 63.56) Based on data from 96 patients in 1 study[5] Follow up 12 months	**0** per 1000	**20** per 1000 **Difference: 20 more per 1000** (95% CI 35 fewer – 74 more)	**Very low** Due to very serious imprecision[6]	We are uncertain whether anifrolumab 900 mg vs. 300 mg increases or decreases malignancy
Adverse events, serious	Relative risk: 0.79 (95% CI 0.35, 1.78) Based on data from 96 patients in 1 study[7] Follow up 12 months	**176** per 1000	**222** per 1000 Difference: **46 fewer per 1000** (95% CI 206 fewer – 115 more)	**Very low** Due to serious imprecision Sparse data[8]	We are uncertain whether anifrolumab 300 mg vs. 900 mg increases or decreases serious adverse events
Adverse events leading to discontinuation	Relative risk: 1.06 (95% CI 0.35, 3.24) Based on data from 96 patients in 1 study[9] Follow up 12 months	**118** per 1000	**111** per 1000 Difference: **7 more per 1000** (95% CI 121 fewer – 134 more)	**Very low** Due to very serious imprecision[10]	We are uncertain whether anifrolumab 300 mg vs. 900 mg increases or decreases discontinuation due to adverse events

Outcome	Study results and measurements Timeframe	Absolute effect estimates Anifrolumab 300	 Anifrolumab 900	Certainty of evidence	Plain text summary
Complete remission	Relative risk: 2.79 (95% CI 1.32, 5.92) Based on data from 96 patients in 1 study[11] Follow up 12 months	**455** per 1000	**163** per 1000 **Difference: 292 more per 1000** (95% CI 108 more – 476 more)	**Low** Sparse data[12]	Anifrolumab 900 mg may decrease complete relapse compared with 300 mg
Relapse	(95% CI: -)	Difference:			No studies were found that looked at annual relapse
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. One study [563]
2. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
3. One study [563]
4. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
5. One study [563]
6. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
7. One study [563]
8. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
9. One study [563]
10. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
11. One study [563]
12. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study

References

[563] Jayne, D.; Rovin, B.; Mysler, E. F.; Furie, R. A.; Houssiau, F. A.; Trasieva, T.; Knagenhjelm, J.; Schwetje, E.; Chia, Y. L.; Tummala, R.; Lindholm, C.. Phase II randomised trial of type I interferon inhibitor anifrolumab in patients with active lupus nephritis. Ann Rheum Dis 2022;81(4):496-506. [PubMed: 35144924]

Table S47.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Obinutuzumab
Comparator: Induction: Placebo

Outcome	Study results and measurements Timeframe	Absolute effect estimates Placebo	 Obinutuzumab	Certainty of evidence	Plain text summary
All-cause mortality	Relative risk: 0.25 (95% CI 0.03 - 2.14) Based on data from 125 patients in 1 study[1] Follow up 24 months	**65** per 1000	**16** per 1000 Difference: **49 fewer per 1000** (95% CI 117 fewer – 20 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether obinutuzumab increases or decreases all-cause mortality
Kidney failure	Relative risk: 0.19 (95% CI 0.01 - 3.89) Based on data from 125 patients in 1 study[3] Follow up 24 months	**33** per 1000	**0** per 1000 Difference: **33 fewer per 1000** (95% CI 86 fewer – 21 more)	**Very low** Due to very serious imprecision[4]	We are uncertain whether obinutuzumab increases or decreases kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.20 (95% CI 0.95 - 1.53) Based on data from 125 patients in 1 study[5] Follow up 24 months	**623** per 1000	**750** per 1000 Difference: **127 more per 1000** (95% CI 34 fewer – 288 more)	**Low** Sparse data[6]	Obinutuzumab may have little or no difference on infections
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Adverse events, serious	Relative risk: 0.85 (95% CI 0.48 - 1.51) Based on data from 125 patients in 1 study[7] Follow up 24 months	**295** per 1000	**250** per 1000 Difference: **45 fewer per 1000** (95% CI 201 fewer – 111 more)	**Very low** Due to very serious imprecision[8]	We are uncertain whether obinutuzumab increases or decreases serious adverse events
Adverse events leading to discontinuation	(95% CI: -)	Difference:			No studies were found that looked at adverse events leading to discontinuation

Outcome	Study results and measurements Timeframe	Absolute effect estimates Placebo	 Obinutuzumab	Certainty of evidence	Plain text summary
Complete remission	Relative risk: 1.55 (95% CI 0.87 - 2.74) Based on data from 125 patients in 1 study[9] Follow up 24 months	**226** per 1000	**349** per 1000 Difference: **123 more per 1000** (95% CI 34 fewer – 281 more)	**Low** Sparse data[10]	Obinutuzumab may have little or no difference on complete remission
Relapse	(95% CI: -)	Difference:			No studies were found that looked at relapse
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. One study [564]
2. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
3. One study [564]
4. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
5. One study [564]
6. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
7. One study [564]
8. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study
9. One study [564]
10. **Risk of bias: Serious. Imprecision: Very Serious.** Sparse data/single study

References

[564]Furie, R. A.; Aroca, G.; Cascino, M. D.; Garg, J. P.; Rovin, B. H.; Alvarez, A.; Fragoso-Loyo, H.; Zuta-Santillan, E.; Schindler, T.; Brunetta, P.; Looney, C. M.; Hassan, I.; Malvar, A.. B-cell depletion with obinutuzumab for the treatment of proliferative lupus nephritis: a randomised, double-blind, placebo-controlled trial. Ann Rheum Dis 2022;81(1):100-107. [PubMed: 34615636]

Table S48.
Population: Patients with proliferative lupus nephritis
Intervention: Induction: Dapirolizumab
Comparator: Induction: Placebo

Outcome	Study results and measurements Timeframe	Absolute effect estimates Placebo	 Dapirolizumab	Certainty of evidence	Plain text summary
All-cause mortality	No events Based on data from 182 patients in 1 study[1] Follow up 6 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI 30 fewer – 30 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether dapirolizumab increases or decreases all-cause mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 0.98 (95% CI 0.69, 1.40) Based on data from 182 patients in 1 study[3] Follow up 6 months	**468** per 1000	**459** per 1000 Difference: **9 fewer per 1000** (95% CI 174 fewer – 157 more)	**Low** Due to very serious imprecision[4]	Dapirolizumab may have little or no difference on infections
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Adverse events, serious	Relative risk: 0.77 (95% CI 0.28, 2.09) Based on data from 182 patients in 1 study[5] Follow up 6 months	**106** per 1000	**81** per 1000 Difference: **25 fewer per 1000** (95% CI 124 fewer – 75 more)	**Very low** Due to very serious imprecision[6]	We are uncertain whether dapirolizumab increases or decreases serious adverse events
Adverse events leading to discontinuation	Relative risk: 1.06 (95% CI 0.04, 25.6) Based on data from 182 patients in 1 study[7] Follow up 6 months	**0** per 1000	**7** per 1000 Difference: **7 more per 1000** (95% CI 26 fewer – 41 more)	**Very low** Due to very serious imprecision[8]	We are uncertain whether dapirolizumab increases or decreases discontinuation due to adverse events
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Relapse	(95% CI: -)	Difference:			No studies were found that looked at complete relapse
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. One study [565]
2. **Risk of bias: Serious. Imprecision: Very Serious.** Single study
3. One study [565]
4. **Risk of bias: Serious. Imprecision: Very Serious.** Single study
5. One study [565]
6. **Risk of bias: Serious. Imprecision: Very Serious.** Single study
7. One study [565]
8. **Risk of bias: Serious. Imprecision: Very Serious.** Single study

References

[565] Furie, R. A.; Bruce, I. N.; Dorner, T.; Leon, M. G.; Leszczy -Ñski, P.; Urowitz, M.; Haier, B.; Jimenez, T.; Brittain, C.; Liu, J.. Phase 2, randomized, placebo-controlled trial of dapirolizumab pegol in patients with moderate-to-severe active systemic lupus erythematosus. Rheumatology 2021;60(11):5397-5407. [PubMed: 33956056]

Table S49.
Population: Patients with proliferative lupus nephritis
Intervention: Maintenance: Hydroxychloroquine, low dose (2-3 mg/kg/d)
Comparator: Maintenance: Hydroxychloroquine, high dose (4-5.5 mg/kg/d)

Outcome	**Study results and measurements** Timeframe	**Absolute effect estimates** High dose	Low dose	**Certainty of evidence**	**Plain text summary**
All-cause mortality	No events Based on data from 73 patients in 1 study[1] Follow up 12 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI 53 fewer – 53 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether hydroxychloroquine low dose increases or decreases all-cause mortality compared with high dose
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Adverse events, serious	No events Based on data from 73 patients in 1 study[3] Follow up 12 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI 53 fewer – 53 more)	**Very low** Due to very serious imprecision[4]	We are uncertain whether hydroxychloroquine low dose increases or decreases serious adverse events compared with high dose
Adverse events leading to discontinuation	No events Based on data from 73 patients in 1 study[5] Follow up 12 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI 53 fewer – 53 more)	**Very low** Due to very serious imprecision[6]	We are uncertain whether hydroxychloroquine low dose increases or decreases discontinuation due to adverse events compared with high dose
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission

Outcome	Study results and measurements Timeframe	Absolute effect estimates High dose	 Low dose	Certainty of evidence	Plain text summary
Relapse	Relative risk: 1.79 (95% CI 0.63, 5.13) Based on data from 73 patients in 1 study[7] Follow up 12 months	**122** per 1000 Difference: **97 more per 1000** (95% CI 78 fewer– 272 more)	**219** per 1000	**Low** Some risk of bias Sparse data[8]	Hydroxychloroquine low dose may have little or no difference on infections compared with high dose
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:			No studies were found that looked at annual GFR loss

1. One study [566]
2. **Risk of bias: Serious. Imprecision: Very Serious.** Single study
3. One study [566]
4. **Risk of bias: Serious. Imprecision: Very Serious.** Single study
5. One study [566]
6. **Risk of bias: Serious. Imprecision: Very Serious.** Single study
7. One study [566]
8. **Risk of bias: Serious. Imprecision: Very Serious.** Single study

References

[566] Zanetti, C. B.; Pedrosa, T.; Kupa, L. V. K.; Aikawa, N. E.; Borba, E. F.; Vendramini, M. B. G.; Silva, C. A.; Pasoto, S. G.; Bonfa, E.. Hydroxychloroquine blood levels in stable lupus nephritis under low dose (2-3 mg/kg/day): 12-month prospective randomized controlled trial. Clin Rheumatol 2021;40(7):2745-2751. [PubMed: 33486596]