DATA SUPPLEMENT

Appendix A. Search strategies

Table S1. Search strategies for systematic review topics

Search dates: May 2018; updated search June 2020, updated search April 19, 2023

Guideline chapter	Nephrotic syndrome in children
Clinical question	Glucocorticoid therapy for nephrotic syndrome in children
Search strategy - CENTRAL	1. MeSH descriptor: [Nephrotic Syndrome] this term only 2. MeSH descriptor: [Nephrosis, Lipoid] this term only 3. "nephrotic syndrome":ti,ab,kw 4. "lipoid nephrosis":ti,ab,kw 5. #1 or #2 or #3 or #4 6. child* or infant*:ti,ab,kw 7. boy* or girl*:ti,ab,kw 8. pediatric* or paediatric*:ti,ab,kw 9. #6 or #7 or #8 10. #5 and #9
Search strategy - MEDLINE	1. nephrotic syndrome/ 2. nephrosis, lipoid/ 3. nephrotic syndrome.tw. 4. lipoid nephrosis.tw. 5. or/1-4 6. exp child/ 7. exp Infant/ 8. child$.tw. 9. infant$.tw. 10. (boy$ or girl$).tw. 11. (pediatric or paediatric).tw. 12. or/7-12 13. and/5,12 14. randomised controlled trial.pt. 15. controlled clinical trial.pt. 16. randomized.ab. 17. placebo.ab. 18. clinical trials as topic/ 19. randomly.ab. 20. (crossover or cross-over).tw. 21. Cross-over Studies/ 22. trial.ti. 23. or/14-22 24. animals/ not (humans/ and animals/) 25. 13 and 23 26. 25 not 24
Search strategy - Embase	1. nephrotic syndrome/ 2. lipoid nephrosis/ 3. nephrotic syndrome.tw. 4. lipoid nephrosis.tw. 5. or/1-4 6. exp Child/ 7. child$.tw. 8. infant$.tw. 9. (boy$ or girl$).tw. 10. (pediatric or paediatric).tw

	11. or/6-10 12. and/5,11 13. randomised controlled trial/ 14. crossover procedure/ 15. double-blind procedure/ 16. single-blind procedure/ 17. random$.tw. 18. factorial$.tw. 19. crossover$ or cross-over$).tw. 20. placebo$.tw. 21. (double$ adj blind$).tw. 22. (singl$ adj blind$).tw. 23. assign$.tw. 24. allocat$.tw. 25. volunteer$.tw. 26. or/13-25 27. 12 and 26
Systematic review topic	Non-glucocorticoid immunosuppressive medications for steroid-sensitive nephrotic syndrome in children
Search strategy - CENTRAL	1. “nephrotic syndrome”:ti,ab,kw 2. (lipoid next nephrosis):ti,ab,kw 3. #1 or #2
Search strategy - MEDLINE	1. nephrotic syndrome/ 2. nephrosis, lipoid/ 3. nephrotic syndrome.tw. 4. lipoid nephrosis.tw. 5. or/1-3 6. (exp Adult/ not (exp Aged/ and exp Child/ or exp Infant/ or exp Adolescent/)) 7. 5 not 6 8. (child* or infant* or babies* or boy* or girl* or pediatric* or paediatric* or adolescen*) 9. and/5,8 10. or/7,9 11. randomised controlled trial.pt. 12. controlled clinical trial.pt. 13. randomized.ab. 14. placebo.ab. 15. clinical trials as topic/ 16. randomly.ab. 17. (crossover or cross-over).tw. 18. Cross-over Studies/ 19. trial.ti. 20. or/11-19 21. animals/ not (humans/ and animals/) 22. 9 and 20 23. 22 not 21
Search strategy - Embase	1. Nephrotic Syndrome/ 2. Lipoid Nephrosis/ 3. nephrotic syndrome.tw. 4. lipoid nephrosis.tw. 5. or/1-4 6. ((Adult/ or Middle Aged/ or exp Aged/) not ((Adult/ or Middle Aged/ or exp Aged/) and (exp Child or exp/Adolescent))

	7. 5 not 6 8. (child* or infant* or babies* or boy* or girl* or pediatric* or paediatric* or adolescen*) 9. and/5,8 10. or/7,9 11. randomised controlled trial/ 12. crossover procedure/ 13. double-blind procedure/ 14. single-blind procedure/ 15. random$.tw. 16. factorial$.tw. 17. crossover$ or cross-over$).tw. 18. placebo$.tw. 19. (double$ adj blind$).tw. 20. (singl$ adj blind$).tw. 21. assign$.tw. 22. allocat$.tw. 23. volunteer$.tw. 24. or/12-24 25. 10 and 24
Systematic review topic	Interventions for steroid-resistant nephrotic syndrome in children
Search strategy - CENTRAL	1. MeSH descriptor: [Nephrotic Syndrome] explode all trees 2. MeSH descriptor: [Nephrosis, Lipoid] explode all trees 3. nephrotic syndrome:ti,ab,kw (Word variations have been searched) 4. lipoid nephrosis:ti,ab,kw (Word variations have been searched) 5. minimal change glomerulonephritis:ti,ab,kw (Word variations have been searched) 6. minimal change nephr*:ti,ab,kw (Word variations have been searched) 7. idiopathic steroid resistant nephrotic syndrome:ti,ab,kw (Word variations have been searched) 8. SRNS:ti,ab,kw (Word variations have been searched) 9. {or #1-#8}
Search strategy - MEDLINE	1. Nephrotic Syndrome/ 2. Nephrosis Lipoid/ 3. nephrotic syndrome.tw. 4. lipoid nephrosis.tw. 5. minimal change glomerulonephritis.tw. 6. minimal change nephr$.tw. 7. idiopathic steroid resistant nephrotic syndrome.tw. 8. or/1-7 9. randomised controlled trial.pt. 10. controlled clinical trial.pt. 11. randomized.ab. 12. placebo.ab. 13. clinical trials as topic/ 14. randomly.ab. 15. (crossover or cross-over).tw. 16. Cross-over Studies/ 17. trial.ti. 18. or/9-17 19. animals/ not (humans/ and animals/)

	20. 8 and 18 21. 20 not 19
Search strategy - Embase	1. Nephrotic Syndrome/ 2. Lipoid Nephrosis/ 3. nephrotic syndrome.tw. 4. lipoid nephrosis.tw. 5. minimal change glomerulonephritis.tw. 6. minimal change nephropathy.tw. 7. idiopathic steroid resistant nephrotic syndrome.tw. 8. or/1-7 9. randomised controlled trial/ 10. crossover procedure/ 11. double-blind procedure/ 12. single-blind procedure/ 13. random$.tw. 14. factorial$.tw. 15. crossover$ or cross-over$).tw. 16. placebo$.tw. 17. (double$ adj blind$).tw. 18. (singl$ adj blind$).tw. 19. assign$.tw. 20. allocat$.tw. 21. volunteer$.tw. 22. or/9-21 23. 8 and 22

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 2020 KDIGO BP in CKD 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 January – May 2020.
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 2020 KDIGO diabetes in CKD guideline
Methods	
Include a research protocol with appropriate eligibility criteria (PICO format)	See *Table 4 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 MC1 – 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
Chapter 2. Immunoglobulin A nephropathy (IgAN)/Immunoglobulin A vasculitis (IgAV)

Table S4.
Population: Patients with IgA nephropathy
Intervention: Targeted-release budesonide (nefecon) for 9 months
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo Nefecon	**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 or ≥30% GFR loss	Hazard ratio: 0.45 (95% CI: 0.26 – 0.75) Based on data from 364 patients in 1 study[1] Follow-up 24 months	**214** per 1000 **115** per 1000 Difference: **99 fewer per 1000** (95% CI: 174 fewer – 23 fewer)	**Moderate** Serious imprecision[2]	Nefecon probably decreases composite kidney failure or ≥30% GFR loss
Infection	Severe: Relative risk: 2.50 (95% CI: 0.49 – 12.7) Based on data from 364 patients in 1 study[3] Follow-up 9 months	**11** per 1000 **27** per 1000 **16 more per 1000** (95% CI: 13 fewer - 46 more)	**Low** Due to very serious imprecision[4]	Nefecon may have little or no difference on severe infection or URI
	URI: Relative risk: 1.20 (95% CI: 0.30 – 4.82) Based on data from 150 patients in 1 study[5] Follow-up 9 months	**50** per 1000 **60** per 1000 **10 more per 1000** (95% CI: 72 fewer - 92 more)	**Low** Due to very serious imprecision[6]	
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 GFR loss 3 years	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss
eGFR, change from baseline, mL/min/1.73 m^2	Measured by: Scale: Higher better Based on data from 480 patients in 2 studies[7] Follow up 9 months	**−4.6** Mean **0.6** Mean Difference: **MD 5.4 higher** (95% CI: 3.8 higher – 7.0 higher)	**High**[8]	Nefecon decreases GFR loss at end of treatment
	Based on data from 295 patients in 1 study[9] Follow up 24 months	**−12.0** Mean **−6.1** Mean Difference: **MD 5.9 higher** (95% CI: 3.4 higher – 9.2 higher)	**Moderate** Serious imprecision[10]	Nefecon probably decreases GFR loss at 24 months
Proteinuria change from baseline, %	Measured by: Scale: Lower better Based on data from 480 patients in 2 studies[11] Follow up 9 months	**−1.6** Mean **−29.3** Mean Difference: **MD 29.0% lower** (95% CI: 36.5% lower – 21.4% lower)	**High**[12]	Nefecon decreases proteinuria at 9 months
	Based on data from 295 patients in 1 study[13] Follow up 24 months	**−1.0** Mean **−30.7** Mean Difference: **MD 30.1% lower** (95% CI: 41.5% lower – 16.4% lower)	**Moderate** Serious imprecision[14]	Nefecon probably decreases proteinuria at 24 months

1. Systematic review with included studies: [NefIgArd 2023] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Serious.** Only data from one study.
3. Systematic review with included studies: [NefIgArd 2023] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Very Serious.** Very wide confidence interval. Data from only one study.
5. Systematic review with included studies: [25] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Very Serious.** Very wide confidence interval. Data from only one study.
7. Systematic review with included studies: [NefIgArd 2023][25] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Low.**
9. Systematic review with included studies: [NefIgArd 2023] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Imprecision: Serious.** Only data from one study.
11. Systematic review with included studies: [NefIgArd 2023][25] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Low.**

13. Systematic review with included studies: [NefIgArd 2023] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Imprecision: Serious.** Only data from one study.

References

[25] Fellstrom BC, Barratt J, Cook H, Coppo R, Feehally J, de Fijter JW, et al. Targeted-release budesonide versus placebo in patients with IgA nephropathy (NEFIGAN): a double-blind, randomised, placebo-controlled phase 2b trial. Lancet 2017;389(10084):2117-2127
9 mo

[NefIgArd 2023] Lafayette R, Kristensen J, Stone A, et al.. Efficacy and safety of a targeted-release formulation of budesonide in patients with primary IgA nephropathy(NefIgArd): 2-year results from a randomised phase 3 trial. Lancet 2023. [PubMed: 37591292]

Table S5.
Population: Patients with IgA nephropathy
Intervention: Tonsillectomy plus standard of care
Comparator: Standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard of care	Tonsillectomy plus standard of care	**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 (95% CI: -) Based on data from 42 patients in 1 study[1] Follow up 12 months	Difference:		**Very low** Due to very serious risk of bias, Due to serious imprecision[2]	There were too few who experienced kidney failure, to determine whether tonsillectomy plus standard of care made a difference
≥50% loss of GFR	Relative risk (95% CI: -) Based on data from 72 patients in 1 study[1] Follow up 12 months	Difference:		**Very low** Due to very serious risk of bias, Due to serious imprecision[3]	There were too few who experienced the ≥50% loss of GFR to determine whether tonsillectomy plus standard of care made a difference
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 (95% CI: -) Based on data from 72 patients in 1 study[1] Follow up 12 months	Difference:		**Very low** Due to very serious risk of bias, Due to serious imprecision[4]	One study reported that there was no difference in achieving complete remission at 12 months (P=0.103). However, we are uncertain of its effect because of

				very low certainty of the evidence.
Remission of proteinuria	Relative risk: 1.9 (95% CI: 1.45 - 2.47) Based on data from 143 patients in 2 studies[5] Follow up 3.5 years	**441** per 1000 **838** per 1000 Difference: **397 more per 1000** (95% CI: 198 more - 648 more)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Tonsillectomy plus other treatment versus other treatment alone may increase remission of proteinuria
Remission of microscopic hematuria	Relative risk: 1.93 (95% CI: 1.47 - 2.53) Based on data from 143 patients in 2 studies[7] Mean follow up 32 months	**456** per 1000 **880** per 1000 Difference: **424 more per 1000** (95% CI: 214 more - 698 more)	**Low** Due to serious risk of bias, Due to serious inconsistency[8]	Tonsillectomy plus other treatment versus other treatment alone may have increase remission of microscopic hematuria
Remission of macroscopic hematuria	Relative risk: 1.33 (95% CI: 0.8 - 2.23) Based on data from 32 patients in 1 study[9] Follow up 24 months	**563** per 1000 **749** per 1000 Difference: **186 more per 1000** (95% CI: 113 fewer - 692 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[10]	We are uncertain whether tonsillectomy plus other treatment versus other treatment alone increases or decreases remission of macroscopic hematuria
Relapse of hematuria	Relative risk: 0.7 (95% CI: 0.51 - 0.98) Based on data from 72 patients in 1 study[11] Follow up 12 months	**783** per 1000 **548** per 1000 Difference: **235 fewer per 1000** (95% CI: 384 fewer - 16 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[12]	Tonsillectomy plus other standard of care versus standard of care alone may decrease relapse of hematuria
Relapse of proteinuria	Relative risk: 0.7 (95% CI: 0.57 - 0.85) Based on data from 73 patients in 1 study[13] Follow up 12 months	**1000** per 1000 **700** per 1000 Difference: **300 fewer per 1000** (95% CI: 430 fewer - 150 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[14]	Tonsillectomy plus other standard of care versus standard of care alone may decrease relapse of proteinuria
Annual GFR loss	Measured by: Scale: - High better	Difference:		No studies were found that looked at annual GFR loss

Creatinine clearance	Measured by: Scale: - High better Based on data from 77 patients in 2 studies[15] Mean follow up 3.5 years	Mean Mean Difference: **MD 3.77 higher** (95% CI: 13.80 lower - 21.35 higher)	**Very low** Due to serious risk of bias, Due to very serious inconsistency, Due to very serious imprecision[16]	We are uncertain whether tonsillectomy plus treatment versus treatment alone increases or decreases creatinine clearance

1. Systematic review with included studies: [34] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, due to no data being reported that could be meta-analysed for complete remission; **Imprecision: Serious.** Only data from one study, Low number of patients.
3. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, due to no data being reported that could be meta-analysed for complete remission; **Imprecision: Serious.** Only data from one study, Low number of patients.
4. Systematic review with included studies: [34] **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, due to no data being reported that could be meta-analysed for complete remission; **Imprecision: Serious.** Only data from one study, Low number of patients.
6. Systematic review [18] with included studies: [71], [82] **Baseline/comparator:** Control arm of reference used for intervention.
7. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Selective outcome reporting; **Imprecision: Serious.** Wide confidence intervals, Low number of patients.
8. Systematic review [137] with included studies: [71], [34], [82] **Baseline/comparator:** Control arm of reference used for intervention.
9. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Selective outcome reporting; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 75%.; **Imprecision: No serious.** Low number of patients.
10. Systematic review with included studies: [78] **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.
12. Systematic review with included studies: [71] **Baseline/comparator:** Control arm of reference used for intervention.
13. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients.
14. Systematic review with included studies: [71] **Baseline/comparator:** Control arm of reference used for intervention.
15. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients.
16. Systematic review [137] with included studies: [78], [82] **Baseline/comparator:** Control arm of reference used for intervention.
17. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Selective outcome reporting; **Inconsistency: Very Serious.** The

magnitude of statistical heterogeneity was high, with I^2:76%., The direction of the effect is not consistent between the included studies; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients.

References

[34] Kawamura T, Yoshimura M, Miyazaki Y, Okamoto H, Kimura K, Hirano K, et al. A multicenter randomized controlled trial of tonsillectomy combined with steroid pulse therapy in patients with immunoglobulin A nephropathy. Nephrology Dialysis Transplantation 2014;29(8):1546-1553
[71] Yang D, He L, Peng X, Liu H, Peng Y, Yuan S, et al. The efficacy of tonsillectomy on clinical remission and relapse in patients with IgA nephropathy: a randomized controlled trial. Renal Failure 2016;38(2):242-248
[78] Kawasaki Y, Takano K, Suyama K, Isome M, Suzuki H, Sakuma H, et al. Efficacy of tonsillectomy pulse therapy versus multiple-drug therapy for IgA nephropathy. Pediatric Nephrology 2006;21(11):1701-1706
[82] Hotta O, Taguma Y, Kurosawa K, Sudo K, Suzuki K, Horigome I. Early intensive therapy for clinical remission of active IgA nephropathy: a three-year follow-up study. Japanese Journal of Nephrology 1993;35(8):967-973
[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews 2011;(3):CD003962

Table S6.
Population: Patients with IgA nephropathy
Intervention: Glucocorticoid (oral) plus supportive therapy (excluding nefecon)
Comparator: Supportive therapy

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Supportive therapy	Glucocorticoid plus supportive therapy	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: 1.45 (95% CI: 0.41 – 5.12) Based on data from 312 patients in 2 studies[1] Mean follow up 29 months	**19** per 1000	**13** per 1000 Difference: **6 more per 1000** (95% CI: 8 fewer - 55 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether glucocorticoid plus supportive therapy made a difference in all-cause mortality
Kidney failure	Relative risk: 0.42 (95% CI: 0.17 – 1.03) Based on data from 772 patients in 4 studies[3] Mean follow up 46 months	**132** per 1000	**214** per 1000 Difference: **124 fewer per 1000** (95% CI: 177 fewer - 6 more)	**Moderate** Due to serious risk of bias[4]	Glucocorticoid plus supportive therapy probably decreases kidney failure (up to 4 years)
≥50% GFR loss	Relative risk: 0.62 (95% CI: 0.45 - 0.84) Based on data from 503 patients in 1 study[5] Follow up 42 months	**309** per 1000	**191** per 1000 Difference: **118 fewer per 1000** (95% CI: 190 fewer - 41 more)	**Moderate** Due to serious imprecision[6]	Glucocorticoid plus supportive therapy probably decreases ≥50% GFR loss
Infection	Reduced dose: Relative risk: 2.31 (95% CI: 0.61 – 8.74) Based on data from 241 patients in 1 study[7] Follow-up 9 months	**25** per 1000	**58** per 1000 Difference: **33 more per 1000** (95% CI: 17 fewer – 83 more)	**Low** Due to serious imprecision[8]	Reduced dose glucocorticoid plus supportive therapy may increase infections
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy

Complete remission	Relative risk: 1.78 (95% CI: 1.09 - 2.89) Based on data from 380 patients in 4 studies[9] Mean follow up 42 months	**326** per 1000 **580** per 1000 Difference: **254 more per 1000** (95% CI: 29 more - 616 more)	**Low** Due to serious risk of bias, Due to serious inconsistency[10]	Glucocorticoid plus supportive therapy may increase complete remission
Doubling of serum creatinine	Relative risk: 0.22 (95% CI: 0.07 - 0.76) Based on data from 160 patients in 2 studies[11] Mean follow up 54 months	**165** per 1000 **36** per 1000 Difference: **129 fewer per 1000** (95% CI: 153 fewer - 40 fewer)	**Moderate** Due to serious risk of bias[12]	Glucocorticoid plus supportive therapy probably decreases doubling of serum creatinine
Adverse events, serious	Relative risk: 1.40 (95% CI: 0.90 – 2.19) Based on data from 403 patients in 2 studies[13] Mean follow up 28 months	**120** per 1000 **172** per 1000 Difference: **48 more per 1000** (95% CI: 12 fewer - 143 more)	**Moderate** Due to serious imprecision[14]	Glucocorticoid plus supportive therapy probably increases serious adverse events
GFR decline ≥15 ml/min/1.73 m^2	Relative risk: 0.74 (95% CI: 0.39 - 1.41) Based on data from 109 patients in 1 study[15] Follow up 36 months	**231** per 1000 **333** per 1000 Difference: **102 more per 1000** (95% CI: 92 fewer - 575 more)	**Low** Due to serious risk of bias, Due to serious imprecision[16]	Glucocorticoid plus supportive therapy may have little or no effect on GFR decline ≥15 m/min/1.73 m^2
Annual GFR loss, ml/min/1.73 m^2	Measured by: Scale: - Lower better Based on data from 309 patients in 2 studies[17] Mean follow up 29 months	**6.6** Mean **1.0** Mean Difference: **MD 5.4 ml/min/1.73 m^2/year lower** (95% CI: 8.6 lower – 2.3 lower)	**High**[18]	Glucocorticoid plus supportive therapy reduces annual GFR loss

1. Systematic review [139] with included studies: [Lv 2022 35579642 TESTING], [54].
   Baseline/comparator: Control arm of reference used for intervention. This analysis is based on short-term follow-up. The STOP-IgAN trial [54] (which lasted 3 years) also reported 10-year follow-up data [Rauen 2020], which had an imprecise, nonsignificant finding: HR 0.71 (95% CI 0.12, 4.32) in 149 patients.
2. **Imprecision: Very serious.** Very wide confidence intervals, Low number of events.
3. Systematic review [139] with included studies: [Lv 2022 35579642], [44], [54], [134]
   Baseline/comparator: Control arm of reference used for intervention. This analysis is based on 4 studies with short-term follow-up [Lv 2022 35579642], [44], [54], [134]. The STOP-IgAN trial [54] (which lasted 3 years) also reported 10-year follow-up data [Rauen 2020], which had an imprecise, nonsignificant finding: HR 0.90 (95% CI 0.47, 1.73) in 149 patients.

4. **Risk of bias: Serious.** Due to inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias.
5. Primary study [Lv 2022 35579642] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Serious.** Only data from one study.
7. Primary study [Lv 2022 35579642] **Baseline/comparator:** Control arm of reference used for intervention. Analysis restricted to reduced-dose glucocorticoid protocol.
8. **Imprecision: Serious.** Wide confidence intervals. Only data from one study.
9. Systematic review [139] with included studies: [45], [134], [44], [54] **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/lack of blinding of outcome assessors, resulting in potential for detection bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with I^2: 60%.
11. Primary study [44], [134] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias.
13. Systematic review [139] with included studies: [54][Lv 2022 35579642]. **Baseline/comparator:** Control arm of reference used for intervention. Analysis restricted to reduced-dose glucocorticoid protocol in TESTING study.
14. **Risk of bias: Serious.** Wide confidence interval.
15. Systematic review [139] with included studies: [54] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Unclear sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study, Low number of patients.
17. Systematic review with included studies: [134], [Rauen 2020]. **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of bias: Low. Consistency: Not serious.** Statistically homogeneous.

References

[44] Lv 2009: Lv J, Zhang H, Chen Y, Li G, Jiang L, Singh AK, et al. Combination therapy of prednisone and ACE inhibitor versus ACE-inhibitor therapy alone in patients with IgA nephropathy: a randomized controlled trial. American Journal of Kidney Diseases 2009;53(1):26-32

[45] Lv J, Zhang H, Wong MG, Jardine MJ, Hladunewich M, Jha V, et al. Effect of oral methylprednisolone on clinical outcomes in patients with IgA nephropathy: the TESTING randomized clinical trial. JAMA 2017;318(5):432-442

[Lv 2022 35579642 TESTING] Lv, J.; Wong, M. G.; Hladunewich, M. A.; Jha, V.; Hooi, L. S.; Monaghan, H.; Zhao, M.; Barbour, S.; Jardine, M. J.; Reich, H. N.; Cattran, D.; Glassock, R.; Levin, A.; Wheeler, D. C.; Woodward, M.; Billot, L.; Stepien, S.; Rogers, K.; Chan, T. M.; Liu, Z. H.; Johnson, D. W.; Cass, A.; Feehally, J.; Floege, J.; Remuzzi, G.; Wu, Y.; Agarwal, R.; Zhang, H.; Perkovic, V.. Effect of Oral Methylprednisolone on Decline in Kidney Function or Kidney Failure in Patients With IgA Nephropathy: The TESTING Randomized Clinical Trial. JAMA 2022;327(19):1888-1898. [PubMed: 35579642]

[54] STOP-IgAN: Rauen T, Eitner F, Fitzner C, Sommerer C, Zeier M, Otte B, et al. Intensive supportive care plus immunosuppression in IgA nephropathy. New England Journal of Medicine 2015;373(23):2225-2236

[Rauen 2020 STOP-IgAN] Rauen, T.; Wied, S.; Fitzner, C.; Eitner, F.; Sommerer, C.; Zeier, M.; Otte, B.; Panzer, U.; Budde, K.; Benck, U.; Mertens, P. R.; Kuhlmann, U.; Witzke, O.; Gross, O.; Vielhauer, V.;

Mann, J. F. E.; Hilgers, R. D.; Floege, J.. After ten years of follow-up, no difference between supportive care plus immunosuppression and supportive care alone in IgA nephropathy. Kidney International 2020;98:1044–1052. [PubMed: 32450154]
[134] Manno 2009 Manno C, Torres DD, Rossini M, Pesce F, Schena FP. Randomized controlled clinical trial of corticosteroids plus ACE-inhibitors with long-term follow-up in proteinuric IgA nephropathy. Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association 2009;24(12):3694-3701
[139] Natale P, Palmer SC, Ruospo M et al. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews 2020;3 CD003965

Table S7.
Population: Patients with IgA nephropathy
Intervention: Renin-angiotensin system inhibitors (RASi)
Comparator: Placebo or no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo or no treatment	RASi	**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 or doubling serum creatinine	Relative risk: 0.25 (95% CI: 0.03 - 2.21) Based on data from 109 patients in 1 study[1] Follow up 26 months	**73** per 1000	**18** per 1000 Difference: **55 fewer per 1000** (95% CI: 71 fewer - 88 more)	**Low** Due to very serious imprecision[2]	RASi may have little or no difference on kidney failure or doubling serum creatinine
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
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
Complete remission of proteinuria	Relative risk: 5.29 (95% CI: 0.27 - 102.49) Based on data from 33 patients in 1 study[3] Follow up 38 months (median)	**0** per 1000	**0** per 1000 Difference: **0 per 1000** (95% CI: 0 - 0)	**Low** Due to very serious imprecision[4]	RASi may have little or no difference on complete remission of proteinuria

Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss
Serum creatinine	Measured by: Scale: - Based on data from 22 patients in 1 study[5] Follow up 3 months	Mean Mean Difference: **MD 0 lower** (95% CI: 23.74 lower - 23.74 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether RASi increases or decreases serum creatinine
Proteinuria	Measured by: Scale: - Based on data from 197 patients in 3 studies[7] Mean follow up 22 months	g/24 h Mean g/24 h Mean Difference: **MD 0.73 lower** (95% CI: 1.06 lower - 0.39 lower)	**Moderate** Due to serious risk of bias[8]	RASi probably decreases proteinuria
Creatinine clearance	Measured by: Scale: - Based on data from 197 patients in 3 studies[9] Mean follow up 22 months	Mean Mean Difference: **MD 6.97 higher** (95% CI: 0.60 lower - 14.54 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	RASi may increase creatinine clearance

1. Systematic review with included studies: [130] **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.
3. Systematic review with included studies: [104] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: No serious.** 14% lost to follow-up (all of these from the ACEi group); **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients.
5. Systematic review with included studies: [99] **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, unclear of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
7. Systematic review with included studies: [99], [130], [104] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** 14% lost to follow-up (all of these from the ACEi group) in the IgACE study. Unclear sequence generation and blinding in Nakamura 2000.
9. Systematic review with included studies: [99], [130], [104] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** 14% lost to follow-up (all of these from the ACEi group) in the IgACE study. Unclear sequence generation and blinding in Nakamura 2000. **Imprecision: Serious.** Large effect size, but nonsignificant with wide confidence intervals.

References

[99] Nakamura T, Ushiyama C, Suzuki S, Hara M, Shimada N, Sekizuka K, et al. Effects of angiotensin-converting enzyme inhibitor, angiotensin II receptor antagonist and calcium antagonist on urinary podocytes in patients with IgA nephropathy. American Journal of Nephrology 2000;20(5):373-379

[104] Coppo R, Peruzzi L, Amore A, Piccoli A, Cochat P, Stone R, et al. IgACE: A Placebo-Controlled, Randomized Trial of Angiotensin-Converting Enzyme Inhibitors in Children and Young People with IgA Nephropathy and Moderate Proteinuria. Journal of the American Society of Nephrology 2007;18(6):1880-1888

[130] Li PK-T, Leung CB, Chow KM et al: Hong Kong study using valsartan in IgA nephropathy (HKVIN): a double-blind, randomized, placebo-controlled study. American journal of kidney diseases: the official journal of the National Kidney Foundation 2006;47(5):751-760

[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews 2011;(3):CD003962

Table S8.
Population: Patients with IgA nephropathy and CKD
Intervention: SGLT2 inhibitor (Dapagliflozin or Empagliflozin) 10 mg daily
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo SGLT2i	**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: 0.30 (95% CI: 0.11- 0.80) Based on data from 270 patients in 1 study[1] Follow up 38 months	**120** per 1000 **36** per 1000 Difference: **84 fewer per 1000** (95% CI: 147 fewer – 20 fewer)	**Moderate** Due to serious imprecision[2]	Dapagliflozin probably decreases kidney failure
Kidney disease progression[3]	Relative risk: 0.49 (95% CI: 0.32-0.74)[4] Based on data from 1087 patients in 2 studies[5] Mean follow up 29 months	**12** per 1000 **67** per 1000 Difference: **65 fewer per 1000** (95% CI: 86 fewer – 33 fewer)[6]	**High**[7]	SGLT2 inhibitors reduce kidney disease progression
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

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	SGLT2i	**Certainty of the evidence**	**Plain text summary**
Annual GFR loss	Measured by: Scale: - Lower better Based on data from 270 patients in 1 study[8] Follow up 38 months	**−4.7** ml/min/1.73 m^2	**−3.5** ml/min/1.73 m^2 per year Difference: **1.2** (95% CI: −0.12, 2.51)	**Moderate** Due to serious imprecision[9]	Dapagliflozin probably has little or no difference on annual GFR loss
Proteinuria	Measured by: ACR Scale: - Lower better Based on data from 270 patients in 1 study[10] Follow up 38 months	**~1%**	**~−25%** Difference: **−26%** (95% CI: −37, −14)	**Moderate** Due to serious imprecision[11]	Dapagliflozin probably improves proteinuria
Adverse events, serious	Relative risk: 0.63 (95% CI: 0.39 – 1.02) Based on data from 270 patients in 1 study[12] Follow up 38 months	**256** per 1000	**161** per 1000 Difference: **95 fewer per 1000** (95% CI: 191 fewer- 1 more)	**Low** Due to very serious imprecision[13]	Dapagliflozin may decrease serious adverse events

1. Primary study [DAPA-CKD 2021] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Not serious. Imprecision: Serious.** Only data from one study. Note: Large magnitude of effect
3. Halving of eGFR, sustained low eGFR, kidney failure, or death from kidney failure.
4. Relative risk (RR) as reported by existing systematic review [Nuffield NHS]; however, n/N data do not align with reported RR for EMPA-KIDNEY. Based on reported n/N data: RR = 0.53 (0.36, 0.78).
5. Primary study [DAPA-CKD 2021][EMPA-KIDNEY 2023] **Baseline/comparator:** Control arm of reference used for intervention.
6. Based on RR estimate from reported n/N data: 60 fewer per 1000 (81 fewer to 28 fewer).
7. **Risk of bias: Not serious. Consistency: Not serious. Imprecision: Not serious.**
8. Primary study [DAPA-CKD 2021] **Baseline/comparator:** Control arm of reference used for intervention.
9. **Risk of bias: Not serious. Imprecision: Serious.** Only data from one study
10. Primary study [DAPA-CKD 2021] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Risk of bias: Not serious. Imprecision: Serious.** Only data from one study
12. Primary study [DAPA-CKD 2021] **Baseline/comparator:** Control arm of reference used for intervention.
13. **Risk of bias: Not serious. Imprecision: Very serious.** Only data from one study, Wide confidence interval

References

[DAPA-CKD 2021] Wheeler, D. C.; Toto, R. D.; Stefansson, B. V.; Jongs, N.; Chertow, G. M.; Greene, T.; Hou, F. F.; McMurray, J. J. V.; Pecoits-Filho, R.; Correa-Rotter, R.; Rossing, P.; Sjostrom, C. D.; Umanath, K.; Langkilde, A. M.; Heerspink, H. J. L. A pre-specified analysis of the DAPA-CKD trial demonstrates the effects of dapagliflozin on major adverse kidney events in patients with IgA nephropathy. Kidney International 2021;100:215-224. [PubMed: 33878338]

[EMPA-KIDNEY 2023] The EMPA-KIDNEY Collaborative Group. Empagliflozin in Patients with Chronic Kidney Disease. New Engl J Med 2023; 388:117-127. [PubMed: 36331190]

[Nuffield NHS] Impact of diabetes on the effects of sodium glucose co-transporter-2 inhibitors on kidney outcomes: collaborative meta-analysis of large placebo-controlled trials.
Nuffield Department of Population Health Renal Studies Group; SGLT2 inhibitor Meta-Analysis Cardio-Renal Trialists' Consortium. Impact of diabetes on the effects of sodium glucose co-transporter-2 inhibitors on kidney outcomes: collaborative meta-analysis of large placebo-controlled trials. Lancet. 2022;400(10365):1788-1801. [PMID: 36351458]

Table S9.
Population: Patients with IgA nephropathy
Intervention: Sparsentan 400 mg daily
Comparator: Irbesartan 300 mg daily

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Irbesartan	Sparsentan	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.33 (95% CI: 0.01- 8.13) Based on data from 404 patients in 1 study[1] Follow up 25 months	**5** per 1000	**0** per 1000 Difference: **5 fewer per 1000** (95% CI: 15 fewer - 5 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether sparsentan increases or decreases mortality compared with irbesartan
Kidney failure	Relative risk: 5.00 (95% CI: 0.24- 103.5) Based on data from 404 patients in 1 study[3] Follow up 25 months	**10** per 1000	**0** per 1000 Difference: **10 more per 1000** (95% CI: 4 fewer - 24 more)	**Very low** Due to very serious imprecision[4]	We are uncertain whether sparsentan increases or decreases kidney failure compared with irbesartan
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
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: 2.70 (95% CI: 1.74 – 4.17) Based on data from 404 patients in 1 study[5] Follow up 25 months	**114** per 1000	**307** per 1000 Difference: **193 more per 1000** (95% CI: 116 more - 270 more)	**Moderate** Due to serious imprecision[6]	Sparsentan probably increases complete remission compared with irbesartan

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Irbesartan	Sparsentan	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Annual GFR loss	Measured by: CKD-EPI Scale: - Higher difference better Based on data from 404 patients in 1 study[7] Follow up 25 months	**−3.9** ml/min/1.73 m^2	**−2.9** ml/min/1.73 m^2 per year Difference: **1.0** (95% CI: −0.03, 1.94)	**Low** Due to very serious imprecision[8]	Sparsentan may reduce annual GFR loss compared with irbesartan
Proteinuria	Measured by: PCR Scale: - Lower better Based on data from 404 patients in 1 study[9] Follow up 25 months	**−42.8%**	**−4.4%** Difference (%): **−40%** (95% CI: −50, −28)	**Moderate** Due to serious imprecision[10]	Sparsentan probably reduces proteinuria compared with irbesartan
Adverse events, serious[11]	Relative risk: 1.06 (95% CI: 0.81 – 1.37) Based on data from 404 patients in 1 study[12] Follow up 25 months	**351** per 1000	**371** per 1000 Difference: **20 more per 1000** (95% CI: 74 fewer- 113 more)	**Low** Due to serious imprecision, Due to indirectness[13]	Sparsentan may have little or no difference on serious adverse events compared with irbesartan

1. Primary study [PROTECT 2023] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias:** No serious risk of bias. **Imprecision: Very serious.** Only data from one study, Very wide confidence interval due to few events.
3. Primary study [PROTECT 2023] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias:** No serious risk of bias. **Imprecision: Very serious.** Only data from one study, Very wide confidence interval due to few events.
5. Primary study [PROTECT 2023] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias:** No serious risk of bias. **Imprecision: Serious.** Only data from one study.
7. Primary study [PROTECT 2023] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias:** No serious risk of bias. **Imprecision: Very serious.** Only data from one study. Nonsignificant estimate of difference.
9. Primary study [PROTECT 2023] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias:** No serious risk of bias. **Imprecision: Serious.** Only data from one study.
11. Includes COVID-19 infections
12. Primary study [PROTECT 2023] **Baseline/comparator:** Control arm of reference used for intervention.

13. **Risk of bias:** No serious risk of bias. **Imprecision: Serious.** Only data from one study. **Indirectness: Serious.** Includes COVID-19 infections, likely biasing any estimate of treatment-related adverse events toward the null.

References

[PROTECT 2023] Rovin BH, Barratt J, Heerspink HJL, Alpers CE, Bieler S, Chae DW, Diva UA, Floege J, Gesualdo L, Inrig JK, Kohan DE, Komers R, Kooienga LA, Lafayette R, Maes B, Małecki R, Mercer A, Noronha IL, Oh SW, Peh CA, Praga M, Preciado P, Radhakrishnan J, Rheault MN, Rote WE, Tang SCW, Tesar V, Trachtman H, Trimarchi H, Tumlin JA, Wong MG, Perkovic V; DUPRO steering committee and PROTECT Investigators.. Efficacy and safety of sparsentan versus irbesartan in patients with IgA nephropathy (PROTECT): 2-year results from a randomised, active-controlled, phase 3 trial. Lancet 2023;Online ahead of print:S0140-6736(23)02302-4. [DOI: 10.1016/ S0140-6736(23)02302-4; PubMed: 37931634]

Table S10.
Population: Patients with IgA vasculitis and severe kidney disease
Intervention: Prednisone
Comparator: Placebo or supportive therapy

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo or supportive therapy	Prednisone	**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% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
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
Development of kidney disease[1] any time after treatment	Relative risk: 0.74 (95% CI: 0.42 - 1.32) Based on data from 746 patients in 5 studies[2] Mean follow up 36.3 months	**143** per 1000	**106** per 1000 Difference: **37 fewer per 1000** (95% CI: 83 fewer - 46 more)	**Moderate** Due to serious risk of bias[3]	Prednisone compared with placebo or supportive treatment probably has little or no difference on development of persistent kidney disease
Continuing kidney disease	Relative risk: 0.51 (95% CI: 0.24 - 1.11)	**100** per 1000	**51** per 1000	**Moderate**	Prednisone compared with placebo or

6 months	Based on data from 379 patients in 3 studies[4] Mean follow up 44.3 months	Difference: **49 fewer per 1000** (95% CI: 76 fewer - 11 more)	Due to serious risk of bias[5]	supportive treatment may have little or no difference on continuing kidney disease at 6 months
Continuing kidney disease 12 months	Relative risk: 1.06 (95% CI: 0.38 - 2.91) Based on data from 455 patients in 3 studies[6] Mean follow up 18 months	**84** per 1000 **89** per 1000 Difference: **5 more per 1000** (95% CI: 52 fewer - 160 more)	**Low** Due to serious risk of bias, Due to serious imprecision[7]	Prednisone compared with placebo or supportive treatment alone may have little or no difference on continuing kidney disease at 12 months
Development of severe kidney disease[8]	Relative risk: 1.58 (95% CI: 0.42 - 6.0) Based on data from 418 patients in 2 studies[9] Mean follow up 51.5 months	**14** per 1000 **22** per 1000 Difference: **8 more per 1000** (95% CI: 8 fewer - 70 more)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Prednisone compared with placebo or supportive treatment may have little or no difference on development of severe kidney disease
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Development or persistence of kidney disease (proteinuria, development of nephrotic syndrome or acute nephritic syndrome as defined by the investigators)
2. Systematic review [157] with included studies: [140], [144], [149], [156], [146] **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias.
4. Systematic review [157] with included studies: [144], [149], [146] **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias.
6. Systematic review [157] with included studies: [146], [144], [140] **Baseline/comparator:** Control arm of reference used for intervention.
7. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Wide confidence intervals, due to few events.
8. Kidney disease with nephrotic range proteinuria, hypertension, or reduced kidney function
9. Systematic review [157] with included studies: [149], [140] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** large loss to follow up of 30%; **Imprecision: Serious.** due to low events, Wide confidence intervals.

References

[140] Dudley J, Smith G, Llewelyn-Edwards A, Bayliss K, Pike K, Tizard J. Randomised, double-blind, placebo-controlled trial to determine whether steroids reduce the incidence and severity of nephropathy in Henoch-Schonlein Purpura (HSP). Archives of Disease in Childhood 2013;98(10):756-763

[144] Huber AM, King J., McLaine P., Klassen T., Pothos M. A randomized, placebo-controlled trial of prednisone in early Henoch Schonlein purpura [ISRCTN85109383]. BMC Medicine 2004;2 7-7

[146] Mollica F, Li Volti S, Garozzo R, Russo G. Effectiveness of early prednisone treatment in preventing the development of nephropathy in anaphylactoid purpura. European Journal of Pediatrics 1992;151(2):140-144

[149] Ronkainen J, Koskimies O, Ala-Houhala M, Antkainen M, Merenmies J, Rajantie J, et al. Early prednisone therapy in Henoch-Schonlein purpura: a randomized double-blind, placebo-controlled trial. Journal of Pediatrics 2006;149(2):241-247

[156] Islek I, Sezer T, Totan M, Cakir M, Kucukoduk S. The effect of profilactic prednisolon therapy on renal involvement in henoch schonlein vasculitis [abstract]. In: XXXVI Congress of the European Renal Association European Dialysis & Transplant Association; 1999 Sep 5-8; Madrid (Spain). 1999;

[157] Hahn D, Hodson EM, Willis NS, Craig JC. Interventions for preventing and treating kidney disease in Henoch-Schönlein Purpura (HSP). The Cochrane Database of Systematic Reviews 2015;(8):CD005128

Appendix D. Data supplement - Additional SoF tables developed as part of the evidence review
Chapter 2. Immunoglobulin A nephropathy (IgAN)/Immunoglobulin A vasculitis (IgAV)

Table S11.
Population: Patients with IgA nephropathy
Intervention: Oral glucocorticoid
Comparator: Placebo or usual care (non-RAS blockade)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/usual care	Oral glucocorticoid	**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: 0.51 (95% CI: 0.29 - 0.89) Based on data from 319 patients in 6 studies[1] Mean follow up 42 months	**232** per 1000	**118** per 1000 Difference: **114 fewer per 1000** (95% CI: 165 fewer - 26 fewer)	**Moderate** Due to serious risk of bias[2]	Oral glucocorticoid probably decreases kidney failure
≥50% GFR loss	Relative risk: 0.47 (95% CI: 0.09 - 2.39) Based on data from 64 patients in 1 study[3] Follow up 12 months	**129** per 1000	**61** per 1000 Difference: **68 fewer per 1000** (95% CI: 117 fewer - 179 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether oral glucocorticoid increases or decreases ≥50% GFR loss
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Complete remission	Relative risk: 15.0 (95% CI: 0.92 - 243.52) Based on data from 34 patients in 1 study[5] Follow up >12 months	**0** per 1000	**0** per 1000 Difference: **0 per 1000** (95% CI: 0 - 0)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to serious inconsistency[6]	We are uncertain whether oral glucocorticoid increases or decreases complete remission
	Relative risk: 0.45	**326** per 1000	**147** per 1000	**Moderate**	Oral glucocorticoid slightly probably

Doubling of serum creatinine	(95% CI: 0.29 - 0.69) Based on data from 341 patients in 6 studies[7] Mean follow up 50 months	Difference: **179 fewer per 1000** (95% CI: 231 fewer - 101 fewer)	Due to serious risk of bias[8]	decreases doubling of serum creatinine
Annual GFR loss	Measured by: Scale: -	Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [57], [39], [33], [69], [36], [31] **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 concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting, due to other issue
3. Systematic review [139] with included studies: [69] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Only data from one study, Wide confidence intervals
5. Systematic review [139] with included studies: [39] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high; **Imprecision: Serious.** Wide confidence intervals, Only data from one study
7. Systematic review [139] with included studies: [57], [33], [53], [39], [31], [36] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias

References

[25] Fellstrom BC, Barratt J, Cook H, Coppo R, Feehally J, de Fijter JW, et al. Targeted-release budesonide versus placebo in patients with IgA nephropathy (NEFIGAN): a double-blind, randomised, placebo-controlled phase 2b trial. Lancet 2017;389(10084):2117-2127

[31] Julian BA, Barker C. Alternate-day prednisone therapy in IgA nephropathy. Preliminary analysis of a prospective, randomized, controlled trial. Contributions to Nephrology 1993;104 198-206

[33] Katafuchi R, Kiyoshi I, Mizumasa T, Tanaka H, Ando T, Yanase T, et al. Controlled, prospective trial of steroid treatment in IgA nephropathy: a limitation of low-dose prednisolone therapy. American Journal of Kidney Diseases 2003;41(5):972-983

[36] Kobayashi Y, Hiki Y, Kokubo T, Horii A, Tateno S. Steroid therapy during the early stage of progressive IgA nephropathy. A 10-year follow-up study. Nephron 1996;72(2):237-242

[39] Lai KN, Lai FM, Ho CP, Chan KW. Corticosteroid therapy in IgA nephropathy with nephrotic syndrome: a long-term controlled trial. Clinical Nephrology 1986;26(4):174-180
[47] Manno C, Gesualdo L, D'Altri C, Rossini M, Grandaliano G, Schena FP. Prospective randomized controlled multicenter trial on steroids plus ramipril in proteinuric IgA nephropathy. Journal of Nephrology 2001;14(4):248-252
[53] Pozzi C, Bolasco PG, Fogazzi GB, Andrulli S, Altieri P, Ponticelli C, et al. Corticosteroids in IgA nephropathy: a randomised controlled trial. Lancet 1999;353(9156):883-887
[57] Shoji T, Nakanishi I, Suzuki A, Hayashi T, Togawa M, Okada N, et al. Early treatment with corticosteroids ameliorates proteinuria, proliferative lesions, and mesangial phenotypic modulation in adult diffuse proliferative IgA nephropathy. American Journal of Kidney Diseases 2000;35(2):194-201
[69] Hogg RJ, Lee J, Nardelli N, Julian BA, Cattran D, Waldo B, Wyatt R, Jennette JC, Sibley R, Hyland K, Fitzgibbons L, Hirschman G, Donadio JV, Holub BJ: Clinical trial to evaluate omega-3 fatty acids and alternate day prednisone in patients with IgA nephropathy: report from the Southwest Pediatric Nephrology Study Group. Clinical journal of the American Society of Nephrology: CJASN 2006;1(3):467-474
[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S12.
Population: Patients with IgA nephropathy
Intervention: Glucocorticoid (i.v. or oral)
Comparator: Placebo or usual care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/usual care	Glucocorticoid	**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: 0.14 (95% CI: 0.01 - 2.68) Based on data from 86 patients in 1 study[1] Follow up 6 years	**70** per 1000	**10** per 1000 Difference: **60 fewer per 1000** (95% CI: 69 fewer - 118 more)	**Very low** Due to very serious risk of bias, Due to serious imprecision[2]	We are uncertain whether glucocorticoid improves or worsen kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Malignancy	Relative risk: 1.0 (95% CI: 0.06 - 15.48) Based on data from 86 patients in 1 study[3] Follow up 6 years	**23** per 1000	**23** per 1000 Difference: **0 per 1000** (95% CI: 22 fewer - 333 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[4]	There were too few who experienced the malignancy to determine whether glucocorticoid made a difference
Infection	(95% CI: -)	Difference:			No studies were found that looked at infections
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [53] **Baseline/comparator:** Control arm of reference used for intervention.

2. **Risk of bias: Very Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to Four patients in the control group received steroids as rescue therapy; **Imprecision: Serious.** Only data from one study
3. Systematic review [139] with included studies: [53] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, due to [reason]

References

[53] Pozzi C, Bolasco PG, Fogazzi GB, Andrulli S, Altieri P, Ponticelli C, et al. Corticosteroids in IgA nephropathy: a randomised controlled trial. Lancet 1999;353(9156):883-887
[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S13.
Population: Patients with IgA nephropathy
Intervention: Methylprednisolone combined with alternative low-dose prednisone
Comparator: Prednisone, full dose

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Full-dose prednisone	~~Methylprenisolone~~Methylprednisolone + low-dose prednisone	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: (95% CI: -) Based on data from 86 patients in 1 study[1] Follow up 18 months	**0** per 1000	**0** per 1000 Difference: **0 per 1000** (95% CI: 44 fewer - 44 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether methylprednisolone + low-dose prednisone increases or decreases mortality
Kidney failure	(95% CI: -)		Difference:		No studies were found that looked at kidney failure
≥50% GFR loss	(95% CI: -)		Difference:		No studies were found that looked at ≥50% GFR loss
Infection	0.36 (95% CI: 0.18 – 0.71) Based on data from 87 patients in 1 study[3] Follow up 18 months	**500** per 1000	**178** per 1000 Difference: **322 fewer per 1000** (95% CI: 509 fewer - 135 more)	**Moderate** Due to serious risk of bias, Due to serious imprecision, Upgraded due to Large magnitude of effect[4]	Methylprednisolone + low-dose prednisone probably decreases infection
Malignancy	(95% CI: -)		Difference:		No studies were found that looked at malignancy
Complete remission	1.07 (95% CI: 0.75 – 1.53) Based on data from 86 patients in 1 study[5] Follow up 18 months	**561** per 1000	**600** per 1000 Difference: **39 more per 1000** (95% CI: 167 fewer - 245 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether methylprednisolone + low-dose prednisone increases or decreases complete remission

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Full-dose prednisone	~~Methylprenisolone~~Methylprednisolone + low-dose prednisone	**Certainty of the evidence**	**Plain text summary**
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss
Proteinuria	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at proteinuria
Adverse events, serious	(95% CI: -)	Difference:			No studies were found that looked at serious adverse events

1. Primary study [Li 2022] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** No blinding of participants and outcome assessors **Imprecision: Very serious.** Only data from one study, no events
3. Primary study [Li 2022] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** No blinding of participants and outcome assessors **Imprecision: Serious.** Only data from one study. **Upgrade: Large magnitude of effect.**
5. Primary study [Li 2022] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** No blinding of participants and outcome assessors **Imprecision: Very serious.** Only data from one study, wide confidence interval

References

[Li 2022] Li, Y.; Fu, R.; Gao, J.; Wang, L.; Duan, Z.; Tian, L.; Ge, H.; Ma, X.; Zhang, Y.; Li, K.; Xu, P.; Tian, X.; Chen, Z.. Effect of pulsed intravenous methylprednisolone with alternative low-dose prednisone on high-risk IgA nephropathy: a 18-month prospective clinical trial. Scientific Reports 2022;12. [PubMed: 34996948]

Table S14.
Population: Patients with IgA nephropathy (crescent percentage 1-49%)
Intervention: i.v. Methylprednisolone months 1, 2, 3 (0.5 g/d x 3 d per mo), then oral 0.4 mg/kg/d x 6 mo
Comparator: i.v. Methylprednisolone months 1, 3, 5 (0.5 g/d x 3 d per mo), then oral 0.4 mg/kg/d x 6 mo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** i.v. Methylprednisolone months 1, 3, 5	**Absolute effect estimates** i.v. Methylprednisolone months 1, 2, 3	**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% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection	Relative risk: 0.19 (95% CI: 0.02-1.70) Based on data from 74 patients in 1 study[1] Follow up 6 months	**132** per 1000	**28** per 1000 Difference: **104 fewer per 1000** (95% CI: 224 fewer – 16 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether i.v. methylprednisolone months 1,2,3 increases or decreases infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	Relative risk: 1.28 (95% CI: 0.48-3.42) Based on data from 74 patients in 1 study[3] Follow up 6 months	**316** per 1000	**389** per 1000 Difference: **73 more per 1000** (95% CI: 144 fewer – 290 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether i.v. methylprednisolone months 1,2,3 increases or decreases complete remission

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** i.v. Methylprednisolone months 1, 3, 5	 i.v. Methylprednisolone months 1, 2, 3	**Certainty of the evidence**	**Plain text summary**
Annual GFR loss	Measured by: Scale: -	Difference:			No studies were found that looked at annual GFR loss
Proteinuria	Measured by: change Scale: - Lower better Based on data from 74 patients in 1 study[5] Follow up 6 months	**−1.01** g/d	**−1.40** g/d Difference: **−0.39 (−1.00, 0.22)**	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether i.v. methylprednisolone months 1, 2, 3 increases or decreases proteinuria
Adverse events, withdrawal due to	Relative risk: 0.24 (95% CI: 0.03 – 2.28) Based on data from 74 patients in 1 study[7] Follow up 6 months	**105** per 1000	**28** per 1000 Difference: **77 fewer per 1000** (95% CI: 189 fewer- 34 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether i.v. methylprednisolone months 1,2,3 increases or decreases withdrawal due to adverse events

1. Primary study [Liang 2022] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious. Unclear allocation concealment,** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very serious.** Only data from one study, wide confidence interval.
3. Primary study [Liang 2022] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very serious.** Only data from one study, wide confidence interval.
5. Primary study [Liang 2022] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very serious.** Only data from one study, wide confidence interval.
7. Primary study [Liang 2022] **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/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very serious.** Only data from one study, wide confidence interval.

References

[Liang 2022] Liang, M.; Xiong, L.; Li, A.; Zhou, J.; Huang, Y.; Huang, M.; Zhang, X.; Shi, H.; Su, N.; Wei, Y.; Jiang, Z.. The effectiveness and safety of corticosteroid therapy for IgA nephropathy with crescents: a prospective, randomized, controlled study. BMC Nephrol 2022;23(40). [PubMed: 35062886]

Table S15.
Population: Patients with IgA nephropathy
Intervention: Fluticasone propionate inhaled 2x/day (+ supportive care)
Comparator: Supportive care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Supportive care / Fluticasone	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:		No studies were found that looked at mortality
Kidney failure	(95% CI: -)	Difference:		No studies were found that looked at kidney failure
≥50% GFR loss	(95% CI: -)	Difference:		No studies were found that looked at ≥50% GFR loss
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
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss
Proteinuria	Measured by: Scale: - Lower better Based on data from 142 patients in 1 study[1] Follow up 9 months	**−0.1** g/d / **−0.9** g/d Difference: **−0.8** (−1.0, −0.6)	**Low** Due to serious imprecision[2]	Inhaled fluticasone may reduce proteinuria

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Supportive care	 Fluticasone	**Certainty of the evidence**	**Plain text summary**
Adverse events, serious	Relative risk: (95% CI: –) Based on data from 142 patients in 1 study[3] Follow up 9 months	**0** per 1000	**0** per 1000 Difference: **0 more per 1000** (95% CI: 27 fewer - 27 more)	**Very low** Due to very serious imprecision[4]	We are uncertain whether inhaled fluticasone increases or decreases serious adverse events

1. Primary study [Sun 2023] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Serious.** Only data from one study
3. Primary study [Sun 2023] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Very Serious.** Only data from one study, no events.

References

[Sun 2023] Sun, L.; Zi, X.; Wang, Z.; Zhang, X.. The clinical efficacy of fluticasone propionate combined with ACEI/ARB in the treatment of immunoglobulin A nephropathy. BMC Nephrol 2023;24. [PubMed: 36949400]

Table S16.
Population: Patients with IgA nephropathy
Intervention: Cyclophosphamide then azathioprine plus glucocorticoid
Comparator: Antihypertensive therapy (non-RAS blockade)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the evidence**	**Plain text summary**
		Antihypertensive therapy (non-RAS blockade)	Cyclophosphamide then azathioprine plus glucocorticoid		
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Kidney failure	Relative risk: 0.27 (95% CI: 0.11 - 0.66) Based on data from 38 patients in 1 study[1] Follow up 2-6 years	**789** per 1000	**213** per 1000 Difference: **576 fewer per 1000** (95% CI: 702 fewer - 268 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Cyclophosphamide then azathioprine plus glucocorticoid may decrease kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection	Relative risk: 3.0 (95% CI: 0.13 - 69.31) Based on data from 38 patients in 1 study[3] Follow up 2-6 years	Difference:		**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	There were too few who experienced the infection to determine whether cyclophosphamide then azathioprine plus glucocorticoid made a difference
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission[5]	(95% CI: -)	Difference:			Cyclophosphamide then azathioprine plus glucocorticoid may have little or no difference on complete remission

Adverse events	(95% CI: -)	Difference:		No studies were found that looked at adverse events
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [20] **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 concealment of allocation during randomization process, resulting in potential for selection bias, Selective outcome reporting, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study
3. Systematic review with included studies: [20] **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 concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study
5. STOP-IgAN Study - Complete remission (defined as proteinuria with a protein-to-creatinine ratio of <0.2 and stable kidney function with a decrease in the eGFR of <5 ml per minute per 1.73 m2 from the baseline eGFR at the end of the 3-year trial phase)

References

[20] Ballardie FW, Roberts IS. Controlled prospective trial of prednisolone and cytotoxics in progressive IgA nephropathy. Journal of the American Society of Nephrology 2002;13(1):142-148
[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S17.
Population: Patients with IgA nephropathy
Intervention: Cyclophosphamide plus glucocorticoid
Comparator: Glucocorticoid alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Glucocorticoid alone	Cyclophosphamide plus glucocorticoid	**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% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
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: 0.78 (95% CI: 0.44 - 1.39) Based on data from 24 patients in 1 study[1] Follow up 6 months	**750** per 1000	**585** per 1000 Difference: **165 fewer per 1000** (95% CI: 420 fewer - 292 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Cyclophosphamide plus glucocorticoid may have little or no difference on complete remission
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [56] **Baseline/comparator:** Control arm of reference used for intervention.

2. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Wide confidence intervals, Low number of patients

References

[56] Shen P, Li Y, Wang Z, Wang W, Ren H, Zhang W, et al. A prospective randomized study on the efficacy of corticosteroid combined with cyclophosphamide or FK506 in primary IGA nephropathy with mild or moderate renal injury [abstract]. Nephrology Dialysis Transplantation 2013;28(Suppl 1):i175-i75
[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S18.
Population: Patients with IgA nephropathy
Intervention: Cyclophosphamide plus antiplatelet/anticoagulant
Comparator: Usual care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Usual care	Cyclophosphamide plus antiplatelet/anticoagulant	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	(95% CI: -)[1]	Difference:			No studies were found that looked at all-cause mortality
Kidney failure	Relative risk: 0.31 (95% CI: 0.03 - 2.85) Based on data from 100 patients in 2 studies[2] Mean follow up 27 months	**42** per 1000	**13** per 1000 Difference: **29 fewer per 1000** (95% CI: 41 fewer - 78 more)	**Low** Due to serious risk of bias, Due to serious imprecision[3]	Cyclophosphamide plus antiplatelet/anticoagulant may have little or no difference on kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
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
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. **Baseline/comparator:** Control arm of reference used for intervention.

2. Systematic review [139] with included studies: [61], [63] **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting (adverse events and all-cause mortality not reported (Walker 1990)), due to other bias (imbalance in duration of follow up and proteinuria between treatment groups, Woo 1987); **Imprecision: Serious.** Wide confidence intervals

References

[54] Rauen T, Eitner F, Fitzner C, Sommerer C, Zeier M, Otte B, et al. Intensive supportive care plus immunosuppression in IgA nephropathy. New England Journal of Medicine 2015;373(23):2225-2236
[61] Walker RG, Yu SH, Owen JE, Kincaid-Smith P. The treatment of mesangial IgA nephropathy with cyclophosphamide, dipyridamole and warfarin: a two-year prospective trial. Clinical Nephrology 1990;34(3):103-107
[63] Woo KT, Chiang GS, Lim CH. Follow-up renal biopsies in IgA nephritic patients on triple therapy. Clinical Nephrology 1987;28(6):304-305
[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S19.
Population: Patients with IgA nephropathy
Intervention: Azathioprine plus glucocorticoid
Comparator: Placebo or usual care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/usual care	Azathioprine plus glucocorticoid	**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: 3.14 (95% CI: 0.13 - 72.96) Based on data from 43 patients in 1 study[1] Follow up 60 months (median)	**0** per 1000	**0** per 1000 Difference: **0 per 1000** (95% CI: 0 - 0)	**Very low** Due to very serious risk of bias, Due to serious imprecision[2]	There were too few events of kidney failure to determine whether azathioprine plus glucocorticoid made a difference
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Complete remission	Relative risk: 5.94 (95% CI: 2.03 - 17.34) Based on data from 43 patients in 1 study[3] Follow up 60 months (median)	**136** per 1000	**808** per 1000 Difference: **672 more per 1000** (95% CI: 140 more - 2222 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Azathioprine plus glucocorticoid may increases complete remission
Annual GFR loss	Measured by:				

3 years	Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [27] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Selective outcome reporting, Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study, Wide confidence intervals, Only data from one study
3. Systematic review [139] with included studies: [27] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients

References

[27] Harmankaya O, Ozturk Y, Basturk T, Obek A, Kilicarslan I. Efficacy of immunosuppressive therapy in IgA nephropathy presenting with isolated hematuria. International Urology & Nephrology 2002;33(1):167-171

[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S20.
Population: Patients with IgA nephropathy
Intervention: Azathioprine, glucocorticoid, and antiplatelet/anticoagulant
Comparator: Antiplatelet/anticoagulant

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the evidence**	**Plain text summary**
		Antiplatelet/anticoagulant	Azathioprine, glucocorticoid, and antiplatelet/anticoagulant		
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Kidney failure	Relative risk: 0.34 (95% CI: 0.07 - 1.64) Based on data from 74 patients in 1 study[1] Follow up 2 years	**147** per 1000	**50** per 1000 Difference: **97 fewer per 1000** (95% CI: 137 fewer - 94 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Azathioprine, glucocorticoid, and anticoagulant/antiplatelet may have little or no difference on kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
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: 1.13 (95% CI: 0.76 - 1.7) Based on data from 74 patients in 1 study[3] Follow up 2 years	**529** per 1000	**598** per 1000 Difference: **69 more per 1000** (95% CI: 127 fewer - 370 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Azathioprine, glucocorticoid, and anticoagulant/antiplatelet may have little or no difference on complete remission
Annual GFR loss	Measured by:				

3 years	Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [67] **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, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Wide confidence intervals
3. Primary study [66] **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: Serious.** Only data from one study, Low number of patients

References

[66] Yoshikawa N, Honda M, Iijima K, Awazu M, Hattori S, Nakanishi K, et al. Steroid treatment for severe childhood IgA nephropathy: a randomized, controlled trial. Clinical Journal of The American Society of Nephrology: CJASN 2006;1(3):511-517

[67] Yoshikawa N, Ito H, Sakai T, Takekoshi Y, Honda M, Awazu, et al. A controlled trial of combined therapy for newly diagnosed severe childhood IgA nephropathy. The Japanese Pediatric IgA Nephropathy Treatment Study Group. Journal of the American Society of Nephrology 1999;10(1):101-109

[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S21.
Population: Patients with IgA nephropathy
Intervention: Azathioprine
Comparator: Glucocorticoid alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Glucocorticoid alone	Azathioprine	**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: 7.36 (95% CI: 2.46 - 22.05) Based on data from 46 patients in 1 study[1] Follow up 7 years	**385** per 1000	**2834** per 1000 Difference: **2449 more per 1000** (95% CI: 562 more - 8104 more)	**Very low** Due to very serious risk of bias, Due to serious imprecision[2]	We are uncertain whether azathioprine increases or decreases kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection	Relative risk: 0.85 (95% CI: 0.14 - 5.1) Based on data from 68 patients in 2 studies[3] Mean follow up 48 months	**83** per 1000	**71** per 1000 Difference: **12 fewer per 1000** (95% CI: 71 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 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 GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [52] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study, Wide confidence intervals
3. Systematic review [139] with included studies: [58], [52] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[52] Pozzi C, Andrulli S, Pani A, Scaini P, Del Vecchio L, Fogazzi G, et al. Addition of azathioprine to corticosteroids does not benefit patients with IgA nephropathy. Journal of the American Society of Nephrology 2010;21(10):1783-1790

[58] Stangou M, Ekonomidou D, Giamalis P, Liakou H, Tsiantoulas A, Pantzaki A, et al. Steroids and azathioprine in the treatment of IgA nephropathy. Clinical & Experimental Nephrology 2011;15(3):373-380

[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S22.
Population: Patients with IgA nephropathy
Intervention: Azathioprine, glucocorticoids, and anticoagulants
Comparator: Glucocorticoids alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Glucocorticoids alone	Azathioprine, glucocorticoids, and anticoagulants	**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% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
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: 1.24 (95% CI: 1.01 - 1.52) Based on data from 78 patients in 1 study[1] Follow up 2 years	**744** per 1000	**923** per 1000 Difference: **179 more per 1000** (95% CI: 7 more - 387 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Azathioprine, glucocorticoids, and anticoagulants may increase complete remission
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [66] **Baseline/comparator:** Control arm of reference used for intervention.

2. **Risk of bias: Serious.** Selective outcome reporting, 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

[66] Yoshikawa N, Honda M, Iijima K, Awazu M, Hattori S, Nakanishi K, et al. Steroid treatment for severe childhood IgA nephropathy: a randomized, controlled trial. Clinical Journal of The American Society of Nephrology: CJASN 2006;1(3):511-517

[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S23.
Population: Patients with IgA nephropathy
Intervention: Calcineurin inhibitor plus glucocorticoids
Comparator: Glucocorticoids alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Glucocorticoids alone	Calcineurin inhibitor plus glucocorticoids	**Certainty of the evidence**	**Plain text summary**
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection	Relative risk: 0.31 (95% CI: 0.03 - 2.74) Based on data from 48 patients in 1 study[1] Follow up 12 months	**130** per 1000	**40** per 1000 Difference: **90 fewer per 1000** (95% CI: 126 fewer - 226 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether calcineurin inhibitor plus glucocorticoids increases or decreases infection
Malignancy	Relative risk: 0.36 (95% CI: 0.02 - 8.45) Based on data from 48 patients in 1 study[3] Follow up 12 months	**40** per 1000	**14** per 1000 Difference: **26 fewer per 1000** (95% CI: 39 fewer - 298 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether calcineurin plus glucocorticoids increases or decreases malignancy
Complete remission	Relative risk: 0.91 (95% CI: 0.6 - 1.39) Based on data from 72 patients in 2 studies[5] Mean follow up 9 months	**541** per 1000	**492** per 1000 Difference: **49 fewer per 1000** (95% CI: 216 fewer - 211 more)	**Low** Due to very serious risk of bias[6]	Calcineurin inhibitor plus glucocorticoids may have little or no difference on complete remission
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality

Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [41] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Selective outcome reporting, Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Very Serious.** Only data from one study, due to few infections, Low number of patients
3. Systematic review [139] with included studies: [41] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Low number of patients, only data from one study, due to few malignancy events
5. Systematic review [139] with included studies: [56], [41] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: No serious.** Low number of patients

References

[40] Lai KN, Lai FM, Li PK, Vallance-Owen J. Cyclosporin treatment of IgA nephropathy: a short term controlled trial. British Medical Journal Clinical Research Ed 1987;295(6607):1165-1168
[41] Liu H, Xu X, Fang Y, Ji J, Zhang X, Yuan M, et al. Comparison of glucocorticoids alone and combined with cyclosporine a in patients with IgA nephropathy: a prospective randomized controlled trial. Internal Medicine 2014;53(7):675-681
[56] Shen P, Li Y, Wang Z, Wang W, Ren H, Zhang W, et al. A prospective randomized study on the efficacy of corticosteroid combined with cyclophosphamide or FK506 in primary IGA nephropathy with mild or moderate renal injury [abstract]. Nephrology Dialysis Transplantation 2013;28(Suppl 1):i175-i75
[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S24.
Population: Patients with IgA nephropathy
Intervention: Mycophenolate mofetil
Comparator: Placebo or usual care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo or usual care	Mycophenolate mofetil	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: 0.93 (95% CI: 0.10 - 8.77) Based on data from 218 patients in 2 studies[1] Mean follow up 24 months	**9** per 1000	**9** per 1000 Difference: **0 per 1000** (95% CI: 26 fewer - 25 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: 1.12 (95% CI: 0.31 – 4.02) Based on data from 236 patients in 3 studies[3] Mean follow up 28 months	**80** per 1000	**81** per 1000 Difference: **1 more per 1000** (95% CI: 55 fewer - 241 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
≥50% GFR loss	Relative risk: 0.74 (95% CI: 0.11 – 5.09) Based on data from 202 patients in 2 studies[5] Follow up 12 months	**250** per 1000	**118** per 1000 Difference: **132 fewer per 1000** (95% CI: 223 fewer - 1000 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision, Due to serious inconsistency[6]	We are uncertain whether mycophenolate mofetil increases or decreases ≥50% GFR loss
Infection	Relative risk: 1.17 (95% CI: 0.73 – 1.87) Based on data from 344 patients in 5 studies[7] Mean follow up 23 months	**138** per 1000	**175** per 1000 Difference: **37 more per 1000** (95% CI: 37 fewer - 120 more)	**Low** Due to very serious risk of bias, Due to serious imprecision[8]	Mycophenolate mofetil may have little or no difference on infection
Malignancy	Relative risk: 2.02 (95% CI: 0.55 - 7.38) Based on data from 136 patients in 3 studies[9] Mean follow up 20 months	**50** per 1000	**101** per 1000 Difference: **51 more per 1000** (95% CI: 22 fewer - 319 more)	**Very low** Due to very serious imprecision, Due to very serious risk of bias[10]	We are uncertain whether mycophenolate mofetil increases or decreases malignancy

Complete remission	Relative risk: 2.08 (95% CI: 0.63 – 6.91) Based on data from 116 patients in 3 studies[11] Mean follow up 14 months	**55** per 1000 **131** per 1000 Difference: **76 more per 1000** (95% CI: 20 fewer - 322 more)	**Low** Due to serious risk of bias, Due to serious imprecision[12]	Mycophenolate mofetil may increase complete remission
Annual GFR loss	Measured by: Scale: - Lower better Based on data from 28 patients in 1 study[13] Follow up 12 months	Mean Mean Difference: **MD 2 higher** (95% CI: 25.15 lower - 29.15 higher)	**Very low** Due to very serious risk of bias, Due to serious imprecision[14]	We are uncertain whether mycophenolate mofetil increases or decreases annual GFR loss
Adverse events, serious	Relative risk: 1.67 (95% CI: 0.36 – 7.68) Based on data from 281 patients in 2 studies[15] Mean follow up 24 months	**28** per 1000 **54** per 1000 Difference: **26 more per 1000** (95% CI: 18 fewer - 187 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[16]	We are uncertain whether mycophenolate mofetil increases or decreases serious adverse events

1. Systematic review [139] with included studies: [Han 2022], [Hou 2023] 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, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision**: Very Serious. Wide confidence intervals, Low number of events.
3. Systematic review [139] with included studies: [26], [46] [Hou 2023]. **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, one trial (Frisch 2005) stopping earlier than scheduled, resulting in potential for overestimating benefits.; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients
5. Systematic review with included studies: [26] [Hou 2023]. **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Trial stopping earlier than scheduled, resulting in potential for overestimating benefits; **Imprecision: Very Serious.** Wide confidence intervals, Low number of events; **Inconsistency: Serious.** 2 studies in opposite directions.
7. Systematic review [139] with included studies: [60], [19], [46] [Han 2022] [Hou 2023] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Very Serious.** Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting. Other bias due to termination of the trail after an independent Data and Safety Monitoring Committee met in person or by teleconference recommended termination of the trial. There were no safety issues leading to this decision. Baseline characteristics were balanced across treatment groups (2nd NA

IgAN, 2004); **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, few events

9. Systematic review [139] with included studies: [46], [19] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Very Serious.** Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting. Other issue due to termination of the trail early without any safety issues for this (2nd NA IgAN 2004); **Imprecision: Very Serious.** Wide confidence intervals, due to few events
11. Systematic review [139] with included studies: [26], [60] [Han 2022] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting, Incomplete data and/or large loss to follow up. Due to other bias, the study was terminated early after the second scheduled interim analysis done by the independent study monitor revealed a trend towards a worse outcome in the mycophenolate mofetil group that would have made it highly unlikely to show a benefit for mycophenolate mofetil given our rate of recruitment and our target sample size (Frisch 2005); **Imprecision: Serious.** Wide confidence intervals
13. Systematic review [139] with included studies: [19] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Only data from one study, Low number of patients
15. Included studies: [Han 2022], [Hou 2023] Baseline/comparator: Control arm of reference used for intervention.
16. **Risk of bias**: Serious. Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision**: Very Serious. Wide confidence intervals.

References

[19] Hogg RJ, Bay RC, Jennette JC, Sibley R, Kumar S, Fervenza FC, Appel G, Cattran D, Fischer D, Hurley RM, Cerda J, Carter B, Jung B, Hernandez G, Gipson D, Wyatt RJ. Randomized controlled trial of mycophenolate mofetil in children, adolescents, and adults with IgA nephropathy. American journal of kidney diseases: the official journal of the National Kidney Foundation 2015;66(5):783-791

[26] Frisch G, Lin J, Rosenstock J, Markowitz G, D'Agati V, Radhakrishnan J, et al. Mycophenolate mofetil (MMF) vs placebo in patients with moderately advanced IgA nephropathy: a double-blind randomized controlled trial. Nephrology Dialysis Transplantation 2005;20(10):2139-2145

[46] Maes BD, Oyen R, Claes K, Evenepoel P, Kuypers D, Vanwalleghem J, et al. Mycophenolate mofetil in IgA nephropathy: results of a 3-year prospective placebo-controlled randomized study. Kidney International 2004;65(5):1842-1849

[60] Tang S, Leung JC, Chan LY, Lui YH, Tang CS, Kan CH, et al. Mycophenolate mofetil alleviates persistent proteinuria in IgA nephropathy. Kidney International 2005;68(2):802-812

[Han 2022] Han, S. Y.; Jung, C. Y.; Lee, S. H.; Lee, D. W.; Lee, S.; Kim, C. D.; Choi, B. S.; Kim, B. S.. A multicenter, randomized, open-label, comparative, phase IV study to evaluate the efficacy and safety of combined treatment with mycophenolate mofetil and corticosteroids in advanced immunoglobulin A nephropathy. Kidney Res Clin Pract 2022;41(4):452-461. [PubMed: 35545228]

[Hou 2023] Hou, F. F.; Xie, D.; Wang, J.; Xu, X.; Yang, X.; Ai, J.; Nie, S.; Liang, M.; Wang, G.; Jia, N.. Effectiveness of Mycophenolate Mofetil Among Patients With Progressive IgA Nephropathy: A Randomized Clinical Trial. JAMA Open 2023;6(2):1-14. [PubMed: 36745456]

[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S25.
Population: Patients with IgA nephropathy with GFR ≤60 ml/min/1.73 m^2
Intervention: Cyclophosphamide then azathioprine plus glucocorticoid
Comparator: Supportive therapy

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Supportive therapy	Cyclophosphamide then azathioprine plus glucocorticoid	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: 2.89 (95% CI: 0.12 - 67.96) Based on data from 53 patients in 1 study[1] Follow up 36 months	Difference: **fewer**		**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether cyclophosphamide then azathioprine plus glucocorticoid increases or decreases all-cause mortality
Kidney failure	Relative risk: 4.8 (95% CI: 0.6 - 38.14) Based on data from 49 patients in 1 study[3] Follow up 36 months	**42** per 1000	**202** per 1000 Difference: **160 more per 1000** (95% CI: 17 fewer - 1560 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Cyclophosphamide then azathioprine plus glucocorticoid may have little or no difference on kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Malignancy	Relative risk: 4.82 (95% CI: 0.24 - 95.88) Based on data from 53 patients in 1 study[5] Follow up 36 months	Difference: **fewer**		**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	There were too few who experienced the malignancy to determine whether cyclophosphamide then azathioprine plus glucocorticoid made a difference
Complete remission[7]	Relative risk: 2.89 (95% CI: 0.32 - 26.02)	**38** per 1000	**110** per 1000 Difference: **72 more per 1000** (95% CI: 26 fewer - 951 more)	**Low** Due to serious risk of bias, Due to serious imprecision[9]	Cyclophosphamide then azathioprine plus glucocorticoid may have little or no

	Based on data from 53 patients in 1 study[8] Follow up 36 months			difference on complete remission
Adverse events	Relative risk: 2.73 (95% CI: 1.28 - 5.83) Based on data from 53 patients in 1 studies[10] Follow up 36 months	**259** per 1000 **707** per 1000 Difference: **448 more per 1000** (95% CI: 73 more - 1251 more)	**Low** Due to serious risk of bias, Due to serious imprecision[11]	Cyclophosphamide then azathioprine plus glucocorticoid may increase adverse events
GFR decline ≥15 m/min/1.73m^2	Relative risk: 1.44 (95% CI: 0.6 - 3.49) Based on data from 53 patients in 1 study[12] Follow up 36 months	**231** per 1000 **333** per 1000 Difference: **102 more per 1000** (95% CI: 92 fewer - 575 more)	**Low** Due to serious risk of bias, Due to serious imprecision[13]	Cyclophosphamide then azathioprine plus glucocorticoid may have little or no difference on GFR decline ≥15 m/min/1.73m^2
Annual GFR loss	Measured by: Scale: - Lower better[14]	Difference:		No studies were found that looked at annual GFR loss

1. Primary study [54] **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/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
3. Systematic review [139] with included studies: [54] **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, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Selective outcome reporting; **Imprecision: Serious.** Wide confidence intervals
5. Systematic review [139] with included studies: [54] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, due to few events
7. STOP-IgAN Study - Complete remission (defined as proteinuria with a protein-to-creatinine ratio of <0.2 and stable kidney function with a decrease in the eGFR of <5 ml per minute per 1.73 m2 from the baseline eGFR at the end of the 3-year trial phase)
8. Systematic review [139] with included studies: [54] **Baseline/comparator:** Control arm of reference used for intervention.

9. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study
10. Systematic review [139] with included studies: [54] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.**
12. Systematic review [139] with included studies: [54] **Baseline/comparator:** Control arm of reference used for intervention.
13. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study, Wide confidence intervals
14. No studies available [54] **Baseline/comparator:** Control arm of reference used for intervention.

References

[54] Rauen T, Eitner F, Fitzner C, Sommerer C, Zeier M, Otte B, et al. Intensive supportive care plus immunosuppression in IgA nephropathy. New England Journal of Medicine 2015;373(23):2225-2236

[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S26.
Population: Patients with IgA nephropathy
Intervention: Mycophenolate mofetil plus glucocorticoid
Comparator: Glucocorticoid alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Glucocorticoid alone	Mycophenolate mofetil plus glucocorticoid	**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: 0.2 (95% CI: 0.01 - 4.2) Based on data from 174 patients in 1 studies[1] Follow up 12 months	**23** per 1000	**5** per 1000 Difference: **18 fewer per 1000** (95% CI: 23 fewer - 74 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether mycophenolate mofetil plus glucocorticoid increases or decreases kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Infection	Relative risk: 1.37 (95% CI: 0.83 - 2.24) Based on data from 175 patients in 1 study[3] Follow up 12 months	**227** per 1000	**311** per 1000 Difference: **84 more per 1000** (95% CI: 39 fewer - 281 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Mycophenolate mofetil plus glucocorticoid may have little or no difference on infection
Complete remission	Relative risk: 0.99 (95% CI: 0.68 - 1.46) Based on data from 174 patients in 1 study[5] Follow up 12 months	**375** per 1000	**371** per 1000 Difference: **4 fewer per 1000** (95% CI: 120 fewer - 173 more)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Mycophenolate mofetil plus glucocorticoid may have little or no difference on complete remission

Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [30] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up, 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, due to few events
3. Systematic review [139] with included studies: [30] **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, Selective outcome reporting; **Imprecision: Serious.** Only data from one study
5. Systematic review [139] with included studies: [30] **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: Serious.** Only data from one study

References

[30] Hou JH, Le WB, Chen N., Wang WM, Liu ZS, Liu D, et al. Mycophenolate mofetil combined with prednisone versus full-dose prednisone in IgA nephropathy with active proliferative lesions: a randomized controlled trial. American Journal of Kidney Diseases 2017;69(6):788-795

[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S27.
Population: Patients with IgA nephropathy
Intervention: Mycophenolate mofetil plus RASi
Comparator: RASi alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** RASi alone	Mycophenolate mofetil RASi	**Certainty of the evidence**	**Plain text summary**
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
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Kidney failure	Relative risk: 0.22 (95% CI: 0.05 - 0.9) Based on data from 40 patients in 1 study[1] Follow up 18 months	**450** per 1000	**99** per 1000 Difference: **351 fewer per 1000** (95% CI: 427 fewer - 45 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Mycophenolate mofetil plus RASi may decrease kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [60] **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: Serious.** Only data from one study, Low number of patients, due to few events

References

[60] Tang S, Leung JC, Chan LY, Lui YH, Tang CS, Kan CH, et al. Mycophenolate mofetil alleviates persistent proteinuria in IgA nephropathy. Kidney International 2005;68(2):802-812
[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S28.
Population: Patients with IgA nephropathy
Intervention: Leflunomide
Comparator: No leflunomide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** No leflunomide / Leflunomide	**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% GFR loss	(95% CI: -)	Difference:		No studies were found that looked at ≥50% GFR loss
Infection – leflunomide versus placebo	Relative risk: 3.0 (95% CI: 0.12 - 72.77) Based on data from 200 patients in 1 study[1] Follow up 6 months	**0** per 1000 / **0** per 1000 Difference: **0 per 1000** (95% CI: 0 - 0)	**Low** Due to very serious imprecision[2]	There were too few who experienced the infection to determine whether leflunomide made a difference
Malignancy	(95% CI: -)	Difference:		No studies were found that looked at malignancy
Complete remission – leflunomide versus RASi	Relative risk: 1.17 (95% CI: 0.68 - 2.0) Based on data from 46 patients in 1 study[3] Follow up 6 months	**500** per 1000 / **585** per 1000 Difference: **85 more per 1000** (95% CI: 160 fewer - 500 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	Leflunomide may have little or no difference on complete remission
Complete remission – leflunomide versus glucocorticoid	Relative risk: 1.63 (95% CI: 0.56 - 4.7) Based on data from 49 patients in 1 study[5] Follow up 3 months	**500** per 1000 / **585** per 1000 Difference: **85 more per 1000** (95% CI: 160 fewer - 500 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	Leflunomide may have little or no difference on complete remission

Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [64] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, due to few/no infections;
3. Systematic review [139] with included studies: [43] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Selective outcome reporting, Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection 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 [139] with included studies: [68] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Selective outcome reporting, Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection 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

References

[43] Lou T, Wang C, Chen Z, Shi C, Tang H, Liu X, et al. Randomised controlled trial of leflunomide in the treatment of immunoglobulin A nephropathy. Nephrology 2006;11(2):113-116

[64] Wu J., Duan SW, Sun XF, Li WG, Wang YP, Liu WH, et al. Efficacy of leflunomide, telmisartan, and clopidogrel for immunoglobulin A nephropathy: a randomized controlled trial. Chinese Medical Journal 2016;129(16):1894-1903

[68] Zhang XZ, He Q, Luo TC, Lin ST. Efficacy and safety of leflunomide in the treatment of IgA nephropathy: preliminary results from a randomized, corticosteroid controlled, multi-center clinical trial [abstract no: SA-PO168]. Journal of the American Society of Nephrology 2004;15(Oct):337A-337A

[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S29.
Population: Patients with IgA nephropathy
Intervention: Leflunomide plus low-dose glucocorticoid
Comparator: High-dose glucocorticoid

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** High-dose glucocorticoid	**Absolute effect estimates** Leflunomide plus low-dose glucocorticoid	**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: 0.68 (95% CI: 0.17 - 2.65) Based on data from 85 patients in 1 study[1] Follow up 12 months	**111** per 1000	**75** per 1000 Difference: **36 fewer per 1000** (95% CI: 92 fewer - 183 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision,[2]	We are uncertain whether leflunomide plus low-dose glucocorticoid increases or decreases kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Infection	Relative risk: 0.64 (95% CI: 0.11 – 3.81) Based on data from 193 patients in 2 studies[3] Mean follow up 18 months	**117** per 1000	**61** per 1000 Difference: **56 fewer per 1000** (95% CI: 54 fewer - 171 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether leflunomide plus low-dose glucocorticoid increases or decreases infection
Complete remission	Relative risk: 1.01 (95% CI: 0.65 - 1.57) Based on data from 182 patients in 2 studies[5] Mean follow up 18 months	**356** per 1000	**359** per 1000 Difference: **3 more per 1000** (95% CI: 124 fewer - 203 more)	**Very low** Due to serious imprecision, Due to very serious risk of bias[6]	We are uncertain whether leflunomide plus low-dose glucocorticoid increases or decreases complete remission

Relapse	Relative risk: 0.33 (95% CI: 0.07 – 1.64) Based on data from 108 patients in 1 study[7] Follow up 24 months	**102** per 1000 **34** per 1000 Difference: **68 fewer per 1000** (95% CI: 169 fewer - 32 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether leflunomide plus low-dose glucocorticoid increases or decreases relapse
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss
GFR	Measured by: Scale: - High better Based on data from 85 patients in 1 study[9] Follow up 12 months	Mean Mean Difference: **MD 3.77 higher** (95% CI: 8.82 lower - 16.36 higher)	**Very low** Due to serious imprecision, Due to very serious risk of bias[10]	We are uncertain whether leflunomide plus low-dose glucocorticoid increases or decreases GFR (any measure)

1. Systematic review [139] with included studies: [49] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** due to severe imprecision in treatment estimate (consistent with appreciable benefit or harm), due to only data from one study
3. Systematic review [139] with included studies: [49], [Ni 2021] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals
5. Systematic review [139] with included studies: [49], [Ni 2021] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Imprecision: Serious.** Wide confidence intervals
7. Systematic review [139] with included studies: [Ni 2021] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Very wide confidence intervals
9. Primary study [49] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Serious.** Only data from one study

References

[49] Min L, Wang Q, Cao L, Zhou W, Yuan J, Zhang M, et al. Comparison of combined leflunomide and low-dose corticosteroid therapy with full-dose corticosteroid monotherapy for progressive IgA nephropathy. Oncotarget 2017;8(29):48375-44838

[Ni 2021] Ni Z ; Zhang, Z.; Yu, Z.; Lu, F.; Mei, C.; Ding, X.; Yuan, W.; Zhang, W.; Jiang, G.; Sun, M.; He, L.; Deng, Y.; Pang, H.; Qian, J.. Leflunomide plus low-dose prednisone in patients with progressive IgA nephropathy: a multicenter, prospective, randomized, open-labeled, and controlled trial. Renal Failure 2021;43(1):1214-1221. [PubMed: 34396911]

[85] Donadio JV, Bergstralh EJ, Offord KP, Spencer DC, Holley KE. A controlled trial of fish oil in IgA nephropathy. Mayo Nephrology Collaborative Group. New England Journal of Medicine 1994;331(18):1194-1199

[91] Bennett WM, Walker RG, Kincaid-Smith P. Treatment of IgA nephropathy with eicosapentanoic acid (EPA): a two-year prospective trial. Clinical Nephrology 1989;31(3):128-131

[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S30.
Population: Patients with IgA nephropathy
Intervention: Mizoribine
Comparator: No mizoribine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** No mizoribine	Mizoribine	**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: 1.0 (95% CI: 0.07 - 14.95) Based on data from 42 patients in 1 study[1] Follow up 30 months	**48** per 1000	**48** per 1000 Difference: **0 per 1000** (95% CI: 45 fewer - 670 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether mizoribine improves or worsens kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection – mizoribine plus RASi versus RASi	Relative risk: 0.59 (95% CI: 0.11 - 3.29) Based on data from 64 patients in 1 study[3] Follow up 12 months	**100** per 1000	**59** per 1000 Difference: **41 fewer per 1000** (95% CI: 89 fewer - 229 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether mizoribine plus RASi increases or decreases infection
Infection - mizoribine plus glucocorticoids versus glucocorticoids	Relative risk: 7.0 (95% CI: 0.38 - 127.32) Based on data from 40 patients in 1 study[5] Follow up 25 months	**0** per 1000	**0** per 1000 Difference: **0 per 1000** (95% CI: 0 - 0)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	There were too few who experienced the infection to determine whether mizoribine plus glucocorticoid made a difference
Infection - mizoribine plus glucocorticoid (i.v. + oral) versus	Relative risk: 7.0 (95% CI: 0.38 - 127.32) Based on data from 64 patients in 1 study[7]	**0** per 1000	**0** per 1000 Difference: **0 per 1000** (95% CI: 0 - 0)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	There were too few who experienced the infection to determine whether mizoribine made a difference

glucocorticoid alone	Follow up 25 months			
Malignancy	Relative risk: 3.0 (95% CI: 0.13 - 69.7) Based on data from 42 patients in 1 study[9] Follow up 30 months	**0** per 1000 **0** per 1000 Difference: **0 per 1000** (95% CI: 0 - 0)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[10]	We are uncertain whether mizoribine improves or worsens malignancy
Complete remission	Relative risk: 1.9 (95% CI: 1.06 - 3.43) Based on data from 24 patients in 1 study[11] Follow up 30 months	**466** per 1000 **885** per 1000 Difference: **419 more per 1000** (95% CI: 28 more - 1132 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[12]	We are uncertain whether mizoribine improves or worsen complete remission
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [28] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study, due to few patients with kidney failure
3. Systematic review [139] with included studies: [65] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study
5. Systematic review [139] with included studies: [48] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study, due to few infections
7. Systematic review [139] with included studies: [48] **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/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study

9. Systematic review [139] with included studies: [28] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients, Only data from one study, due to few patients with malignancy
11. Systematic review [139] with included studies: [28] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Low number of patients, Only data from one study

References

[28] Hirai K, Ookawara S, Kitano T, Miyazawa H, Ito K, Ueda Y, et al. Efficacy and safety of adding mizoribine to standard treatment in patients with immunoglobulin A nephropathy: A randomized controlled trial. Kidney Research and Clinical Practice 2017;36(2):159-166
[48] Masutani K, Tsuchimoto A, Yamada T, Hirakawa M, Mitsuiki K, Katafuchi R, et al. Comparison of steroid-pulse therapy and combined with mizoribine in IgA nephropathy: a randomized controlled trial. Clinical & Experimental Nephrology 2016;20(6):896-903
[65] Xie Y, Huang S, Wang L, Miao L, Zhang A, Li Y, et al. Efficacy and safety of mizoribine combined with losartan in the treatment of IgA nephropathy: a multicenter, randomized, controlled study. American Journal of the Medical Sciences 2011;341(5):367-372
[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S31.
Population: Patients with IgA nephropathy
Intervention: Atacicept 25 mg or 75 mg subcutaneous 1x/week
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	Atacicept	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: (95% CI: -) Based on data from 16 patients in 1 study[1] Follow up 11 months	**0** per 1000	**0** per 1000 Difference: **0 per 1000** (95% CI: 248 fewer - 248 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether atacicept increases or decreases mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
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

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	Atacicept	**Certainty of the evidence**	**Plain text summary**
GFR loss 6 months	Measured by: CKD-EPI Scale: - Lower better Based on data from 15 patients in 1 study[3] Follow up 24 weeks	**~ −9** ml/min/1.73 m^2	**~ −5** ml/min/1.73 m^2 loss Difference: ~4 [difference of difference of median values]	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether atacicept increases or decreases GFR loss
Proteinuria 6 months	Measured by: PCR Scale: - Lower better Based on data from 13 patients in 1 study[5] Follow up 24 weeks	**~ 0.4** mg/mg	**~ −0.4** mg/mg Difference: ~−0.8 [difference of difference of median values]	**Very low** Due to very serious imprecision[6]	We are uncertain whether atacicept increases or decreases proteinuria
Adverse events, serious	Relative risk: 1.36 (95% CI: 0.18 – 10.1) Based on data from 16 patients in 1 study[7] Follow up 11 months	**200** per 1000	**273** per 1000 Difference: **73 more per 1000** (95% CI: 366 fewer - 511 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether atacicept increases or decreases serious adverse events

1. Primary study [Barratt 2020] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** High attrition rate; **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates, no events.
3. Primary study [Barratt 2020] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** High attrition rate; **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates, rough estimates based on reported median values.
5. Primary study [Barratt 2020] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** High attrition rate; **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates, rough estimates based on reported median values.
7. Primary study [Barratt 2020] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** High attrition rate; **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates.

References

[Barratt 2020] Barratt, J.; Tumlin, J.; Suzuki, Y.; Kao, A.; Aydemir, A.; Pudota, K.; Jin, H.; Gohring, H.; Appel, G.. Randomized Phase II JANUS Study of Atacicept in Patients With IgA Nephropathy and Persistent Proteinuria. Kidney Int Rep 2022;7:1831-1841. [PubMed: 35967104]

Table S32.
Population: Patients with IgA nephropathy
Intervention: Telitacicept 160 mg or 240 mg subcutaneous 1x/week
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	Telitacicept	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: (95% CI: -) Based on data from 44 patients in 1 study[1] Follow up 6 months	**0** per 1000	**0** per 1000 Difference: **0 per 1000** (95% CI: 114 fewer - 114 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether telitacicept increases or decreases mortality
Kidney failure	Relative risk: (95% CI: -) Based on data from 44 patients in 1 study[3] Follow up 6 months	**0** per 1000	**0** per 1000 Difference: **0 per 1000** (95% CI: 114 fewer - 114 more)	**Very low** Due to very serious imprecision[4]	We are uncertain whether telitacicept increases or decreases kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection, upper respiratory	Relative risk: 0.86 (95% CI: 0.40 – 1.84) Based on data from 44 patients in 1 study[5] Follow up 6 months	**429** per 1000	**367** per 1000 Difference: **62 fewer per 1000** (95% CI: 365 fewer - 241 more)	**Very low** Due to very serious imprecision[6]	We are uncertain whether telitacicept increases or decreases upper respiratory infections
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

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	Telitacicept	**Certainty of the evidence**	**Plain text summary**
GFR loss 6 months	Measured by: CKD-EPI Scale: - Lower better Based on data from 42 patients in 1 study[7] Follow up 24 weeks	**−7.3** ml/min/1.73 m^2	**3.4** ml/min/1.73 m^2 loss Difference: **10.7 (−8.3, 29.8)**	**Very low** Due to very serious imprecision[8]	We are uncertain whether telitacicept increases or decreases GFR loss
Proteinuria 6 months	Measured by: Scale: - Lower better Based on data from 42 patients in 1 study[9] Follow up 24 weeks	**−0.3** g/d	**−0.4** g/d Difference: **−0.1 (−1.0, 0.7)**	**Very low** Due to very serious imprecision[10]	We are uncertain whether telitacicept increases or decreases proteinuria
Adverse events, serious	Relative risk: 1.40 (95% CI: 0.16 – 12.3) Based on data from 44 patients in 1 study[11] Follow up 11 months	**71** per 1000	**100** per 1000 Difference: **29 more per 1000** (95% CI: 144 fewer - 201 more)	**Very low** Due to very serious imprecision[12]	We are uncertain whether telitacicept increases or decreases serious adverse events

1. Primary study [Lv 2022 36938094] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates, no events.
3. Primary study [Lv 2022 36938094] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates.
5. Primary study [Lv 2022 36938094] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates, no events.
7. Primary study [Lv 2022 36938094] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates.
9. Primary study [Lv 2022 36938094] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates.
11. Primary study [Lv 2022 36938094] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates.

References

[Lv 2022 36938094] Lv, J.; Liu, L.; Hao, C.; Li, G.; Fu, P.; Xing, G.; Zheng, H.; Chen, N.; Wang, C.; Luo, P.; Xie, D.; Zuo, L.; Li, R.; Mao, Y.; Dong, S.; Zhang, P.; Wang, Y.; Qin, W.; Wang, W.; Li, L.;

Jiao, W.; Fang, J.; Zhang, H.. Randomized Phase 2 Trial of Telitacicept in Patients With IgA Nephropathy With Persistent Proteinuria. Kidney Int Rep 2022;8:499-506. [PubMed: 36938094]

Table S33.
Population: Patients with IgA nephropathy
Intervention: Narsoplimab 370 mg intravenously 1x/week
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo Narsoplimab	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:		No studies were found that looked at mortality
Kidney failure	(95% CI: -)	Difference:		No studies were found that looked at kidney failure
≥50% GFR loss	(95% CI: -)	Difference:		No studies were found that looked at ≥50% GFR loss
Infection, upper respiratory	Relative risk: 1.00 (95% CI: 0.08 – 12.6) Based on data from 12 patients in 1 study[1] Follow up 18 weeks	**167** per 1000 **167** per 1000 Difference: **0 per 1000** (95% CI: 430 fewer - 430 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether narsoplimab increases or decreases upper respiratory infections
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

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo Narsoplimab	**Certainty of the evidence**	**Plain text summary**
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss
Proteinuria	Measured by: % reduction Scale: - Lower better Based on data from 9 patients in 1 study[3] Follow up 18 weeks	**−18.0%** [median] **−18.4%** [median] Difference [in median values]: **−0.4%**	**Very low** Due to very serious imprecision[4]	We are uncertain whether telitacicept increases or decreases proteinuria
Adverse events, serious	Relative risk: 2.00 (95% CI: 0.24 – 16.6) Based on data from 12 patients in 1 study[1] Follow up 18 weeks	**167** per 1000 **333** per 1000 Difference: **167 more per 1000** (95% CI: 301 fewer - 634 more)	**Very low** Due to very serious imprecision[2]	We are uncertain whether narsoplimab increases or decreases serious adverse events

1. Primary study [Lafayette 2020] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** High, uneven attrition rate; **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates, no events.
3. Primary study [Lafayette 2020] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** High, uneven attrition rate; **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates, rough estimates based on reported median values.
5. Primary study [Lafayette 2020] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates, no events.
7. Primary study [Lafayette 2020] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates.
9. Primary study [Lafayette 2020] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** High attrition rate; **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates.
11. Primary study [Lafayette 2020] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** High attrition rate; **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimates.

References

[Lafayette 2020] Lafayette, R. A.; Rovin, B. H.; Reich, H. N.; Tumlin, J. A.; Floege, J.; Barratt, J.. Safety, Tolerability and Efficacy of Narsoplimab, a Novel MASP-2 Inhibitor for the Treatment of IgA Nephropathy. Kidney Int Rep 2020;5(2032–2041). [PubMed: 33163724]

Table S34.
Population: Patients with IgA nephropathy
Intervention: RASi
Comparator: Symptomatic treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Symptomatic treatment	RASi	**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% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
>50% increase in serum creatinine	Relative risk: 0.23 (95% CI: 0.07 - 0.7) Based on data from 44 patients in 1 study[1] Follow up 2.3 months	**571** per 1000	**131** per 1000 Difference: **440 fewer per 1000** (95% CI: 531 fewer - 171 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	ACEi compared with symptomatic treatment may decrease >50% increase in serum creatinine
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Annual GFR loss 3 years	Measured by: Scale: - Lower better				No studies were found that

		Difference:		looked at annual GFR loss
Serum creatinine	Measured by: Scale: - Lower better Based on data from 168 patients in 3 studies[3] Mean follow up 31 months	Mean Mean Difference: **MD 39.37 lower** (95% CI: 71.95 lower - 6.80 lower)	**Moderate** Due to serious risk of bias[4]	RASi compared with symptomatic treatment probably decreases serum creatinine
Proteinuria	Measured by: Scale: - Lower better Based on data from 168 patients in 3 studies[5] Mean follow up 31 months	g/24 h Mean g/24 h Mean Difference: **MD 1.16 lower** (95% CI: 1.52 lower - 0.81 lower)	**Moderate** Due to serious risk of bias[6]	RASi compared to symptomatic treatment probably decreases proteinuria
Proteinuria – ACEi + ARB versus ARB or ACEi alone	Measured by: Scale: - Lower better Based on data from 67 patients in 2 studies[7] Mean follow up 7.5 months	g/24 h Mean g/24 h Mean Difference: **MD 0.49 lower** (95% CI: 0.72 lower - 0.25 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	ACEi + ARB compared with ACEi or ARB alone may decrease proteinuria
Creatinine clearance	Measured by: Scale: - High better Based on data from 127 patients in 2 studies[9] Mean follow up 10.4 months	Mean Mean Difference: **MD 23.26 higher** (95% CI: 10.40 higher - 36.12 higher)	**Moderate** Due to serious risk of bias[10]	RASi compared with symptomatic treatment probably improves creatinine clearance

1. Systematic review with included studies: [97] **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: Serious.** Only data from one study, Low number of patients.
3. Systematic review with included studies: [114], [123], [97] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias.
5. Systematic review with included studies: [97], [114], [123] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias.
7. Systematic review with included studies: [117], [100] **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/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Low number of patients.

9. Systematic review with included studies: [97], [114] **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/lack of blinding of outcome assessors, resulting in potential for detection bias.

References

[97] Praga M, Gutiérrez E, González E, Morales E, Hernández E. Treatment of IgA nephropathy with ACE inhibitors: a randomized and controlled trial. Journal of the American Society of Nephrology 2003;14(6):1578-1583
[100] Nakamura T, Inoue T, Sugaya T, Kawagoe Y, Suzuki T, Ueda Y, et al. Beneficial effects of olmesartan and temocapril on urinary liver-type fatty acid-binding protein levels in normotensive patients with immunoglobulin A nephropathy. American Journal of Hypertension 2007;20(11):1195-1201
[114] Shi X, Chen X, Liu S, Zhuang Y, Zhang Y. The effects of angiotensin-converting enzyme inhibitor on IgA nephropathy and the influencing factors. Zhonghua Nei Ke Za Zhi [Chinese Journal of Internal Medicine] 2002;41(6):399-403
[117] Horita Y, Tadokoro M, Taura K, Suyama N, Taguchi T, Miyazaki M, et al. Low-dose combination therapy with temocapril and losartan reduces proteinuria in normotensive patients with immunoglobulin A nephropathy. Hypertension Research - Clinical & Experimental 2004;27(12):963-970
[123] Woo KT, Lau YK, Wong KS, Chiang GS. ACEI/ATRA therapy decreases proteinuria by improving glomerular permselectivity in IgA nephritis. Kidney international 2000;58(6):2485-2491
[136] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews 2011;(3):CD003962

Table S35.
Population: Patients with IgA nephropathy
Intervention: RASi plus glucocorticoid
Comparator: Glucocorticoid alone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Glucocorticoid alone	Glucocorticoid plus RASi	**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% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
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	Relative risk: 1.08 (95% CI: 0.84 - 1.39) Based on data from 38 patients in 1 study[1] Follow up 24 months	**833** per 1000	**900** per 1000 Difference: **67 more per 1000** (95% CI: 133 fewer - 325 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Glucocorticoid plus RASi may have little or no difference on complete remission
Annual GFR loss	Measured by: Scale: - Lower better Based on data from 38 patients in 1 study[3] Follow up 24 months	Difference: **MD 16 higher** (95% CI: 6.89 lower - 38.89 higher)		**Low** Due to serious risk of bias, Due to serious imprecision[4]	Glucocorticoid plus RAS inhibition may increase annual GFR loss

1. Systematic review [139] with included studies: [29] **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, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients
3. Primary study [29] **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; **Imprecision: Serious.** Only data from one study

References

[29] Horita Y, Tadokoro M, Taura K, Ashida R, Hiu M, Taguchi T, et al. Prednisolone co-administered with losartan confers renoprotection in patients with IgA nephropathy. Renal Failure 2007;29(4):441-446
[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S36.
Population: Patients with IgA nephropathy
Intervention: ARB plus glucocorticoid plus tonsillectomy
Comparator: Glucocorticoid plus tonsillectomy

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the evidence**	**Plain text summary**
		Glucocorticoid plus tonsillectomy	Glucocorticoid plus tonsillectomy plus ARB		
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% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
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: 0.93 (95% CI: 0.56 - 1.53) Based on data from 77 patients in 1 study[1] Follow up 24 months	**459** per 1000	**427** per 1000 Difference: **32 fewer per 1000** (95% CI: 202 fewer - 243 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether glucocorticoid plus tonsillectomy plus ARB increases or decreases complete remission
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [139] with included studies: [37] **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, Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Low number of patients, Only data from one study, Wide confidence intervals

References

[37] Kohagura K, Arima H, Miyasato H, Chang TH, Kobori H, Iseki K, et al. Effects of candesartan on clinical remission in IgA nephropathy treated with steroid pulse therapy and tonsilectomy (CAST IgA Study) - a randomized control study [abstract no: TH-PO661]. Journal of the American Society of Nephrology 2015;26(Abstracts):240A-240A

[139] Natale P, Palmer SC, Ruospo M, Saglimbene VM, Craig JC, Vecchio M, Samuels JA, Molony DA, Schena FP, Strippoli GF. Immunosuppressive agents for treating IgA nephropathy. The Cochrane Database of Systematic Reviews. 2020;3 CD003965

Table S37.
Population: Patients with IgA nephropathy
Intervention: ARB, prednisolone, and antiplatelet
Comparator: Prednisolone plus antiplatelet

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Prednisolone plus antiplatelet	ARB, prednisolone, and antiplatelet	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
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 failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Mean	Mean Difference:		No studies were found that looked at annual GFR loss
Serum creatinine	Measured by: Scale: - Lower better	Mean	Mean Difference: **MD 8.84 lower**	**Low** Due to serious risk of bias, Due to	ARB, prednisolone, and antiplatelet may have little or no

	Based on data from 38 patients in 1 study[1] Follow up 2 years	(95% CI: 20.10 lower - 2.42 higher)	serious imprecision[2]	difference on serum creatinine
Proteinuria	Measured by: Scale: - Lower better Based on data from 38 patients in 1 study[3] Follow up 2 years	g/24 hr Mean g/24 hr Mean Difference: **MD 0.20 lower** (95% CI: 0.26 lower - 0.14 lower)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	ARB, prednisolone, and antiplatelet may decrease proteinuria
Creatinine clearance	Measured by: Scale: - High better Based on data from 38 patients in 1 study[5] Follow up 2 years	ml/min Mean ml/min Mean Difference: **MD 16 higher** (95% CI: 6.89 lower - 38.89 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether ARB, prednisolone, and antiplatelet increases or decreases creatinine clearance

1. Systematic review [137] with included studies: [29] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear blinding of participants and personnel, resulting in potential for performance bias, unclear blinding of outcome assessors, resulting in potential for detection bias, 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; **Imprecision: Serious.** Only data from one study, Low number of patients
3. Systematic review [137] with included studies: [29] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Unclear blinding of participants and personnel, resulting in potential for performance bias, unclear blinding of outcome assessors, resulting in potential for detection bias, 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; **Imprecision: Serious.** Only data from one study, Low number of patients
5. Systematic review [137] with included studies: [29] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Unclear blinding of participants and personnel, resulting in potential for performance bias, unclear blinding of outcome assessors, resulting in potential for detection bias, 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; **Imprecision: Very Serious.** Only data from one study, Low number of patients, Wide confidence intervals

References

[29] Horita Y, Tadokoro M, Taura K, Ashida R, Hiu M, Taguchi T, et al. Prednisolone co-administered with losartan confers renoprotection in patients with IgA nephropathy. Renal Failure 2007;29(4):441-446
[97] Praga M, Gutiérrez E, González E, Morales E, Hernández E. Treatment of IgA nephropathy with ACE inhibitors: a randomized and controlled trial. Journal of the American Society of Nephrology 2003;14(6):1578-1583
[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S38.
Population: Patients with IgA nephropathy
Intervention: Fish oil
Comparator: Placebo or no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo or no treatment	Fish oil	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	Relative risk: 0.93 (95% CI: 0.06 - 14.44) Based on data from 106 patients in 1 study[1] Follow up 24 months	**20** per 1000	**19** per 1000 Difference: **1 fewer per 1000** (95% CI: 19 fewer - 269 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether fish oil increases or decreases all-cause mortality
Kidney failure	Relative risk: 1.01 (95% CI: 0.34 - 2.97) Based on data from 143 patients in 2 studies[3] Mean follow up 24 months	**85** per 1000	**86** per 1000 Difference: **1 more per 1000** (95% CI: 56 fewer - 167 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether fish oil increases or decreases kidney failure
>50% loss in creatinine clearance	Relative risk: 1.87 (95% CI: 0.63 - 5.55) Based on data from 60 patients in 1 study[5] Follow up 24 months	**138** per 1000	**258** per 1000 Difference: **120 more per 1000** (95% CI: 51 fewer - 628 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether fish oil increases or decreases >50% decrease in creatinine clearance
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
>50% increase in serum creatinine	Relative risk: 0.2 (95% CI: 0.06 - 0.65) Based on data from 106 patients in 1 study[7]	**275** per 1000	**55** per 1000 Difference: **220 fewer per 1000** (95% CI: 258 fewer - 96 fewer)	**Low** Due to serious risk of bias, Due to very serious imprecision, Upgraded due to	Fish oil may increase in serum creatinine by >50%

	Follow up 24 months		Large magnitude of effect[8]	
Complete remission	(95% CI: -)	Difference:		No studies were found that looked at complete remission
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss
Creatinine clearance	Measured by: Scale: - High better Based on data from 69 patients in 2 studies[9] Mean follow up 15 months	ml/min Mean ml/min Mean Difference: **MD 15.57 lower** (95% CI: 34.94 lower - 3.79 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[10]	We are uncertain whether fish oil increases or decreases creatinine clearance

1. Systematic review with included studies: [85] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
3. Systematic review with included studies: [85], [91] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients
5. Systematic review with included studies: [101] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Large loss to follow up, 72% completed 2 years (67% prednisone, 80% O3FA, 83% placebo); **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
7. Systematic review with included studies: [85] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Only data from one study, Low number of patients; **Upgrade: Large magnitude of effect.**
9. Systematic review with included studies: [95], [91] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Low number of patients

References

[85] Donadio JV, Bergstralh EJ, Offord KP, Spencer DC, Holley KE. A controlled trial of fish oil in IgA nephropathy. Mayo Nephrology Collaborative Group. New England Journal of Medicine 1994;331(18):1194-1199
[91] Bennett WM, Walker RG, Kincaid-Smith P. Treatment of IgA nephropathy with eicosapentanoic acid (EPA): a two-year prospective trial. Clinical Nephrology 1989;31(3):128-131
[95] Pettersson EE, Rekola S, Berglund L, Sundqvist KG, Angelin B, Diczfalusy U, et al. Treatment of IgA nephropathy with omega-3-polyunsaturated fatty acids: a prospective, double-blind, randomized study. Clinical Nephrology 1994;41(4):183-190
[101] Hogg RJ. A randomized, placebo-controlled, multicenter trial evaluating alternate-day prednisone and fish oil supplements in young patients with immunoglobulin A nephropathy. Scientific Planning Committee of the IgA Nephropathy Study. American Journal of Kidney Diseases 1995;26(5):792-796
[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S39.
Population: Patients with IgA nephropathy
Intervention: Fish oil
Comparator: Symptomatic treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Symptomatic treatment	Fish oil	**Certainty of the evidence**	**Plain text summary**
>50% increase in serum creatinine	Relative risk: 0.17 (95% CI: 0.02 - 1.21) Based on data from 28 patients in 1 study[1] Follow up 4 years	**429** per 1000	**73** per 1000 Difference: **356 fewer per 1000** (95% CI: 420 fewer - 90 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether fish oil increases or decreases >50% increase in serum creatinine
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Kidney failure	Relative risk: 0.17 (95% CI: 0.02 - 1.21) Based on data from 28 patients in 1 study[3] Follow up 4 years	**429** per 1000	**73** per 1000 Difference: **356 fewer per 1000** (95% CI: 420 fewer - 90 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether fish oil increases or decreases kidney failure
>50% loss in GFR	Relative risk: 0.14 (95% CI: 0.02 - 1.01) Based on data from 28 patients in 1 studies[5] Follow up 4 years	**500** per 1000	**70** per 1000 Difference: **430 fewer per 1000** (95% CI: 490 fewer - 5 more)	**Low** Due to serious risk of bias, Due to very serious imprecision, Due to serious imprecision[6]	Fish oil may decrease >50% loss in GFR slightly. However, the effect estimates do cross the line of no effect.
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy

Glucocorticoid-related adverse events	(95% CI: -)	Difference:		No studies were found that looked at glucocorticoid-related adverse events
Creatinine clearance	Measured by: Scale: - High better Based on data from 28 patients in 1 study[7] Follow up 4 years	Mean Mean Difference: **7 higher** (95% CI: 10.13 lower - 24.13 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether fish oil increases or decreases >50% increase creatinine clearance
Annual GFR loss	Based on data from 28 patients in 1 study Follow up 4 years	In the fish oil group (n=14), the mean annual change in GFR was -1.4 ml/min/1.73 m² per year (SD not reported) and in the symptomatic treatment group (n=14), the mean annual change in GFR was -3 ml/min/1.73 m² per year (SD not reported).)	**Very low** Due to serious risk of bias, Due to very serious imprecision[9]	We are uncertain whether fish oil increases or decreases annual GFR loss

1. Systematic review with included studies: [93] **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, Only data from one study, Low number of patients
3. Systematic review with included studies: [93] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** High lost to follow-up with 33% lost to follow-up in fish oil group and 22% in symptomatic treatment group. No intention-to-treat analysis undertaken; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
5. Systematic review with included studies: [93] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Serious.** Wide confidence intervals, Only data from one study, Low number of patients
7. Systematic review with included studies: [93] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
9. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up; **Imprecision: Very Serious.** Only data from one study, Low number of patients and no measure of variance provided

References

[93] Alexopoulos E, Stangou M, Pantzaki A, Kirmizis D, Memmos D. Treatment of severe IgA nephropathy with omega-3 fatty acids: the effect of a "very low dose" regimen. Renal Failure 2004;26(4):453-459

[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S40.
Population: Patients with IgA nephropathy
Intervention: Fish oil plus ACEi or ARB
Comparator: ACEi or ARB

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** ACEi or ARB	Fish oil plus ACEi or ARB	**Certainty of the evidence**	**Plain text summary**
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Malignancy[1]	(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
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at 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
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss
Creatinine clearance	Measured by: Scale: - High better Based on data from 30 patients in 1 study[2]	**67.7** ml/min Mean	**93.9** ml/min Mean Difference: **MD 26.20 higher**	**Low** Due to serious risk of bias, Due to serious imprecision[3]	Fish oil plus ACEi or ARBs may improve creatinine clearance slightly

	Follow up 6 months	(95% CI: 1.01 higher - 51.39 higher)		

1. No studies
2. Systematic review with included studies: [94] **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[94] Costanzi S, Ferraro M, Sturniolo A, Passalacqua S, D'Alonzo S, Tullio T, et al. Combined treatment with renin-angiotensin system blockers and polyunsaturated fatty acids in IgA nephropathy: promising results on proteinuria at six months [abstract]. Nephrology Dialysis Transplantation 2006;21(Suppl 4): iv295-iv295

[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S41.
Population: Patients with IgA nephropathy
Intervention: Anticoagulant
Comparator: Placebo or no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo or no treatment	Anticoagulant	**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[1]	Relative risk: 0.28 (95% CI: 0.04 - 2.07) Based on data from 21 patients in 1 study[2] Follow up 3 years	**364** per 1000	**102** per 1000 Difference: **262 fewer per 1000** (95% CI: 349 fewer - 389 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[3]	We are uncertain whether anticoagulant increases or decreases kidney failure
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
Remission of proteinuria[4]	Relative risk: 0.95 (95% CI: 0.19 - 4.6) Based on data from 49 patients in 1 study[5] Follow up 6 months	**125** per 1000	**119** per 1000 Difference: **6 fewer per 1000** (95% CI: 101 fewer - 450 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether anticoagulant increases or decreases remission of proteinuria
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Annual loss in GFR	Measured by: Scale: - Lower better				

		Difference:		No studies were found that looked at annual loss in GFR
Creatinine clearance	Measured by: Scale: - High better Based on data from 21 patients in 1 studies[7] Follow up 3 years	ml/min Mean ml/min Mean Difference: **MD 21 higher** (95% CI: 0.19 lower - 42.19 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether anticoagulant increases or decreases creatinine clearance

1. Antiplatelet: Dipyridamole Dose: 75 mg 3 times/d Anticoagulant: Warfarin Dose: INR 1.3 to 1.5 versus no treatment
2. Systematic review [137] with included studies: [77] **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of bias: Serious.** Selective outcome reporting, 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
4. Sulodexide versus placebo 50% Reduction in UPCR proteinuria
5. Systematic review [137] with included studies: [92] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
7. Systematic review with included studies: [77] **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, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[77] Lee GSL, Choong HL, Chiang GSC, Woo KT. Three-year randomized controlled trial of dipyridamole and low-dose warfarin in patients with IgA nephropathy and renal impairment. Nephrology 1997;3(1):117-121

[92] Bang K, Chin HJ, Chae DW, Joo KW, Kim YS, Kim S, et al. Anti-proteinuric effect of sulodexide in immunoglobulin A nephropathy. Yonsei Medical Journal 2011;52(4):588-594

[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S42.
Population: Patients with IgA nephropathy
Intervention: Anticoagulant
Comparator: Other nonimmunosuppressive treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Other nonimmunosuppressive treatment	Anticoagulant	**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
Complete remission[1]	Relative risk: 0.27 (95% CI: 0.16 - 0.46) Based on data from 262 patients in 1 study[2] Follow up 6 months	**500** per 1000	**865** per 1000 Difference: **365 more per 1000** (95% CI: 230 more - 525 more)	**Low** Due to very serious risk of bias, Due to serious imprecision, Upgraded due to Large magnitude of effect[3]	Dipyridamole compared with hirudin may decrease complete remission
≥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
Adverse events	Relative risk: 1.38 (95% CI: 0.86 - 2.22)	**181** per 1000	**250** per 1000 Difference: **69 more per 1000** (95% CI: 25 fewer - 221 more)	**Very low** Due to very serious risk of bias, Due to very	We are uncertain whether dipyridamole versus hirudin increases or

	Based on data from 262 patients in 1 study[4] Follow up 6 months		serious imprecision[5]	decreases adverse events
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss
Creatinine clearance[6]	Measured by: Scale: - High better Based on data from 38 patients in 1 study[7] Follow up 33 months	ml/min Mean ml/min Mean Difference: **MD 6 higher** (95% CI: 17.60 lower - 29.60 higher)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether dipyridamole + aspirin versus vitamin B increases or decreases creatinine clearance
Creatinine clearance[9]	Measured by: Scale: - High better Based on data from 262 patients in 1 study[10] Follow up 6 months	ml/min Mean ml/min Mean Difference: **MD 15.90 lower** (95% CI: 19.99 lower - 11.81 lower)	**Low** Due to very serious risk of bias, Due to serious imprecision, Upgraded due to Large magnitude of effect[11]	Dipyridamole versus hirudin may decrease creatinine clearance

1. Dipyridamole versus Hirudin
2. Systematic review with included studies: [76] **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of bias: Very Serious.** Selective outcome reporting, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, 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; **Upgrade: Large magnitude of effect.**
4. Systematic review with included studies: [76] **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
6. Dipyridamole + aspirin versus Vitamin B
7. Systematic review with included studies: [88] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Very Serious.** Incomplete data and/or large loss to follow up, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
9. Dipyridamole versus hirudin

10. Systematic review [137] with included studies: [76] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Risk of bias: Very Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients; **Upgrade: Large magnitude of effect.**

References

[76] Li KL, He YN, Zuo HW, Wang HM, Ding HL, Yang JR. [Efficacy of hirudin in treating immunoglobulin A nephropathy with hematuria: a randomized controlled trial]. [Chinese]. Zhong Xi Yi Jie He Xue Bao [Journal of Chinese Integrative Medicine] 2008;6(3):253-257

[88] Chan MK, Kwan SY, Chan KW, Yeung CK. Controlled trial of antiplatelet agents in mesangial IgA glomerulonephritis. American Journal of Kidney Diseases 1987;9(5):417-421

[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S43.
Population: Patients with IgA nephropathy
Intervention: Anticoagulant plus other treatment
Comparator: Other treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Other treatment	Anticoagulant plus other treatment	**Certainty of the evidence**	**Plain text summary**
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
All-cause mortality	Relative risk (95% CI: -) Based on data from 200 patients in 1 study[1] Follow up 6 months	Difference: **fewer**		**Low** Due to serious risk of bias, Due to serious imprecision[2]	There were too few who experienced the all-cause mortality, to determine whether clopidogrel plus telmisartan versus telmisartan alone made a difference
Kidney failure[3]	Relative risk: 0.28 (95% CI: 0.06 - 1.34) Based on data from 115 patients in 2 studies[4] Mean follow up 30 months	**111** per 1000	**31** per 1000 Difference: **80 fewer per 1000** (95% CI: 104 fewer - 38 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[5]	We are uncertain whether ticlopidine plus ACEi versus ACEi alone increases or decreases kidney failure
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection[6]	Relative risk: 1.0 (95% CI: 0.06 - 15.77) Based on data from 200 patients in 1 study[7] Follow up 6 months	**10** per 1000	**10** per 1000 Difference: **0 per 1000** (95% CI: 9 fewer - 148 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether clopidogrel plus telmisartan versus telmisartan alone increases or decreases infection

Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss
Change in creatinine clearance	Measured by: Scale: - High better Based on data from 20 patients in 1 study[9] Follow up 24 months	ml/min Mean ml/min Mean Difference: **MD 7 higher** (95% CI: 10.62 lower - 24.62 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[10]	We are uncertain whether defibrotide plus prednisone versus prednisone alone improves or worsens change in creatinine clearance
eGFR	Measured by: Scale: - High better Based on data from 84 patients in 1 studies[11] Follow up 24 months	ml/min/1.73m^2 Mean ml/min/1.73m^2 Mean Difference: **MD 1.28 lower** (95% CI: 6.73 lower - 4.17 higher)	**Low** Due to very serious imprecision[12]	Clopidine + ARB versus ARB alone may have little or no difference on eGFR

1. Systematic review with included studies: [64] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Serious.** Only data from one study, due to no events
3. Ticlopidine +ACEi versus ACEi
4. Systematic review with included studies: [129], [96] **Baseline/comparator:** Control arm of reference used for intervention.
5. **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, Unclear 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
6. Clopidogrel plus telmisartan versus telmisartan alone
7. Systematic review [137] with included studies: [64] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
9. Systematic review [137] with included studies: [110] **Baseline/comparator:** Control arm of reference used for intervention.
10. **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, unclear blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
11. Systematic review with included studies: [96] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[64] Wu J, Duan SW, Sun XF, Li WG, Wang YP, Liu WH, et al. Efficacy of leflunomide, telmisartan, and clopidogrel for immunoglobulin A nephropathy: a randomized controlled trial. Chinese Medical Journal 2016;129(16):1894-1903
[96] Cheng G, Liu D, Margetts P, Liu L, Zhao Z, Liu Z, et al. Valsartan combined with clopidogrel and/or leflunomide for the treatment of progressive immunoglobulin A nephropathy. Nephrology 2015;20(2):77-84
[110] Frasca GM, Martello M, Canova C, Isola E, Vangelista A, Bonomini V. Defibrotide treatment and disease progression in patients with IgA nephropathy and impaired renal function at diagnosis. Clinical Drug Investigation 1997;13(4):185-191
[129] Cheng IKP, Fang GX, Wong MC, Ji YL, Chan KW, Yeung HWD. A randomized prospective comparison of nadolol, captopril with or without ticlopidine on disease progression in IgA nephropathy. Nephrology 1998;4((1-2)):19-26
[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S44.
Population: Patients with IgA nephropathy
Intervention: Antioxidant
Comparator: Other treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Other treatment / Antioxidant	**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 (95% CI: -) Based on data from 68 patients in 1 study[1] Follow up 36 months	Difference: **fewer**	**Low** Due to serious risk of bias, Due to serious imprecision[2]	There were too few who experienced the kidney failure to determine whether probucol compared to ARB made a difference
≥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 infections
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 eGFR loss 3 years	Measured by: Scale: - Lower better Based on data from 68 patients in 1 study[3] Follow up 36 months	Mean / Mean Difference: **MD 1.36 higher** (95% CI: 0.32 higher - 2.40 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Probucol compared with ARB alone may increase annual eGFR loss

1. Systematic review [137] with included studies: [70] **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: Serious.** Wide confidence intervals, Only data from one study, Low number of patients
3. Systematic review with included studies: [70] **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, Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients

References

[70] Ye Z, Zhang L, Xu L, Shi W, Hu H, Shi X, et al. Probucol combined with valsartan in immunoglobulin A nephropathy: a multi-center, open labelled, randomized controlled study. Nephrology 2014;19(1):40-46

[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S45.
Population: Patients with IgA nephropathy
Intervention: Statins
Comparator: Placebo or no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo or no treatment / Statins	**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
Annual GFR loss	Measured by: Scale: - High better	Difference:		No studies were found that looked at annual GFR loss
eGFR	Based on data from 21 patients in 1 study Follow up 6 months	After the duration of therapy, the statins arm (n=13) had an eGFR of 85 ml/min/1.73 m² (IQR: 70-147); the placebo arm (n=8) had an eGFR of 77	**Very low** Due to serious risk of bias, Due to very serious imprecision[1]	We are uncertain whether statins increase or decrease eGFR

		ml/min/1.73 m² (IQR: 47-92)		

1. **Risk of bias: Serious.** Selective outcome reporting, 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; **Imprecision: Very Serious.** Only data from one study, Low number of patients

References

[90] Buemi M, Allegra A, Corica F, Aloisi C, Giacobbe M, Pettinato G, et al. Effect of fluvastatin on proteinuria in patients with immunoglobulin A nephropathy. Clinical Pharmacology & Therapeutics 2000;67(4):427-431

[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S46.
Population: Patients with IgA nephropathy
Intervention: Statins plus other treatment
Comparator: Other treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Other treatment	Statins plus other treatment	**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
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss
Creatinine clearance	Measured by: Scale: - High better Based on data from 30 patients in 1 study[1]	ml/min Mean Difference: **MD 22.60 higher**	ml/min Mean	**Very low** Due to very serious risk of bias, Due to serious imprecision[2]	We are uncertain whether statins plus other treatment improves or worsen creatinine clearance

	Follow up 12 months	(95% CI: 11.83 higher - 33.37 higher)		

1. Systematic review [137] with included studies: [80] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Selective outcome reporting, 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; **Imprecision: Serious.** Only data from one study, Low number of patients

References

[79] Kano K, Nishikura K, Yamada Y, Arisaka O. No effect of fluvastatin on the bone mineral density of children with minimal change glomerulonephritis and some focal mesangial cell proliferation, other than an ameliorating effect on their proteinuria. Clinical Nephrology 2005;63(2):74-79
[80] Kano K, Nishikura K, Yamada Y, Arisaka O. Effect of fluvastatin and dipyridamole on proteinuria and renal function in childhood IgA nephropathy with mild histological findings and moderate proteinuria. Clinical Nephrology 2003;60(2):85-89
[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S47.
Population: Patients with IgA nephropathy
Intervention: Phenytoin
Comparator: Placebo or no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo or no treatment	Phenytoin	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
≥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
Remission of hematuria	Relative risk: 4.47 (95% CI: 0.58 - 34.57) Based on data from 36 patients in 1 study[1] Follow up not reported	**59** per 1000	**264** per 1000 Difference: **205 more per 1000** (95% CI: 25 fewer - 1981 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether phenytoin increases or decreases remission of hematuria
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
Creatinine clearance	Measured by: Scale: - High better	ml/min Mean	ml/min Mean	**Very low**	We are uncertain whether phenytoin

	Based on data from 47 patients in 1 studies[3] Follow up not reported	Difference: **MD 6.00 lower** (95% CI: 28.05 lower - 16.05 higher)	Due to serious risk of bias, Due to very serious imprecision[4]	improves or worsens creatinine clearance

1. Systematic review [137] with included studies: [81] **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, unclear blinding of participants and personnel, resulting in potential for performance bias, unclear of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
3. Primary study [86] **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, unclear blinding of participants and personnel, resulting in potential for performance bias, unclear of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[81] Houssin A, Denis J, Spiesser R. Phenytoin in treatment of Berger's Disease. Ouest Medical 1984;37(4):211-215

[86] Clarkson AR, Seymour AE, Woodroffe AJ, McKenzie PE, Chan YL, Wootton AM. Controlled trial of phenytoin therapy in IgA nephropathy. Clinical Nephrology 1980;13(5):215-218

[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S48.
Population: Patients with IgA nephropathy
Intervention: Vitamin E
Comparator: Placebo or no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo or no treatment	Vitamin E	**Certainty of the evidence**	**Plain text summary**
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Kidney failure	Relative risk (95% CI: -) Based on data from 55 patients in 1 study[1] Follow up 24 months	Difference: **fewer**			There were too few who experienced the kidney failure to determine whether vitamin E made a difference
≥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
Annual loss of GFR	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual loss of GFR
Creatinine clearance	Measured by: Scale: - High better	**112** ml/min Mean	**127** ml/min Mean	**Very low**	We are uncertain whether vitamin E

	Based on data from 55 patients in 1 study[2] Follow up 24 months	Difference: **MD 15 higher** (95% CI: 7.08 lower - 37.08 higher)	Due to serious risk of bias, Due to very serious imprecision[3]	increases or decreases creatinine clearance

1. Systematic review [137] with included studies: [89] **Baseline/comparator:** Control arm of reference used for intervention.
2. Systematic review with included studies: [89] **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of bias: Serious.** 69% completed study to at least 1 year; number not reported for each group. No intention-to-treat analysis was conducted; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[89] Chan JC, Mahan JD, Trachtman H, Scheinman J, Flynn JT, Alon US, et al. Vitamin E therapy in IgA nephropathy: a double-blind, placebo-controlled study. Pediatric Nephrology 2003;18(10):1015-1019
[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews 2011;(3):CD003962

Table S49.
Population: Patients with IgA nephropathy
Intervention: Vitamin D
Comparator: Placebo or no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo or no treatment	Vitamin D	**Certainty of the evidence**	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference: **fewer**			No studies were found that looked at all-cause mortality
Kidney failure	(95% CI: -)	Difference:			No studies were found that looked at kidney failure
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Infection	Relative risk: 0.74 (95% CI: 0.22 - 2.43) Based on data from 50 patients in 1 study[1] Follow up 11 months	**208** per 1000	**154** per 1000 Difference: **54 fewer per 1000** (95% CI: 162 fewer - 297 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether vitamin D increases or decreases infection
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Adverse events	Relative risk: 0.72 (95% CI: 0.32 - 1.63) Based on data from 50 patients in 1 study[3] Follow up 11 months	**375** per 1000	**270** per 1000 Difference: **105 fewer per 1000** (95% CI: 255 fewer - 236 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether vitamin D increases or decreases adverse events
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission

Annual loss in eGFR	Measured by: Scale: - Lower better Based on data from 50 patients in 1 study[5] Follow up 11 months	ml/min/1.73 m^2 Mean ml/min/1.73 m^2 Mean Difference: **MD 0.00 higher** (95% CI: 16.61 lower - 16.61 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether vitamin D improves or worsens annual loss in GFR

1. Systematic review [137] with included studies: [74] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
3. Systematic review [137] with included studies: [74] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
5. Systematic review [137] with included studies: [74] **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, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[74] Liu LJ, Lv JC, Shi SF, Chen YQ, Zhang H., Wang HY. Oral calcitriol for reduction of proteinuria in patients with IgA nephropathy: a randomized controlled trial. American Journal of Kidney Diseases 2012;59(1):67-74

[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S50.
Population: Patients with IgA nephropathy
Intervention: Sodium cromoglycate
Comparator: Placebo or no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/no treatment	Sodium cromoglycate	**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	(95% CI: -)	Difference:			No studies were found that looked at 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	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Annual loss of GFR	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual loss of GFR
Creatinine clearance	Measured by: Scale: - High better Based on data from 30 patients in 1 study[1]	**78.6** ml/min Mean	**87** ml/min Mean Difference: **8.4 higher** (95% CI: 10.19 lower - 26.99 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether sodium cromoglycate increases or decreases creatinine clearance

	Follow up 3.5 months			

1. Systematic review [137] with included studies: [73] **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, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[73] Sato M, Takayama K, Kojima H, Koshikawa S. Sodium cromoglycate therapy in IgA nephropathy: a preliminary short-term trial. American Journal of Kidney Diseases 1990;15(2):141-146
[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S51.
Population: Patients with IgA nephropathy
Intervention: Allopurinol
Comparator: Placebo or no treatment

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo/no treatment	Allopurinol	**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
Annual GFR loss	Measured by: Scale: - High better	Difference:			No studies were found that looked at annual GFR loss
eGFR	Measured by: Scale: - High better Based on data from 40 patients in 1 study[1] Follow up 6 months	**68.9** Mean Difference: **MD 4.30 higher** (95% CI: 17.89 lower - 26.49 higher)	**73.2** Mean	**Very low** Due to very serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether allopurinol improves or worsen eGFR

1. Systematic review [137] with included studies: [72] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[72] Shi Y, Chen W, Jalal D, Li Z, Chen W, Mao H, et al. Clinical outcome of hyperuricemia in IgA nephropathy: a retrospective cohort study and randomized controlled trial. Kidney & Blood Pressure Research 2012;35(3):153-160

[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962

Table S52.
Population: Patients with IgA nephropathy
Intervention: Hydroxychloroquine
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	Hydroxychloroquine	**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
>50% decrease in proteinuria	Relative risk: 3.13 (95% CI: 1.17 - 8.36) Based on data from 53 patients in 1 study[1] Follow up 6 months	**154** per 1000	**482** per 1000 Difference: **328 more per 1000** (95% CI: 26 more - 1133 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Hydroxychloroquine may improve >50% decrease in proteinuria
Adverse events	Relative risk: 0.5	**67** per 1000	**34** per 1000	**Very low**	We are uncertain whether

	(95% CI: 0.05 - 5.22) Based on data from 53 patients in 1 study[3] Follow up 6 months	Difference: **33 fewer per 1000** (95% CI: 64 fewer - 283 more)	Due to serious risk of bias, Due to very serious imprecision[4]	hydroxychloroquine increases or decreases adverse events
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Primary study [139] **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; **Imprecision: Serious.** Only data from one study, Low number of patients.
3. Primary study [139] **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; **Imprecision: Very Serious.** Only data from one study, Low number of patients, Wide confidence intervals.

References

[137] Reid S, Cawthon PM, Craig JC, Samuels JA, Molony DA, Strippoli GF. Non-immunosuppressive treatment for IgA nephropathy. The Cochrane Database of Systematic Reviews. 2011;(3):CD003962
[139] Liu LJ, Yang YZ, Shi SF, Bao YF, Yang C, Zhu SN, Sui GL, Chen YQ, Lv JC, Zhang H. Effects of Hydroxychloroquine on Proteinuria in IgA Nephropathy: A Randomized Controlled Trial. American Journal of Kidney Diseases 2019;74(1):15-22

Table S53.
Population: Patients with IgA vasculitis and severe kidney disease
Intervention: Cyclosporine
Comparator: Methylprednisolone

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Methylprednisolone	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 kidney failure
≥50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
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[1] 3 months	Relative risk: 1.88 (95% CI: 0.95 - 3.69) Based on data from 15 patients in 1 study[2] Follow up 2.9 years	**500** per 1000	**940** per 1000 Difference: **440 more per 1000** (95% CI: 25 fewer - 1345 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[3]	We are uncertain whether cyclosporine improves or worsen number with remission at 3 months
Complete remission at last follow-up[4]	Relative risk: 1.37 (95% CI: 0.74 - 2.54) Based on data from 15 patients in 1 study[5] Mean follow up 6.3 years	**625** per 1000	**856** per 1000 Difference: **231 more per 1000** (95% CI: 162 fewer - 963 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether cyclosporine improves or worsen number with remission at last follow-up

Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. PCR <200 or urine protein <40 mg/m²/h
2. Primary study [146] **Baseline/comparator:** Control arm of reference used for intervention.
3. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up (No SD provided with means of urinary protein and SCr at last follow-up. Duration of study not defined); **Imprecision: Very Serious.** Only data from one study, Low number of patients, due to few events
4. PCR < 200 or urine protein < 40 mg/m²/h
5. Primary study [146] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: No serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Incomplete data and/or large loss to follow up (No SD provided with means of urinary protein and SCr at last follow-up. Duration of study not defined); **Imprecision: Very Serious.** Low number of patients, Only data from one study, due to few events

References

[146] Jauhola O, Ronkainen J, Koskimies O, Ala-Houhala M, Arikoski P, Holtta T, et al. Outcome of Henoch-Schoenlein purpura 8 years after the treatment with placebo or prednisone at disease onset [abstract]. Pediatric Nephrology 2011;26(9):1678-1678

[158] Hahn D, Hodson EM, Willis NS, Craig JC. Interventions for preventing and treating kidney disease in Henoch-Schönlein Purpura (HSP). The Cochrane Database of Systematic Reviews 2015;(8):CD005128

Table S54.
Population: Patients with IgA vasculitis and severe kidney disease
Intervention: Mycophenolate mofetil
Comparator: Azathioprine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Azathioprine	Mycophenolate mofetil	**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
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at 50% GFR loss
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Remission of proteinuria 1 year	Relative risk: 1.09 (95% CI: 0.82 - 1.44) Based on data from 26 patients in 1 studies[1] Mean follow up 66 months	**846** per 1000	**922** per 1000 Difference: **76 more per 1000** (95% CI: 152 fewer - 372 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	We are uncertain whether mycophenolate mofetil increases or decreases remission of proteinuria at 1 year
Relapse	Relative risk: 0.67 (95% CI: 0.13 - 3.35) Based on data from 26 patients in 1 study[3] Mean follow up 66 months	**231** per 1000	**155** per 1000 Difference: **76 fewer per 1000** (95% CI: 201 fewer - 543 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether mycophenolate mofetil increases or decreases relapse

Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss
Creatinine clearance	Measured by: Scale: - High better Based on data from 26 patients in 1 studies[5] Mean follow up 66 months	**107** ml/min Mean **110** ml/min Mean Difference: **MD 3.00 higher** (95% CI: 14.83 lower - 20.83 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Mycophenolate mofetil may have little or no difference on creatinine clearance

1. Primary study [142] **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/lack of blinding of outcome assessors, resulting in potential for detection bias, due to (One author a consultant for Novartis; no full-text publication after 5 years); **Imprecision: Serious.** Only data from one study, Low number of patients, due to few events
3. Primary study [142] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to other issue (one author a consultant for Novartis; no full-text publication after 5 years); **Imprecision: Very Serious.** Low number of patients, Only data from one study, due to patients who had relapse of HSP
5. Primary study [142] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to other issue (one author was a consultant for Novartis; no full-text publication after 5 years); **Imprecision: Serious.** Low number of patients, Only data from one study

References

[142] Fuentes Y, Valverde S, Velasquez-Jones L, Romero B, Ramón G, Medeiros M. Comparison of azathioprine vs mofetil mycophenolate for Henoch-Schonlein nephritis treatment [abstract]. Pediatric Nephrology 2010;25(9):1802-1802

[158] Hahn D, Hodson EM, Willis NS, Craig JC. Interventions for preventing and treating kidney disease in Henoch-Schönlein Purpura (HSP). The Cochrane Database of Systematic Reviews 2015;(8):CD005128

Table S55.
Population: Patients with IgA vasculitis and severe kidney disease
Intervention: Mycophenolate mofetil
Comparator: Leflunomide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Leflunomide	Mycophenolate mofetil	**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% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at 50% GFR loss
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
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss
24-hour urine proteinuria 3 months	Measured by: Scale: - Based on data from 19 patients in 1 study[1] Follow up 9 months	**220** Mean	**580** Mean Difference: **MD 360 higher** (95% CI: 43.35 lower - 763.35 higher)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether mycophenolate mofetil increases or decreases 24-hour

				urine proteinuria at three months
24-hour urine proteinuria 9 months	Measured by: Scale: - Based on data from 19 patients in 1 study[3] Follow up 9 months	**31** Mean **80** Mean Difference: **MD 49 higher** (95% CI: 3.09 higher - 94.91 higher)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Mycophenolate mofetil may increase 24-hour urine proteinuria at 9 months

1. Primary study [140] **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, Selective outcome reporting (not all expected outcomes not reported); **Imprecision: Very Serious.** Low number of patients, Only data from one study
3. Primary study [140] **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, not all expected outcomes were recorded; **Imprecision: Serious.** Low number of patients, Only data from one study

References

[140] Du Y, Zhang Z, Hou L, Qin K, Wang X, Wu Y. Comparison of Leflunomide and Mycophenolate mofetil in children with Henoch-Schonlein nephritis [abstract]. Pediatric Nephrology 2016;31(10):1817-1817

[158] Hahn D, Hodson EM, Willis NS, Craig JC. Interventions for preventing and treating kidney disease in Henoch-Schönlein Purpura (HSP). The Cochrane Database of Systematic Reviews 2015;(8):CD005128

Table S56.
Population: Patients with IgA vasculitis and severe kidney disease
Intervention: Cyclophosphamide
Comparator: Supportive therapy

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Supportive therapy	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	Relative risk: 0.75 (95% CI: 0.18 - 3.05) Based on data from 56 patients in 1 studies[1] Follow up 6.93 ± 3.32 years in patients who recovered; 6.57 ± 4.1 years in group with persistent abnormalities; 3.71 ± 2.14 years in patients progressing to kidney failure	**143** per 1000	**107** per 1000 Difference: **36 fewer per 1000** (95% CI: 117 fewer - 293 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether 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	(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

Persistent kidney disease	Relative risk: 1.07 (95% CI: 0.65 - 1.78) Based on data from 56 patients in 1 study[3] Follow up 6.93 ± 3.32 years in patients who recovered; 6.57 ± 4.1 years in group with persistent abnormalities	**500** per 1000 **535** per 1000 Difference: **35 more per 1000** (95% CI: 175 fewer - 390 more)	**Low** Due to serious risk of bias, Due to very serious imprecision, Due to serious imprecision[4]	Cyclophosphamide may have little or no difference on persistent kidney disease
Persistent severe kidney disease[5]	Relative risk: 0.88 (95% CI: 0.37 - 2.09) Based on data from 56 patients in 1 studies[6] Follow up 6.93 ± 3.32 years in patients who recovered; 6.57 ± 4.1 years in group with persistent abnormalities; 3.71 ± 2.14 years in patients progressing to kidney failure	**286** per 1000 **252** per 1000 Difference: **34 fewer per 1000** (95% CI: 180 fewer - 312 more)	**Low** Due to serious risk of bias, Due to serious imprecision[7]	Cyclophosphamide may have little or no difference on persistent severe kidney disease
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Primary study [151] **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.** Only data from one study, due to few patients having kidney failure
3. Primary study [151] **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: Serious.** Only data from one study
5. Decreased GFR, severe proteinuria, kidney failure
6. Primary study [151] **Baseline/comparator:** Control arm of reference used for intervention.
7. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: Serious.** Only data from one study, due to low number of persistent kidney disease events

References

[151] Tarshish P, Bernstein J, Edelmann CJr. Henoch-Schonlein purpura nephritis: course of disease and efficacy of cyclophosphamide. Pediatric Nephrology 2004;19(1):51-56

[158] Hahn D, Hodson EM, Willis NS, Craig JC. Interventions for preventing and treating kidney disease in Henoch-Schönlein Purpura (HSP). The Cochrane Database of Systematic Reviews. 2015;(8):CD005128

Table S57.
Population: Patients with IgA vasculitis and severe kidney disease
Intervention: Cyclophosphamide plus glucocorticoids
Comparator: Glucocorticoids

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates**		**Certainty of the evidence**	**Plain text summary**
		Glucocorticoids	Cyclophosphamide plus glucocorticoids		
All-cause mortality	Relative risk: 0.19 (95% CI: 0.02 - 1.5) Based on data from 54 patients in 1 study[1] Follow up 12 months	**207** per 1000	**39** per 1000 Difference: **168 fewer per 1000** (95% CI: 203 fewer - 104 more)	**Low** Due to very serious imprecision[2]	Cyclophosphamide plus glucocorticoids may have little or no difference on all-cause mortality
Kidney failure	Relative risk: 1.17 (95% CI: 0.07 - 19.67) Based on data from 54 patients in 1 study[3] Follow up 12 months	**34** per 1000	**40** per 1000 Difference: **6 more per 1000** (95% CI: 32 fewer - 635 more)	**Low** Due to very serious imprecision[4]	Cyclophosphamide plus glucocorticoids may have little or no difference on kidney failure at 12 months
≥ 50% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection	Relative risk: 0.81 (95% CI: 0.36 - 1.81) Based on data from 54 patients in 1 study[5] Follow up 12 months	**345** per 1000	**279** per 1000 Difference: **66 fewer per 1000** (95% CI: 221 fewer - 279 more)	**Low** Due to serious imprecision, Due to serious risk of bias[6]	Cyclophosphamide plus glucocorticoids may have little or no difference on infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Glucocorticoid-related adverse events - diabetes induction	Relative risk: 0.99 (95% CI: 0.38 - 2.57)	**241** per 1000	**239** per 1000 Difference: **2 fewer per 1000** (95% CI: 149 fewer - 378 more)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Cyclophosphamide plus glucocorticoids may have little or no difference on diabetes induction

	Based on data from 54 patients in 1 study[7] Follow up 12 months			
Complete remission[9] 6 months	Relative risk: 1.16 (95% CI: 0.26 - 5.24) Based on data from 54 patients in 1 study[10] Follow up 12 months	**103** per 1000 **119** per 1000 Difference: **16 more per 1000** (95% CI: 76 fewer - 437 more)	**Low** Due to serious risk of bias, Due to serious imprecision[11]	Cyclophosphamide plus glucocorticoids may have little or no difference on complete remission
eGFR <60 ml/min/1.73 m^2 12 months	Relative risk: 0.79 (95% CI: 0.33 - 1.93) Based on data from 34 patients in 1 study[12] Follow up 12 months	**421** per 1000 **333** per 1000 Difference: **88 fewer per 1000** (95% CI: 282 fewer - 392 more)	**Moderate** Due to serious imprecision[13]	Cyclophosphamide plus glucocorticoids probably has little or no difference on the number of patients with eGFR <60 ml/min/1.73 m^2 at 12 months
Kidney function improvement >50% 12 months	Relative risk: 0.3 (95% CI: 0.04 - 2.4) Based on data from 35 patients in 1 study[14] Follow up 12 months	**211** per 1000 **63** per 1000 Difference: **148 fewer per 1000** (95% CI: 203 fewer - 295 more)	**Moderate** Due to serious risk of bias, Due to serious imprecision[15]	Cyclophosphamide plus glucocorticoids may have little or no difference on kidney function improvement >50% at 12 months
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Primary study [149] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: No serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Only data from one study, due to not many mortality events
3. Primary study [149] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: No serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Only data from one study, due to not many patients with kidney failure
5. Primary study [149] **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, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study
7. Primary study [149] **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/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study, due to few events
9. BVAS = 0 at 6 months
10. Systematic review [158] with included studies: [149] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study
12. Primary study [149] **Baseline/comparator:** Control arm of reference used for intervention.
13. **Risk of bias: No serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study, due to few patients with eGFR <60ml/min
14. Primary study [149] **Baseline/comparator:** Control arm of reference used for intervention.
15. **Risk of bias: No serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study, due to few patients with kidney function improvement > 50%

References

[149] Pillebout E, Alberti C, Guillevin L, Ouslimani A, Thervet E, Cesar study Group. Addition of cyclophosphamide to steroids provides no benefit compared with steroids alone in treating adult patients with severe Henoch Schonlein Purpura. Kidney International 2010;78(5):495-502

[158] Hahn D, Hodson EM, Willis NS, Craig JC: Interventions for preventing and treating kidney disease in Henoch-Schönlein Purpura (HSP). The Cochrane Database of Systematic Reviews 2015;(8):CD005128

Table S58.
Population: Patients with IgA vasculitis (HSP), children
Intervention: Tacrolimus 0.05 mg/kg oral 2x/day
Comparator: Cyclophosphamide 10 mg/kg i.v. x 2 days each 2 weeks

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Cyclophosphamide	Tacrolimus	**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% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection	Relative risk: 1.14 (95% CI: 0.57 - 2.27) Based on data from 61 patients in 1 study[1] Follow up 2 months	**323** per 1000	**367** per 1000 Difference: **44 more per 1000** (95% CI: 194 fewer – 282 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether tacrolimus increases or decreases infection compared with cyclophosphamide
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	Relative risk: 0.86 (95% CI: 0.29 - 2.52) Based on data from 61 patients in 1 study[3] Follow up 2 months	**194** per 1000	**167** per 1000 Difference: **27 fewer per 1000** (95% CI: 220 fewer – 166 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether tacrolimus increases or decreases complete remission compared with cyclophosphamide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Cyclophosphamide	Tacrolimus	**Certainty of the evidence**	**Plain text summary**
Annual GFR loss	Measured by: Scale: -	Difference:			No studies were found that looked at annual GFR loss
Proteinuria	Measured by: Scale: -	Difference:			No studies were found that looked at proteinuria
Adverse events	(95% CI: -)	Difference:			No studies were found that looked at adverse events

1. Primary study [Wu 2022] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very serious.** Unclear allocation concealment, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; Uneven attrition due to noncompliance. **Imprecision: Very serious.** Only data from one study, wide confidence interval.
3. Primary study [Wu 2022] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very serious.** Unclear allocation concealment, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; Uneven attrition due to noncompliance. **Imprecision: Very serious.** Only data from one study, wide confidence interval.

References

[Wu 2022] Wu, D.; Ma, R.; Wang, X.; Yang, Y.. Efficacy and Safety of Tacrolimus in the Treatment of Pediatric Henoch-Schonlein Purpura Nephritis. Paediatr Drugs 2022;24:389–401. [PubMed: 35508891]

Table S59.
Population: Patients with IgA vasculitis (HSP), children
Intervention: Tacrolimus 0.05 mg/kg oral 2x/day
Comparator: Mycophenolate mofetil 10-15 mg/kg oral 2x/day

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Mycophenolate mofetil	Tacrolimus	**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% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection	Relative risk: 0.68 (95% CI: 0.38 – 1.23) Based on data from 56 patients in 1 study[1] Follow up 2 months	**538** per 1000	**367** per 1000 Difference: **172 fewer per 1000** (95% CI: 430 fewer – 86 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether tacrolimus increases or decreases infection compared with mycophenolate mofetil
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	Relative risk: 1.44 (95% CI: 0.38 – 5.47) Based on data from 61 patients in 1 study[3] Follow up 2 months	**115** per 1000	**167** per 1000 Difference: **51 more per 1000** (95% CI: 130 fewer – 233 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether tacrolimus increases or decreases complete remission compared with mycophenolate mofetil

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Mycophenolate mofetil	Tacrolimus	**Certainty of the evidence**	**Plain text summary**
Annual GFR loss	Measured by: Scale: -	Difference:			No studies were found that looked at annual GFR loss
Proteinuria	Measured by: Scale: -	Difference:			No studies were found that looked at proteinuria
Adverse events	(95% CI: -)	Difference:			No studies were found that looked at adverse events

1. Primary study [Wu 2022] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very serious.** Unclear allocation concealment, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; Uneven attrition due to noncompliance. **Imprecision: Very serious.** Only data from one study, wide confidence interval.
3. Primary study [Wu 2022] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very serious.** Unclear allocation concealment, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; Uneven attrition due to noncompliance. **Imprecision: Very serious.** Only data from one study, wide confidence interval.

References

[Wu 2022] Wu, D.; Ma, R.; Wang, X.; Yang, Y.. Efficacy and Safety of Tacrolimus in the Treatment of Pediatric Henoch-Schonlein Purpura Nephritis. Paediatr Drugs 2022;24:389–401. [PubMed: 35508891]

Table S60.
Population: Patients with IgA vasculitis (HSP), children
Intervention: Tacrolimus 0.1– 0.15 mg/kg/day oral
Comparator: Control (no tacrolimus)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Control Tacrolimus	**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% GFR loss	(95% CI: -)	Difference:		No studies were found that looked at ≥50% GFR loss
Infection	Relative risk: 0.57 (95% CI: 0.44 – 0.73) Based on data from 170 patients in 1 study[1] Follow up 2 years	**807** per 1000 **460** per 1000 Difference: **347 fewer per 1000** (95% CI: 482 fewer – 213 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Tacrolimus may decrease infection
Malignancy	(95% CI: -)	Difference:		No studies were found that looked at malignancy
Complete remission	Relative risk: 1.13 (95% CI: 0.99 – 1.29) Based on data from 165 patients in 1 study[3] Follow up 2 years	**790** per 1000 **893** per 1000 Difference: **103 more per 1000** (95% CI: 8 fewer – 213 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Tacrolimus may increase complete remission

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Control	Tacrolimus	**Certainty of the evidence**	**Plain text summary**
Annual GFR loss	Measured by: Scale: -	Difference:			No studies were found that looked at annual GFR loss
Proteinuria	Measured by: g/d Scale: - Lower better Based on data from 170 patients in 1 study[5] Follow up 2 years	**−2.01** g/d	**−2.07** g/d	**Low** Due to serious risk of bias, Due to serious imprecision[6]	Tacrolimus may have little or no difference on proteinuria
		Difference: 0.06 (**−0.28, 0.16)**			
Adverse events	(95% CI: -)	Difference:			No studies were found that looked at adverse events

1. Primary study [Zhang 2021] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear blinding of participants and personnel, resulting in potential for performance bias, Unclear blinding of outcome assessors, resulting in potential for detection bias. **Imprecision: Serious.** Only data from one study.
3. Primary study [Zhang 2021] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Unclear blinding of participants and personnel, resulting in potential for performance bias, Unclear blinding of outcome assessors, resulting in potential for detection bias. **Imprecision: Serious.** Only data from one study.
5. Primary study [Zhang 2021] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Unclear blinding of participants and personnel, resulting in potential for performance bias, Unclear blinding of outcome assessors, resulting in potential for detection bias. **Imprecision: Serious.** Only data from one study.

References

[Zhang 2021] Zhang, H.; Li, X.; Xu, H.; Ran, F.; Zhao, G.. Effect and safety evaluation of tacrolimus and tripterygium glycosides combined therapy in treatment of Henoch-Schonlein purpura nephritis. Int J Urol 2021;28:1157-1163.

Table S61.
Population: Patients with IgA vasculitis (HSP), children
Intervention: Cyclophosphamide
Comparator: Mycophenolate mofetil

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Mycophenolate mofetil	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% GFR loss	(95% CI: -)	Difference:			No studies were found that looked at ≥50% GFR loss
Infection	Relative risk: 0.92 (95% CI: 0.39 – 2.13) Based on data from 125 patients in 2 studies[1] Follow up 2 & 12 months	**407** per 1000	**379** per 1000 Difference: **28 fewer per 1000** (95% CI: 248 fewer – 460 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether cyclophosphamide increases or decreases infection compared with mycophenolate mofetil
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	Relative risk: 0.92 (95% CI: 0.56 – 1.53) Based on data from 125 patients in 2 studies[3] **Follow up 2-3 months**	**339** per 1000	**318** per 1000 Difference: **21 fewer per 1000** (95% CI: 149 fewer – 180 more)	**Very low** Due to very serious risk of bias, Due to very serious imprecision[5]	We are uncertain whether cyclophosphamide increases or decreases complete remission compared with mycophenolate mofetil

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Mycophenolate mofetil	Cyclophosphamide	**Certainty of the evidence**	**Plain text summary**
	Relative risk: 0.94 (95% CI: 0.74 – 1.20) Based on data from 68 patients in 1 study[4] **Follow up 12 months**	**818** per 1000	**771** per 1000 Difference: **47 fewer per 1000** (95% CI: 238 fewer – 145 more)		
Annual GFR loss	Measured by: Scale: -	Difference:			No studies were found that looked at annual GFR loss
Proteinuria	Measured by: Scale: -	Difference:			No studies were found that looked at proteinuria
Adverse events	(95% CI: -)	Difference:			No studies were found that looked at adverse events

1. Primary studies [Wu 2022][Geng 2021] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very serious.** Unclear allocation concealment, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; Uneven attrition due to noncompliance. **Imprecision: Very serious.** Very wide confidence interval.
3. Primary studies [Wu 2022][Geng 2021] **Baseline/comparator:** Control arm of reference used for intervention.
4. Primary study [Geng 2021] **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of bias: Very serious.** Unclear allocation concealment, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; Uneven attrition due to noncompliance. **Imprecision: Serious.** Wide confidence interval.

References

[Geng 2021] Geng, H. Y.; Chen, C. Y.; Li, H. R.; Tu, J.; Du, P. W.; Xia, H.. Efficacy and safety of mycophenolate mofetil versus cyclophosphamide in the treatment of Henoch-Schonlein purpura nephritis with nephrotic-range proteinuria in children: a prospective randomized controlled trial. Zhongguo Dang Dai Er Ke Za Zhi 2021;23:338-342.

[Wu 2022] Wu, D.; Ma, R.; Wang, X.; Yang, Y.. Efficacy and Safety of Tacrolimus in the Treatment of Pediatric Henoch-Schonlein Purpura Nephritis. Paediatr Drugs 2022;24:389–401. [PubMed: 35508891]