**DATA SUPPLEMENT**

**Appendix A. Search strategies**

*Table S1. Search strategies for systematic review topics*

Search dates: May 2018; updated search June 2020, updated search August 22, 2024

| Guideline chapter | Immunoglobulin A nephropathy (IgAN)/Immunoglobulin A vasculitis (IgAV) |
|---|---|
| Clinical question | All treatments for adults or children with IgAN or IgAV |
| Search strategy - CENTRAL | 1. MeSH descriptor: [Glomerulonephritis, IGA] explode all trees<br>2. MeSH descriptor: [IgA Vasculitis] explode all trees<br>3. iga next glomeruloneph*<br>4. iga next nephropath*<br>5. IgAGN<br>6. "iga-n" or "igan"<br>7. berger* next disease*<br>8. "immunoglobulin a" next nephropath*<br>9. henoch next scho*nlein next purpura<br>10. allergic next purpura<br>11. anaphylactoid next purpura<br>12. henoch next purpura<br>13. nonthrombocytop*enic next purpura<br>14. iga next vasculitis<br>15. non next thrombocytop*enic next purpura<br>16. leukocytoclastic next vasculitis<br>17. peliosis next rheumatica<br>18. purpura next rheumatica<br>19. rheumatoid next purpura<br>20. scho*nlein next disease<br>21. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 with Publication Year from 2020 to 2024, in Trials |
| Search strategy - MEDLINE | 1. ("Glomerulonephritis, IGA"[Mesh] OR iga glomerulonephritis[tiab] OR iga glomeruloneph*[tiab] OR iga nephropath*[tiab] OR iga neph*[tiab] OR IgAGN[tiab] OR igA-N[tiab] OR berger* disease[tiab] OR (immunoglobulin[tiab] AND (nephropathy[tiab] OR neph*[tiab])) OR "Glomerulonephritis/immunology"[Mesh] OR nephrotic* syndrome[tiab] OR "IgA Vasculitis"[Mesh] OR "schoenlein henoch purpura"[tiab] OR "Schonlein Henoch Purpura"[tiab] OR "allergic purpura"[tiab] OR "anaphylactoid purpura"[tiab] OR "henoch purpura"[tiab] OR "Nonthrombocytopenic Purpura"[tiab] OR "Non thrombocytopenic Purpura"[tiab] OR "leukocytoclastic vasculitis"[tiab] OR "peliosis rheumatica"[tiab] OR "purpura rheumatica"[tiab:~1] OR "rheumatoid purpura"[tiab:~1] OR "schoenlein disease"[tiab:~1] OR "schonlein disease"[tiab:~1] ) AND<br>2. (("Randomized Controlled Trial" [Publication Type] OR "Controlled Clinical Trial" [Publication Type] OR random* OR placebo OR crossover or cross-over OR "Cross-Over Studies"[Mesh] OR trial) NOT ("Animals"[Mesh] NOT "Humans"[Mesh]))<br>Since 1/1/2020 |

| | |
|---|---|
| Search strategy - Embase | 1. (((iga AND nephropathy OR iga) AND glomerulonephritis OR berger*) AND disease OR igagn OR 'iga n' OR immunoglobulin) AND a AND nephropathy<br>2. 'immunoglobulin a nephropathy'<br>3. ((iga AND neph* OR iga) AND glomeruloneph* OR berger*) AND disease OR igagn OR 'iga n'<br>4. 'immunoglobulin a' AND neph*<br>5. 'anaphylactoid purpura'<br>6. henoch AND scho?nlein<br>7. ((allergic AND purpura OR anaphylactoid) AND purpura OR henoch) AND purpura<br>8. (((nonthrombocytop?enic AND purpura OR non) AND thrombocytop?enic AND purpura OR leukocytoclastic) AND purpura OR leukocytoclastic) AND vasculitis<br>9. (((peliosis AND rheumatica OR purpura) AND rheumatica OR rheumatoid) AND purpura OR scho?nlein) AND disease<br>10. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9<br>11. 'randomized controlled trial'<br>12. 'crossover procedure'<br>13. 'double blind procedure'<br>14. 'single blind procedure'<br>15. random* OR factorial* OR crossover* OR cross-over* OR placebo*<br>16. double* AND blind*<br>17. singl* AND blind* OR assign* OR allocat* OR volunteer*<br>18. #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17<br>19. #10 AND #18<br>20. #10 AND #18 AND [01-01-2020]/sd |

## 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 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<br><br>The processes of guideline development are transparent and allow for involvement of all Work Group Members | For guideline group composition – see *Work Group Membership*<br><br>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 August/September 2024. |
| Updating | An update for the guideline 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 guideline |
|---|---|
| Methods | |
| Include a research protocol with appropriate eligibility criteria (PICO format) | See *Table 5 clinical questions 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 | See *Appendix C & D* for summary of findings tables |
| Study selection processes | See *Methods for Guideline Development – Figure 5 – Search yield and study flow diagram* |
| Appraisal of individual studies quality | The summary of findings tables in Appendix C & D provide an assessment of risk of bias for all studies in a comparison between intervention and comparator. |
| Meta-analysis results | See *Appendix C & D* for summary of findings tables for meta-analysis results for all critical and important outcomes |
| Table and figures | See *Appendix C & D* for summary of findings tables |

**References**

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

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

**Table S4**.
Population: Adults 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 |
| | Upper respiratory infection: 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] | Nefecon may have little or no difference on upper respiratory 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:<br>Scale: - Lower better | Difference: | | No studies were found that looked at annual GFR loss |
| eGFR, change from baseline, ml/min per 1.73 $m^2$ | Measured by:<br>Scale: Higher better<br>Based on data from 480 patients in 2 studies[7]<br>Follow up 9 months | **−4.6**<br>Mean<br>**0.6**<br>Mean<br>Difference: **MD 5.4 higher**<br>(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]<br>Follow up 24 months | **−12.0**<br>Mean<br>**−6.1**<br>Mean<br>Difference: **MD 5.9 higher**<br>(95% CI: 3.4 higher – 9.2 higher) | **Moderate**<br>Serious imprecision[10] | Nefecon probably decreases GFR loss at 24 months |
| Proteinuria, change from baseline, % | Measured by:<br>Scale: Lower better<br>Based on data from 480 patients in 2 studies[11]<br>Follow up 9 months | **−1.6**<br>Mean<br>**−29.3**<br>Mean<br>Difference: **MD 29.0% lower**<br>(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]<br>Follow up 24 months | **−1.0**<br>Mean<br>**−30.7**<br>Mean<br>Difference: **MD 30.1% lower**<br>(95% CI: 41.5% lower – 16.4% lower) | **Moderate**<br>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: Adults and children 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 kidney failure events, 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[3] Follow up 12 months | Difference: | | **Very low** Due to very serious risk of bias, Due to serious imprecision[4] | 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[5] Follow up 12 months | Difference: | | **Very low** Due to very serious risk of bias, Due to serious imprecision[6] | 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[7] 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[8] | Tonsillectomy plus standard of care 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[9] 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[10] | Tonsillectomy plus standard of care 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[11] 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[12] | We are uncertain whether tonsillectomy plus standard of care 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[13] 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[14] | Tonsillectomy plus other standard of care 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[15] 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[16] | Tonsillectomy plus other standard of care 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[17] | 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 | We are uncertain whether tonsillectomy plus standard of care increases or |

| | | | | |
|---|---|---|---|---|
| | Mean follow up 3.5 years | | to very serious imprecision[18] | 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. Systematic review with included studies: [34] **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 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.
5. Systematic review with included studies: [34] **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, 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.
7. Systematic review [18] with included studies: [71], [82] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Selective outcome reporting; **Imprecision: Serious.** Wide confidence intervals, Low number of patients.
9. Systematic review [137] with included studies: [71], [82] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Selective outcome reporting; **Inconsistency: Serious.** The magnitude of statistical heterogeneity was high, with $I^2$: 75%.; **Imprecision: No serious.** Low number of patients.
11. Systematic review with included studies: [78] **Baseline/comparator:** Control arm of reference used for intervention. Study conducted in children (in contrast with other included studies, which were conducted in adults).
12. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients.
13. Systematic review with included studies: [71] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients.
15. Systematic review with included studies: [71] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Selective outcome reporting; **Imprecision: Serious.** Only data from one study, Low number of patients.
17. Systematic review [137] with included studies: [78], [82] **Baseline/comparator:** Control arm of reference used for intervention. One study conducted in children [78].
18. **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: Adults with IgA nephropathy
Intervention: Glucocorticoid (oral) plus supportive therapy (excluding nefecon)
Comparator: Supportive therapy

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** | | **Certainty of the evidence** | **Plain text summary** |
|---|---|---|---|---|---|
| | | Supportive therapy | Glucocorticoid plus supportive therapy | | |
| 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 | **13** per 1000 | **19** 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 | **214** per 1000 | **132** per 1000 Difference: **124 fewer per 1000** (95% CI: 177 fewer - 6 more) | **Moderate** Due to serious risk of bias[5] | Glucocorticoid plus supportive therapy probably decreases kidney failure (up to 4 years) |
| | **Reduced dose:** Hazard ratio: 0.26 (95% CI: 0.07 – 1.03) Based on data from 241 patients in 1 study[4] Median follow up 30 months | **83** per 1000 | **25** per 1000 Difference: **59 fewer per 1000** (95% CI: 115 fewer – 2 fewer) | | |
| ≥50% GFR loss | Relative risk: 0.62 (95% CI: 0.45 - 0.84) Based on data from 503 patients in 1 study[6] 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[8] | Glucocorticoid plus supportive therapy probably decreases ≥50% GFR loss |
| | **Reduced dose:** Hazard ratio: 0.30 (95% CI: 0.10 – 0.88) Based on data from 241 patients in 1 study[7] Median follow up 30 months | **100** per 1000 | **41** per 1000 Difference: **59 fewer per 1000** (95% CI: 124 fewer – 7 more) | | |
| Infection | **Reduced dose:** | **17** per 1000 | **41** per 1000 | **Low** | Reduced dose glucocorticoid |

| | | | | |
|---|---|---|---|---|
| | Relative risk: 2.48<br>(95% CI: 0.49 – 12.5)<br>Based on data from 241 patients in 1 study[9]<br>Median follow up 30 months | Difference: **25 more per 1000**<br>(95% CI: 18 fewer – 67 more) | Due to serious imprecision[10] | plus supportive therapy may increase infections |
| Malignancy | (95% CI: - ) | Difference: | | No studies were found that looked at malignancy |
| Complete remission | Relative risk: 1.78<br>(95% CI: 1.09 - 2.89)<br>Based on data from 380 patients in 4 studies[11]<br>Mean follow up 42 months | **326** per 1000 **580** per 1000<br>Difference: **254 more per 1000**<br>(95% CI: 29 more - 616 more) | **Low**<br>Due to serious risk of bias, Due to serious inconsistency[12] | Glucocorticoid plus supportive therapy may increase complete remission |
| Doubling of serum creatinine | Relative risk: 0.22<br>(95% CI: 0.07 - 0.76)<br>Based on data from 160 patients in 2 studies[13]<br>Mean follow up 54 months | **165** per 1000 **36** per 1000<br>Difference: **129 fewer per 1000**<br>(95% CI: 153 fewer - 40 fewer) | **Moderate**<br>Due to serious risk of bias[14] | Glucocorticoid plus supportive therapy probably decreases doubling of serum creatinine |
| Adverse events, serious | Relative risk: 1.40<br>(95% CI: 0.90 – 2.19)<br>Based on data from 403 patients in 2 studies[15]<br>Mean follow up 28 months | **120** per 1000 **172** per 1000<br>Difference: **48 more per 1000**<br>(95% CI: 12 fewer - 143 more) | **Moderate**<br>Due to serious imprecision[17] | Glucocorticoid plus supportive therapy probably increases serious adverse events |
| | **Reduced dose:**<br>Relative risk: 1.98<br>(95% CI: 0.51 – 7.75)<br>Based on data from 241 patients in 1 study[16]<br>Median follow up 30 months | **25** per 1000 **50** per 1000<br>Difference: **25 more per 1000**<br>(95% CI: 23 fewer – 72 more) | | |
| GFR decline ≥15 ml/min per 1.73 $m^2$ | Relative risk: 0.74<br>(95% CI: 0.39 - 1.41)<br>Based on data from 109 patients in 1 study[18]<br>Follow up 36 months | **231** per 1000 **333** per 1000<br>Difference: **102 more per 1000**<br>(95% CI: 92 fewer - 575 more) | **Low**<br>Due to serious risk of bias, Due to serious imprecision[19] | Glucocorticoid plus supportive therapy may have little or no effect on GFR decline ≥15 ml/min per 1.73 $m^2$ |

| | | | | | |
|---|---|---|---|---|---|
| Annual GFR loss, ml/min per 1.73 $m^2$ | Measured by:<br>Scale: - Lower better<br>Based on data from 309 patients in 2 studies[20]<br>Mean follow up 29 months | **6.6**<br>Mean | **1.0**<br>Mean<br><br>Difference: **MD 5.4 ml/min/1.73 $m^2$/year lower**<br>(95% CI: 8.6 lower – 2.3 lower) | **High**[22] | Glucocorticoid plus supportive therapy reduces annual GFR loss |
| | **Reduced dose:**<br>Based on data from 241 patients in 1 study[21]<br>Median follow up 30 months | **3.0**<br>Mean | **0.7**<br>Mean<br><br>Difference: **MD 2.3 ml/min/1.73 $m^2$/year lower**<br>(95% CI: 4.6 lower – 0.03 more) | | |

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. Based on secondary analysis restricted to reduced dose phase.[Kim 2024 39081761].
5. **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.
6. Primary study [Lv 2022 35579642] **Baseline/comparator:** Control arm of reference used for intervention.
7. Based on secondary analysis restricted to reduced dose phase.[Kim 2024 39081761].
8. **Imprecision: Serious.** Only data from one study.
9. Reduced dose primary study [Kim 2024 39081761] **Baseline/comparator:** Control arm of reference used for intervention. Analysis restricted to reduced-dose glucocorticoid protocol.
10. **Imprecision: Serious.** Wide confidence intervals. Only data from one study.
11. Systematic review [139] with included studies: [45], [134], [44], [54] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, 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%.
13. Primary study [44], [134] **Baseline/comparator:** Control arm of reference used for intervention.
14. **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.
15. Systematic review [139] with included studies: [54][Lv 2022 35579642]. **Baseline/comparator:** Control arm of reference used for intervention.
16. Based on secondary analysis restricted to reduced dose phase.[Kim 2024 39081761].
17. **Risk of bias: Serious.** Wide confidence interval.

18. Systematic review [139] with included studies: [54] **Baseline/comparator:** Control arm of reference used for intervention.
19. **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.
20. Systematic review with included studies: [134], [Rauen 2020]. **Baseline/comparator:** Control arm of reference used for intervention.
21. Based on secondary analysis restricted to reduced dose phase.[Kim 2024 39081761].
22. **Risk of bias: Low. Consistency: Not serious.** Statistically homogeneous.

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**Table S7**.
Population: Adults 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 | Measured by: Scale: - Lower better | | | |

| | | | | |
|---|---|---|---|---|
| | | Difference: | | No studies were found that looked at annual GFR loss |
| Serum creatinine | Measured by:<br>Scale: -<br>Based on data from 22 patients in 1 study[5]<br>Follow up 3 months | Mean Mean<br>Difference: **MD 0 lower** (95% CI: 23.74 lower - 23.74 higher) | **Very low**<br>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:<br>Scale: -<br>Based on data from 197 patients in 3 studies[7]<br>Mean follow up 22 months | g/24 h Mean g/24 h Mean<br>Difference: **MD 0.73 lower** (95% CI: 1.06 lower - 0.39 lower) | **Moderate**<br>Due to serious risk of bias[8] | RASi probably decreases proteinuria |
| Creatinine clearance | Measured by:<br>Scale: -<br>Based on data from 197 patients in 3 studies[9]<br>Mean follow up 22 months | Mean Mean<br>Difference: **MD 6.97 higher** (95% CI: 0.60 lower - 14.54 higher) | **Low**<br>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. A small number of participants were children (mean age 20 years, range 9-35 years).
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. A small number of participants in one study [104] were children (mean age 20 years, range 9-35 years).
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. A small number of participants in one study [104] were children (mean age 20 years, range 9-35 years).
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.

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**Table S8.**
Population: Adults with IgA nephropathy and chronic kidney disease
Intervention: Sodium-glucose cotransporter-2 inhibitor (SGLT2i) (dapagliflozin or empagliflozin) 10 mg/d
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] | Hazard ratio: 0.59 (95% CI: 0.42 - 0.84)[4] Based on data from 1087 patients in 2 studies[5] Median follow up 24 months | **162** per 1000 **102** per 1000 Difference: **60 fewer per 1000** (95% CI: 100 fewer – 20 fewer) | **Moderate**[6] | SGLT2 inhibitors probably 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 1087 patients in 2 studies [7] Follow up 24–38 months | **−4.3** ml/min/1.73 $m^2$ | **−2.6** ml/min/1.73 $m^2$ per year<br>Difference: **1.7** (95% CI: 1.1, 2.3) | **High**[8] | SGLT2 inhibitors slow annual GFR loss |
| Proteinuria | Measured by: ACR Scale: - Lower better Based on data from 270 patients in 1 study[9] Follow up 38 months | **~1%** | **~−25%**<br>Difference: **−26%** (95% CI: −37, −14) | **Moderate** Due to serious imprecision[10] | 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[11] Follow up 38 months | **256** per 1000 | **161** per 1000<br>Difference: **95 fewer per 1000** (95% CI: 191 fewer- 1 more) | **Low** Due to very serious imprecision[12] | 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. Based on fixed effect meta-analysis of two studies. Effect sizes heterogeneous between studies (0.29 and 0.67), resulting in incongruous nonsignificant random effects model meta-analysis.
5. Primary study [DAPA-CKD 2021][EMPA-KIDNEY 2024] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Not serious. Consistency: Serious.** Inconsistent effect sizes affecting summary estimate. **Imprecision: Not serious.**
7. Primary study [DAPA-CKD 2021][EMPA-KIDNEY 2024] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Not serious.**
9. Primary study [DAPA-CKD 2021] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Not serious. Imprecision: Serious.** Only data from one study
11. Primary study [DAPA-CKD 2021] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Not serious. Imprecision: Very serious.** Only data from one study, Wide confidence interval

**References**

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**Table S9.**
Population: Adults with IgA nephropathy
Intervention: Sparsentan 400 mg/d
Comparator: Irbesartan 300 mg/d

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Irbesartan | Sparsentan | **Certainty of the 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 all-cause mortality |
| 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 | **0** per 1000 | **10** 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 |
| ≥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 |

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

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**

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**Table S10.**
Population: Children 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 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 may have little or no difference |

| | | | | |
|---|---|---|---|---|
| 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] | 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 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 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.

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

**Table S11.**
Population: Adults with IgA nephropathy
Intervention: Oral glucocorticoid
Comparator: Placebo or usual care (non-renin-angiotensin system blockade)

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Placebo or 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 |
| Doubling of serum creatinine | Relative risk: 0.45 (95% CI: 0.29 - 0.69) | **326** per 1000 | **147** per 1000 Difference: **179 fewer per 1000** | **Moderate** Due to serious risk of bias[8] | Oral glucocorticoid probably slightly decreases doubling of serum creatinine |

| | | | | |
|---|---|---|---|---|
| | Based on data from 341 patients in 6 studies[7] Mean follow up 50 months | (95% CI: 231 fewer - 101 fewer) | | |
| 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**

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**Table S12.**
Population: Adults with IgA nephropathy
Intervention: Glucocorticoid (intravenous or oral)
Comparator: Placebo or usual care

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Placebo or 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: Adults with IgA nephropathy
Intervention: Methylprednisolone combined with alternative low-dose prednisone
Comparator: Full-dose prednisone

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Full-dose prednisone | Methylprenisolone plus 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 plus low-dose prednisone increases or decreases 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 | 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 plus 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 plus low-dose prednisone increases or decreases complete remission |

| **Outcome**<br>Timeframe | **Study results and measurements** | **Absolute effect estimates**<br>Full-dose prednisone | Methylprenisolone plus low-dose prednisone | **Certainty of the evidence** | **Plain text summary** |
|---|---|---|---|---|---|
| Annual GFR loss | Measured by:<br>Scale: - Lower better | Difference: | | | No studies were found that looked at annual GFR loss |
| Proteinuria | Measured by:<br>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: Adults with IgA nephropathy (crescent percentage 1%–49%)
Intervention: Intravenous methylprednisolone at months 1, 2, and 3 (0.5 g/d × 3 d/mo), followed by oral 0.4 mg/kg/d × 6 mo
Comparator: Intravenous methylprednisolone at months 1, 3, and 5 (0.5 g/d × 3 d/mo), followed by oral 0.4 mg/kg/d × 6 mo

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Methyl-prednisolone at months 1, 3, and 5 | **Absolute effect estimates** Methyl-prednisolone at months 1, 2, and 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 intravenous methylprednisolone at months 1, 2, and 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 intravenous methylprednisolone at months 1, 2, and 3 increases or decreases complete remission |

| **Outcome**<br>Timeframe | **Study results and measurements** | **Absolute effect estimates**<br>Methyl-prednisolone at months 1, 3, and 5 | <br>Methyl-prednisolone at months 1, 2, and 3 | **Certainty of the evidence** | **Plain text summary** |
|---|---|---|---|---|---|
| Annual GFR loss | Measured by:<br>Scale: - | Difference: | | | No studies were found that looked at annual GFR loss |
| Proteinuria | Measured by: change<br>Scale: - Lower better<br>Based on data from 74 patients in 1 study[5]<br>Follow up 6 months | **−1.01** g/d | **−1.40** g/d<br><br>Difference: **−0.39 (−1.00, 0.22)** | **Very low**<br>Due to serious risk of bias, Due to very serious imprecision[6] | We are uncertain whether intravenous methylprednisolone months 1, 2, 3 increases or decreases proteinuria |
| Withdrawal due to adverse events | Relative risk: 0.24 (95% CI: 0.03 – 2.28)<br>Based on data from 74 patients in 1 study[7]<br>Follow up 6 months | **105** per 1000 | **28** per 1000<br><br>Difference: **77 fewer per 1000** (95% CI: 189 fewer- 34 more) | **Very low**<br>Due to serious risk of bias, Due to very serious imprecision[8] | We are uncertain whether intravenous 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: Adults with IgA nephropathy
Intervention: Inhaled fluticasone propionate twice daily (plus supportive care)
Comparator: Supportive care

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Supportive care | Inhaled fluticasone propionate | **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 |

| **Outcome**<br>Timeframe | **Study results and measurements** | **Absolute effect estimates**<br>Supportive care | <br>Inhaled fluticasone propionate | **Certainty of the evidence** | **Plain text summary** |
|---|---|---|---|---|---|
| Annual GFR loss | Measured by:<br>Scale: - Lower better | Difference: | | | No studies were found that looked at annual GFR loss |
| Proteinuria | Measured by:<br>Scale: - Lower better<br>Based on data from 142 patients in 1 study[1]<br>Follow up 9 months | **−0.1**<br>g/d<br>Difference:<br>**−0.8** (−1.0, −0.6) | **−0.9**<br>g/d | **Low**<br>Due to serious imprecision[2] | Inhaled fluticasone may reduce proteinuria |
| Adverse events, serious | Relative risk:<br>(95% CI: –)<br>Based on data from 142 patients in 1 study[3]<br>Follow up 9 months | **0**<br>per 1000<br>Difference: **0 more per 1000**<br>(95% CI: 27 fewer - 27 more) | **0**<br>per 1000 | **Very low**<br>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: Adults with IgA nephropathy
Intervention: Cyclophosphamide followed by azathioprine plus glucocorticoid
Comparator: Antihypertensive therapy (non-renin-angiotensin system blockade)

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Antihypertensive therapy | Cyclophosphamide then 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: 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 on infections |
| 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 | Measured by:<br>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**

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[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: Adults 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: Adults 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**

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**Table S19.**
Population: Adults 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 kidney failure events 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: | | | | |

| | | | | |
|---|---|---|---|---|
| | 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**

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**Table S20.**
Population: Children 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: | | | | |

| | | | | |
|---|---|---|---|---|
| | 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

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**Table S21.**
Population: Adults 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**

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**Table S22.**
Population: Children 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

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**Table S23.**
Population: Adults 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** |
|---|---|---|---|---|---|
| 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: 0.31 (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 |

| | | | | |
|---|---|---|---|---|
| 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**

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**Table S24.**
Population: Adults 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 all-cause 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)<br>Based on data from 116 patients in 3 studies[11]<br>Mean follow up 14 months | **55** per 1000 **131** per 1000<br><br>Difference: **76 more per 1000** (95% CI: 20 fewer - 322 more) | **Low**<br>Due to serious risk of bias, Due to serious imprecision[12] | Mycophenolate mofetil may increase complete remission |
| Annual GFR loss | Measured by:<br>Scale: - Lower better<br>Based on data from 28 patients in 1 study[13]<br>Follow up 12 months | Mean Mean<br><br>Difference: **MD 2 higher** (95% CI: 25.15 lower - 29.15 higher) | **Very low**<br>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)<br>Based on data from 281 patients in 2 studies[15]<br>Mean follow up 24 months | **28** per 1000 **54** per 1000<br><br>Difference: **26 more per 1000** (95% CI: 18 fewer - 187 more) | **Very low**<br>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.

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**Table S25.**
Population: Adults with IgA nephropathy with glomerular filtration rate (GFR) ≤60 ml/min per 1.73 $m^2$
Intervention: Cyclophosphamide followed by 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 malignancy events 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 |

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|---|---|---|---|---|
| | 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 study[10] Follow up 36 months | **259** per 1000 **707** per 1000<br>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 ml/min per 1.73 $m^2$ | 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<br>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 ml/min per 1.73 $m^2$ |
| 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.

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**Table S26.**
Population: Adults 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 study[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**

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**Table S27.**
Population: Adults with IgA nephropathy
Intervention: Mycophenolate mofetil plus renin-angiotensin system inhibitor (RASi)
Comparator: RASi alone

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** RASi alone | Mycophenolate mofetil 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 | 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 |
| 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 |
| 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**

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**Table S28.**
Population: Adults 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 infection events 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:<br>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**

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**Table S29.**
Population: Adults 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)<br>Based on data from 108 patients in 1 study[7]<br>Follow up 24 months | **102** per 1000 **34** per 1000<br><br>Difference: **68 fewer per 1000** (95% CI: 169 fewer - 32 more) | **Very low**<br>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:<br>Scale: - Lower better | Difference: | | No studies were found that looked at annual GFR loss |
| GFR, ml/min per 1.83 $m^2$ | Measured by:<br>Scale: - High better<br>Based on data from 85 patients in 1 study[9]<br>Follow up 12 months | Mean Mean<br><br>Difference: **MD 3.77 higher** (95% CI: 8.82 lower - 16.36 higher) | **Very low**<br>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

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**Table S30.**
Population: Adults 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 infection events 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 infection events to determine whether mizoribine made a difference |

| | | | | |
|---|---|---|---|---|
| glucocorticoid alone | Follow up 25 months | | | |
| Malignancy | Relative risk: 3.0 (95% CI: 0.13 - 69.7)<br>Based on data from 42 patients in 1 study[9]<br>Follow up 30 months | **0** per 1000 **0** per 1000<br><br>Difference: **0 per 1000** (95% CI: 0 - 0) | **Very low**<br>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)<br>Based on data from 24 patients in 1 study[11]<br>Follow up 30 months | **466** per 1000 **885** per 1000<br><br>Difference: **419 more per 1000** (95% CI: 28 more - 1132 more) | **Very low**<br>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:<br>Scale: - Lower better | <br>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**

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**Table S31.**
Population: Adults with IgA nephropathy
Intervention: Atacicept 25 or 75 mg subcutaneously once weekly
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 132 patients in 2 studies[1] Follow up 8 and 11 months | **0** per 1000 | **0** per 1000 Difference: **0 per 1000** (95% CI: 37 fewer - 37 more) | **Very low** Due to very serious imprecision[2] | We are uncertain whether atacicept increases or decreases 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: 1.32 (95% CI: 0.76 – 2.28) Based on data from 116 patients in 1 study[3] Follow up 8 and 11 months | 324 per 1000 | 427 per 1000 Difference: **103 more per 1000** (95% CI: 9 fewer - 294 more) | **Low** Due to very serious imprecision[4] | Atacicept may increase 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**<br>Timeframe | **Study results and measurements** | **Absolute effect estimates**<br>Placebo Atacicept | **Certainty of the evidence** | **Plain text summary** |
|---|---|---|---|---|
| GFR loss<br>≥3 years | Measured by:<br>Scale: - Lower better | Difference: | | No studies were found that looked at GFR loss (≥3 years) |
| Proteinuria<br>≥3 years | Measured by:<br>Scale: - Lower better | Difference: | | No studies were found that looked at proteinuria (≥3 years) |
| Adverse events, serious | Relative risk: 0.57 (95% CI:0.12 – 2.69)<br>Based on data from 132 patients in 2 studies[5]<br>Follow up 8 and 11 months | **103** per 1000 **54** per 1000<br>Difference: **49 fewer per 1000** (95% CI: 154 fewer - 57 more) | **Very low**<br>Due to very serious imprecision[6] | We are uncertain whether atacicept increases or decreases serious adverse events |

1. Primary studies [Barratt 2020][Lafayette 2024] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Imprecision: Very Serious.** No events.
3. Primary study [Lafayette 2024] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Imprecision: Very Serious.** Wide confidence interval, single study.
5. Primary studies [Barratt 2020][Lafayette 2024] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Imprecision: Very Serious.** Very wide confidence interval.

**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]

[Lafayette 2024] Lafayette R, Barbour S, Israni R, Wei X, Eren N, Floege J, Jha V, Kim SG, Maes B, Phoon RKS, Singh H, Tesař V, Lin CJF, Barratt J. A phase 2b, randomized, double-blind, placebo-controlled, clinical trial of atacicept for treatment of IgA nephropathy. Kidney Int. 2024;105(6):1306-1315. doi: 10.1016/j.kint.2024.03.012. [PMID: 38552841]

**Table S32.**
Population: Adults with IgA nephropathy
Intervention: Telitacicept 160 or 240 mg subcutaneously once weekly
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 all-cause 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**<br>Timeframe | **Study results and measurements** | **Absolute effect estimates**<br>Placebo | Telitacicept | **Certainty of the evidence** | **Plain text summary** |
|---|---|---|---|---|---|
| GFR loss<br>6 months | Measured by: CKD-EPI<br>Scale: - Lower better<br>Based on data from 42 patients in 1 study[7]<br>Follow up 24 weeks | **−7.3** ml/min/1.73 $m^2$ | **3.4** ml/min/1.73 $m^2$ loss<br>Difference: **10.7 (−8.3, 29.8)** | **Very low**<br>Due to very serious imprecision[8] | We are uncertain whether telitacicept increases or decreases GFR loss |
| Proteinuria<br>6 months | Measured by:<br>Scale: - Lower better<br>Based on data from 42 patients in 1 study[9]<br>Follow up 24 weeks | **−0.3** g/d | **−0.4** g/d<br>Difference: **−0.1 (−1.0, 0.7)** | **Very low**<br>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)<br>Based on data from 44 patients in 1 study[11]<br>Follow up 11 months | **71** per 1000 | **100** per 1000<br>Difference: **29 more per 1000** (95% CI: 144 fewer - 201 more) | **Very low**<br>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: Adults with IgA nephropathy
Intervention: Cemdisiran
Comparator: Placebo

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Placebo | Cemdisiran | **Certainty of the evidence** | **Plain text summary** |
|---|---|---|---|---|---|
| All-cause mortality | Relative risk: (95% CI: -) Based on data from 31 patients in 1 study[1] Mean follow up 32 months | **0** per 1000 | **45** per 1000 Difference: **45 more per 1000** (95% CI: 42 fewer - 132 more) | **Very low** Due to very serious imprecision[2] | We are uncertain whether cemdisiran increases or decreases 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 | (95% CI: - ) | Difference: | | | No studies were found that looked at annual GFR loss |
| Proteinuria, urinary protein-to-creatinine ratio | Measured by: Scale: - Lower better Based on data from 31 patients in 1 study[3] | **1.10** g/24 h | **0.69** g/24 h Difference: MD **0.41 lower** (95% CI: 0.96 - 0.14 higher) | **Very low** Due to very serious imprecision[4] | We are uncertain whether cemdisiran increases or decreases 24-hour |

| | | | | |
|---|---|---|---|---|
| | Mean follow up 32 months | | | urinary protein-to-creatinine ratio |
| Adverse events, serious | Relative risk: (95% CI: -)<br>Based on data from 31 patients in 1 study[5]<br>Mean follow up 32 months | **0** per 1000 **45** per 1000<br>Difference: **45 more per 1000** (95% CI: 42 fewer - 132 more) | **Very low**<br>Due to very serious imprecision[6] | We are uncertain whether cemdisiran increases or decreases serious adverse events |

1. Primary study [Barratt 2024 38214599] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimate.
3. Primary study [Barratt 2024 38214599] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Very Serious.** Only data from one study, small sample with imprecise estimate.
5. Primary study [Barratt 2024 38214599] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimate.

**References**

[Barratt 2024 38214599] Barratt J, Liew A, Yeo SC, Fernström A, Barbour SJ, Sperati CJ, Villanueva R, Wu MJ, Wang D, Borodovsky A, Badri P, Yureneva E, Bhan I, Cattran D; Cemdisiran Phase 2 Study Investigators and Collaborators. Phase 2 Trial of Cemdisiran in Adult Patients with IgA Nephropathy: A Randomized Controlled Trial. Clin J Am Soc Nephrol. 2024 Apr 1;19(4):452-462. doi: 10.2215/CJN.0000000000000384. [PMID: 38214599]

**Table S34.**
Population: Adults with IgA nephropathy
Intervention: Narsoplimab 370 mg intravenously once weekly
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 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, 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:<br>Scale: - Lower better | Difference: | | | No studies were found that looked at annual GFR loss |
| Proteinuria | Measured by: % reduction<br>Scale: - Lower better<br>Based on data from 9 patients in 1 study[3]<br>Follow up 18 weeks | **−18.0%** [median] | **−18.4%** [median]<br>Difference [in median values]: **−0.4%** | **Very low**<br>Due to very serious imprecision[4] | We are uncertain whether narsoplimab increases or decreases proteinuria |
| Adverse events, serious | Relative risk: 2.00 (95% CI: 0.24 – 16.6)<br>Based on data from 12 patients in 1 study[1]<br>Follow up 18 weeks | **167** per 1000 | **333** per 1000<br>Difference: **167 more per 1000** (95% CI: 301 fewer - 634 more) | **Very low**<br>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 S35.**
Population: Adults with IgA nephropathy
Intervention: Fostamatinib 100 or 150 mg
Comparator: Placebo

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Placebo | Fostamatinib | **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 | Based on data from 76 patients in 1 study[1] Mean follow up 24 weeks RR 0.57 (95% CI: 0.21 - 1.52) | **240** per 1000 | **137** per 1000 Difference: **103 fewer per 1000** (95% CI: 295 fewer - 89 more) | **Very low** Due to very serious imprecision[2] | We are uncertain whether fostamatinib increases or decreases upper respiratory or urinary tract 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 | (95% CI: - ) | Difference: | | | No studies were found that looked at annual GFR loss |
| Proteinuria, urinary protein- | Measured by: Scale: - Lower better | **-177.4** g/24 h | **-157.5** g/24 h | **Very low** | We are uncertain whether 150 mg of |

| | | | | |
|---|---|---|---|---|
| to-creatinine ratio | Based on data from 50 patients in 1 study[3] Mean follow up 24 weeks | Difference: NMD **19.9 greater reduction** (95% CI: 211 greater - 171 less) | Due to very serious imprecision[4] | fostamatinib increases or decreases change in 24-hour urinary protein-to-creatinine ratio |
| Adverse events, serious | Based on data from 76 patients in 1 study[5] Mean follow up 24 weeks RR 0.98 (95% CI: 0.19 – 5.00) | **80** per 1000 **78** per 1000 Difference: **2 fewer per 1000** (95% CI: 131 fewer - 128 more) | **Very low** Due to very serious imprecision[6] | We are uncertain whether fostamatinib increases or decreases serious adverse events |

1. Primary study [Tam 2023 38106605] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Very Serious.** Only data from one study, small sample with imprecise estimate.
3. Primary study [Tam 2023 38106605] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimate.
5. Primary study [Tam 2023 38106605] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Very Serious.** Only data from one study, small sample with very imprecise estimate.

**References**

[Tam 2023 38106605]. Tam FWK, Tumlin J, Barratt J, Rovin BH, Roberts ISD, Roufosse C, Cook HT, Bhangal G, Brown AL, Busch M, Dudhiya F, Duliege AM, Fraser DJ, Gale DP, Huang CC, Lai PC, Lee M, Masuda ES, McAdoo SP, Rosenkranz AR, Sommerer C, Sunder-Plassmann G, Szeto CC, Tang SCW, Williamson DE, Willcocks L, Vielhauer V, Kim MJ, Todd L, Zayed H, Tong-Starksen S, Lafayette R. Randomized Trial on the Effect of an Oral Spleen Tyrosine Kinase Inhibitor in the Treatment of IgA Nephropathy. Kidney Int Rep. 2023 Sep 30;8(12):2546-2556. doi: 10.1016/j.ekir.2023.09.024. [PMID: 38106605]

**Table S36.**
Population: Adults with IgA nephropathy
Intervention: Iptacopan 10, 50, 100, or 200 mg
Comparator: Placebo

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Placebo or no treatment | Iptacopan | **Certainty of the evidence** | **Plain text summary** |
|---|---|---|---|---|---|
| All-cause mortality | Based on data from 112 patients in 1 study[1] Mean follow up 3 months | 0 per 1000 | 0 per 1000 Difference: **0 per 1000** (95% CI: 73 fewer - 73 more) | **Very low** and very serious imprecision[2] | We are uncertain whether iptacopan increases or decreases all-cause mortality |
| Kidney failure or doubling serum creatinine | (95% CI: - ) (95% CI: - ) | Difference: | | | No studies were found that looked kidney failure oe doubling of 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 | (95% CI: - ) | Difference: | | | No studies were found that looked at complete remission of proteinuria |
| Annual GFR loss | (95% CI: - ) | | | | |

| | | | | |
|---|---|---|---|---|
| | | Difference: | | No studies were found that looked at annual GFR loss |
| Serum creatinine | (95% CI: - ) | Difference: | | No studies were found that looked at serum creatinine |
| Proteinuria | Measured by:<br>Scale: -<br>Based on data from 51 patients in 1 study[3]<br>Mean follow up 3 months | **-12** g/24 h Mean **-31** g/24 h Mean<br>Difference: NMD **23% greater reduction**<br>(80% CI: 8% less – 34% greater) | **Very low**<br>Due to very serious imprecision[4] | We are uncertain whether iptacopan increases or decreases proteinuria |
| Adverse events, serious | Based on data from 112 patients in 1 study[5]<br>Mean follow up 3 months<br>RR 0.29<br><br>(95% CI: 0.02 – 4.43) | **11** per 1000 **40** per 1000<br><br>Difference: **29 more per 1000**<br>(95% CI: 109 fewer - 52 more) | **Very low**<br>and very serious imprecision[6] | We are uncertain whether iptacopan increases or decreases serious adverse events |

1. Primary study [Zhang 2024 37914086] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Very Serious.** Only data from one study, small sample with imprecise estimate.
3. Primary study [Zhang 2024 37914086] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Very Serious.** Only data from one study, small sample with imprecise estimate.
5. Primary study [Zhang 2024 37914086] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Very Serious.** Only data from one study, small sample with imprecise estimate.

**References**

[Zhang 2024 37914086]. Zhang H, Rizk DV, Perkovic V, Maes B, Kashihara N, Rovin B, Trimarchi H, Sprangers B, Meier M, Kollins D, Papachristofi O, Milojevic J, Junge G, Nidamarthy PK, Charney A, Barratt J. Results of a randomized double-blind placebo-controlled Phase 2 study propose iptacopan as an alternative complement pathway inhibitor for IgA nephropathy. Kidney Int. 2024 Jan;105(1):189-199. doi: 10.1016/j.kint.2023.09.027. Epub 2023 Oct 31. [PMID: 37914086]

**Table S37.**
Population: Adults with IgA nephropathy
Intervention: Sibeprenlimab 2, 4, or 8 mg/kg
Comparator: Placebo

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Placebo | Sibeprenlimab | **Certainty of the evidence** | **Plain text summary** |
|---|---|---|---|---|---|
| Treatment-related mortality | Based on data from 155 patients in 1 study[1] Mean follow up 12 months<br><br>RR 0.11 (95% CI: 0.00-2.65) | 26 per 1000 | 0 per 1000<br><br>Difference: **26 fewer per 1000** (95% CI: 77 fewer - 25 more) | **Very low** Due to very serious imprecision[2] | We are uncertain whether sibeprenlimab increases or decreases treatment-related mortality |
| Kidney failure or doubling serum creatinine | (95% CI: - )<br><br>(95% CI: - ) | Difference: | | | No studies were found that looked at kidney failure or doubling of serum creatinine |
| ≥50% GFR loss | (95% CI: - ) | Difference: | | | No studies were found that looked at ≥50% GFR loss |
| Infection | Based on data from 155 patients in 1 study[3] Mean follow up 12 months<br><br>RR 0.84 (95% CI: 0.59 – 1.18) | 553 per 1000 | 462 Per 1000<br><br>Difference: **91 fewer per 1000** (95% CI: 273 fewer - 90 more) | **Very Low** Due to very serious imprecision[4] | We are uncertain whether sibeprenlimab increases or decreases 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 |

| | | | | |
|---|---|---|---|---|
| Complete remission of proteinuria | (95% CI: - ) | Difference: | | No studies were found that looked at complete remission of proteinuria |
| Annual GFR loss | (95% CI: - ) | Difference: | | No studies were found that looked at annual GFR loss |
| Serum creatinine | (95% CI: - ) | Difference: | | No studies were found that looked at serum creatinine |
| Proteinuria, 24-hour urinary protein-to-creatinine ratio | Measured by:<br>Scale: -<br>Based on data from 76 patients in 1 study[5]<br>Mean follow up 12 months | **-20%** g/24 h Mean **-62%** g/24 h Mean<br>Difference: NMD **42% greater reduction**<br>(95% CI: 37.6% greater – 46.4% greater) | **Low**<br>Due to serious imprecision[6] | 8 mg/kg dose of sibeprenlimab may decrease 24-hour urinary protein-to-creatinine ratio |
| Adverse events, serious | Based on data from 155 patients in 1 study[7]<br>Mean follow up 12 months<br>RR 0.81<br>(95% CI: 0.14 – 4.02) | 53 per 1000 43 Per 1000<br>Difference: **10 fewer per 1000**<br>(95% CI: 90 fewer - 70 more) | **Very Low**<br>Due to very serious imprecision[8] | We are uncertain whether sibeprenlimab increases or decreases serious adverse events |

1. Primary study [Mathur 2024 37916620] Baseline/comparator: Control arm of reference used for intervention.
2. Imprecision: Very serious. Only data from one study, small sample with very imprecise estimate.
3. Primary study [Mathur 2024 37916620] Baseline/comparator: Control arm of reference used for intervention.
4. Imprecision: Very Serious. Only data from one study, small sample with imprecise estimate.
5. Primary study [Mathur 2024 37916620] Baseline/comparator: Control arm of reference used for intervention.
6. Imprecision: Serious. Only data from one study.
7. Primary study [Mathur 2024 37916620] Baseline/comparator: Control arm of reference used for intervention.
8. Imprecision: Very serious. Only data from one study, small sample with very imprecise estimate

**References**

[Mathur 2024 37916620]. Mathur M, Barratt J, Chacko B, Chan TM, Kooienga L, Oh KH, Sahay M, Suzuki Y, Wong MG, Yarbrough J, Xia J, Pereira BJG; ENVISION Trial Investigators Group. A Phase 2 Trial of Sibeprenlimab in Patients with IgA Nephropathy. N Engl J Med. 2024 Jan 4;390(1):20-31. doi: 10.1056/NEJMoa2305635. Epub 2023 Nov 2. [PMID: 37916620]

**Table S38.**
Population: Adults with IgA nephropathy
Intervention: Renin angiotensin system inhibitor (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 may decrease >50% increase in serum creatinine |
| 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 |
| Serum creatinine | Measured by:<br>Scale: - Lower better<br>Based on data from 168 patients in 3 studies[3]<br>Mean follow up 31 months | Mean Mean<br><br>Difference: **MD 39.37 lower** (95% CI: 71.95 lower - 6.80 lower) | **Moderate**<br>Due to serious risk of bias[4] | RASi probably decreases serum creatinine |
| Proteinuria | Measured by:<br>Scale: - Lower better<br>Based on data from 168 patients in 3 studies[5]<br>Mean follow up 31 months | g/24 h Mean g/24 h Mean<br><br>Difference: **MD 1.16 lower** (95% CI: 1.52 lower - 0.81 lower) | **Moderate**<br>Due to serious risk of bias[6] | RASi probably decreases proteinuria |
| Proteinuria – ACEi + ARB versus ARB or ACEi alone | Measured by:<br>Scale: - Lower better<br>Based on data from 67 patients in 2 studies[7]<br>Mean follow up 7.5 months | g/24 h Mean g/24 h Mean<br><br>Difference: **MD 0.49 lower** (95% CI: 0.72 lower - 0.25 lower) | **Low**<br>Due to serious risk of bias, Due to serious imprecision[8] | ACEi + ARB may decrease proteinuria |
| Creatinine clearance | Measured by:<br>Scale: - High better<br>Based on data from 127 patients in 2 studies[9]<br>Mean follow up 10.4 months | Mean Mean<br><br>Difference: **MD 23.26 higher** (95% CI: 10.40 higher - 36.12 higher) | **Moderate**<br>Due to serious risk of bias[10] | RASi 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

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[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 S39.**
Population: Adults with IgA nephropathy
Intervention: Renin angiotensin system inhibitor (RASi) plus glucocorticoid
Comparator: Glucocorticoid alone

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Glucocorticoid alone | RASi 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 |
| 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] | RASi plus glucocorticoid 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] | RASi plus glucocorticoid 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**

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**Table S40.**
Population: Adults with IgA nephropathy
Intervention: Angiotensin II receptor blocker (ARB) plus glucocorticoid plus tonsillectomy
Comparator: Glucocorticoid plus tonsillectomy

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Glucocorticoid plus tonsillectomy | ARB plus glucocorticoid plus tonsillectomy | **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: 0.93 (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 ARB plus glucocorticoid plus tonsillectomy 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 S41.**
Population: Adults with IgA nephropathy
Intervention: Angiotensin II receptor blocker (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 | Measured by:<br>Scale: - Lower better | Mean | Mean<br>Difference: | | No studies were found that looked at annual GFR loss |
| Serum creatinine | Measured by:<br>Scale: - Lower better | Mean | Mean<br>Difference: **MD 8.84 lower** | **Low**<br>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<br>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<br>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 S42.**
Population: Adults 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 | Measured by:<br>Scale: - Lower better | Difference: | | No studies were found that looked at annual GFR loss |
| Creatinine clearance | Measured by:<br>Scale: - High better<br>Based on data from 69 patients in 2 studies[9]<br>Mean follow up 15 months | ml/min Mean ml/min Mean<br><br>Difference: **MD 15.57 lower**<br>(95% CI: 34.94 lower - 3.79 higher) | **Very low**<br>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
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[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: Adults 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** |
|---|---|---|---|---|---|
| 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 study[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 |
| Complete remission | (95% CI: - ) | Difference: | | | No studies were found that looked at complete remission |
| Glucocorticoid-related adverse events | (95% CI: - ) | Difference: | | | No studies were found that looked at glucocorticoid-related adverse events |

| | | | | | |
|---|---|---|---|---|---|
| >50% increase in serum creatinine | Relative risk: 0.17 (95% CI: 0.02 - 1.21)<br>Based on data from 28 patients in 1 study[1]<br>Follow up 4 years | **429** per 1000 | **73** per 1000 | **Very low**<br>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 |
| | | Difference: **356 fewer per 1000** (95% CI: 420 fewer - 90 more) | | | |
| Creatinine clearance | Measured by:<br>Scale: - High better<br>Based on data from 28 patients in 1 study[7]<br>Follow up 4 years | Mean | Mean | **Very low**<br>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 |
| | | Difference: **7 higher** (95% CI: 10.13 lower - 24.13 higher) | | | |
| Annual GFR loss | Based on data from 28 patients in 1 study<br>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**<br>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 S44.**
Population: Adults with IgA nephropathy
Intervention: Fish oil plus angiotensin-converting enzyme inhibitor (ACEi) or angiotensin II receptor blocker (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** |
|---|---|---|---|---|---|
| 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:<br>Scale: - Lower better | Difference: | | | No studies were found that looked at annual GFR loss |
| Creatinine clearance | Measured by:<br>Scale: - High better | **67.7** ml/min Mean | **93.9** ml/min Mean<br>Difference: **MD 26.20 higher** | **Low**<br>Due to serious risk of bias, Due to | Fish oil plus ACEi or ARBs may improve creatinine clearance slightly |

| | | | | |
|---|---|---|---|---|
| | Based on data from 30 patients in 1 study[1] Follow up 6 months | (95% CI: 1.01 higher - 51.39 higher) | serious imprecision[2] | |

1. Systematic review with included studies: [94] **Baseline/comparator:** Control arm of reference used for intervention.
2. **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 S45.**
Population: Adults 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:<br>Scale: - High better<br>Based on data from 21 patients in 1 study[7]<br>Follow up 3 years | ml/min Mean ml/min Mean<br><br>Difference: **MD 21 higher** (95% CI: 0.19 lower - 42.19 higher) | **Very low**<br>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 S46.**
Population: Adults with IgA nephropathy
Intervention: Anticoagulant
Comparator: Other nonimmunosuppressive treatment

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Other non-immunosuppressive 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 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[1] | Relative risk: 1.38 (95% CI: 0.86 - 2.22) Based on data from 262 patients in 1 study[4] | **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 serious imprecision[5] | We are uncertain whether dipyridamole increases or decreases adverse events |

| | | | | |
|---|---|---|---|---|
| | Follow up 6 months | | | |
| Annual GFR loss | Measured by:<br>Scale: - Lower better | Difference: | | No studies were found that looked at annual GFR loss |
| Creatinine clearance[6] | Measured by:<br>Scale: - High better<br>Based on data from 38 patients in 1 study[7]<br>Follow up 33 months | ml/min Mean ml/min Mean<br><br>Difference: **MD 6 higher** (95% CI: 17.60 lower - 29.60 higher) | **Very low**<br>Due to very serious risk of bias, Due to very serious imprecision[8] | We are uncertain whether dipyridamole plus aspirin increases or decreases creatinine clearance |
| Creatinine clearance[1] | Measured by:<br>Scale: - High better<br>Based on data from 262 patients in 1 study[9]<br>Follow up 6 months | ml/min Mean ml/min Mean<br><br>Difference: **MD 15.90 lower** (95% CI: 19.99 lower - 11.81 lower) | **Low**<br>Due to very serious risk of bias, Due to serious imprecision, Upgraded due to Large magnitude of effect[10] | Dipyridamole 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 plus 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. Systematic review [137] with included studies: [76] **Baseline/comparator:** Control arm of reference used for intervention.
10. **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 S47.**
Population: Adults 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** |
|---|---|---|---|---|---|
| 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 all-cause mortality events 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 increases or decreases kidney failure |
| ≥50% loss of GFR | (95% CI: - ) | Difference: | | | No studies were found that looked at ≥50% loss of GFR |
| Malignancy | (95% CI: - ) | Difference: | | | No studies were found that looked at malignancy |
| Complete remission | (95% CI: - ) | Difference: | | | No studies were found that looked at complete remission |
| 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 increases or decreases infection |

| | | | | |
|---|---|---|---|---|
| Annual GFR loss | Measured by:<br>Scale: - Lower better | Difference: | | No studies were found that looked at annual GFR loss |
| Change in creatinine clearance | Measured by:<br>Scale: - High better<br>Based on data from 20 patients in 1 study[9]<br>Follow up 24 months | ml/min Mean ml/min Mean<br><br>Difference: **MD 7 higher** (95% CI: 10.62 lower - 24.62 higher) | **Very low**<br>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:<br>Scale: - High better<br>Based on data from 84 patients in 1 study[11]<br>Follow up 24 months | ml/min/1.73m$^2$ Mean ml/min/1.73m$^2$ Mean<br><br>Difference: **MD 1.28 lower** (95% CI: 6.73 lower - 4.17 higher) | **Low**<br>Due to very serious imprecision[12] | Clopidine plus 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 plus 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
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[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 S48.**
Population: Adults 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 S49.**
Population: Adults 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:<br>Scale: - High better | Difference: | | No studies were found that looked at annual GFR loss |
| eGFR | Based on data from 21 patients in 1 study<br>Follow up 6 months | After the duration of therapy, the statins arm (n=13) had an eGFR of 85 ml/min per 1.73 $m^2$ (IQR: 70–147); the placebo arm (n=8) had an eGFR of 77 | **Very low**<br>Due to serious risk of bias, Due to very serious imprecision[1] | We are uncertain whether statins increase or decrease eGFR |

| | | | | |
|---|---|---|---|---|
| | | ml/min per 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 S50.**
Population: Children 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:<br>Scale: - Lower better | Difference: | | | No studies were found that looked at annual GFR loss |
| Creatinine clearance | Measured by:<br>Scale: - High better<br>Based on data from 30 patients in 1 study[1] | ml/min Mean<br>Difference: **MD 22.60 higher** | ml/min Mean | **Very low**<br>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**

[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 S51.**
Population: Adults 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 |
| 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 |
| 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 |
| 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 study[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 S52.**
Population: Children 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** |
|---|---|---|---|---|---|
| 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 kidney failure events 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 |
| 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 | **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 S53.**
Population: Adults 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 |
| ≥50% loss of GFR | (95% CI: - ) | Difference: | | | No studies were found that looked at ≥50% loss of GFR |
| Malignancy | (95% CI: - ) | Difference: | | | No studies were found that looked at malignancy |
| Infection | Relative risk: 0.74 (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 |
| Complete remission | (95% CI: - ) | Difference: | | | No studies were found that looked at complete remission |
| 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 |

| | | | | |
|---|---|---|---|---|
| Annual loss in eGFR | Measured by:<br>Scale: - Lower better<br>Based on data from 50 patients in 1 study[5]<br>Follow up 11 months | ml/min/1.73 $m^2$ Mean ml/min/1.73 $m^2$ Mean<br><br>Difference: **MD 0.00 higher** (95% CI: 16.61 lower - 16.61 higher) | **Very low**<br>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 S54.**
Population: Adults with IgA nephropathy
Intervention: Sodium cromoglycate
Comparator: Placebo or no treatment

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Placebo or 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 |
| ≥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 loss of GFR | Measured by:<br>Scale: - Lower better | Difference: | | | No studies were found that looked at annual loss of GFR |
| Creatinine clearance | Measured by:<br>Scale: - High better<br>Based on data from 30 patients in 1 study[1] | **78.6** ml/min Mean | **87** ml/min Mean<br>Difference: **8.4 higher** (95% CI: 10.19 lower - 26.99 higher) | **Very low**<br>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 S55.**
Population: Adults with IgA nephropathy
Intervention: Allopurinol
Comparator: Placebo or no treatment

| **Outcome** Timeframe | **Study results and measurements** | **Absolute effect estimates** Placebo or 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:<br>Scale: - High better | Difference: | | | No studies were found that looked at annual GFR loss |
| eGFR | Measured by:<br>Scale: - High better<br>Based on data from 40 patients in 1 study[1]<br>Follow up 6 months | **68.9**<br>Mean<br>Difference: **MD 4.30 higher**<br>(95% CI: 17.89 lower - 26.49 higher) | **73.2**<br>Mean | **Very low**<br>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 S56.**
Population: Adults 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)<br>Based on data from 53 patients in 1 study[3]<br>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:<br>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 S57.**
Population: Children 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 worsens complete 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 worsens complete remission at last follow-up |

| | | | | |
|---|---|---|---|---|
| Annual GFR loss | Measured by:<br>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 S58.**
Population: Children 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 study[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 | Measured by:<br>Scale: - Lower better | Difference: | | No studies were found that looked at annual GFR loss |
| Creatinine clearance | Measured by:<br>Scale: - High better<br>Based on data from 26 patients in 1 study[5]<br>Mean follow up 66 months | **107** ml/min Mean **110** ml/min Mean<br><br>Difference: **MD 3.00 higher** (95% CI: 14.83 lower - 20.83 higher) | **Low**<br>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 S59.**
Population: Children 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:<br>Scale: - Lower better | Difference: | | | No studies were found that looked at annual GFR loss |
| 24-hour urine proteinuria<br>3 months | Measured by:<br>Scale: -<br>Based on data from 19 patients in 1 study[1]<br>Follow up 9 months | **220**<br>Mean | **580**<br>Mean<br>Difference: **MD 360 higher**<br>(95% CI: 43.35 lower - 763.35 higher) | **Very low**<br>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 3 months |
| 24-hour urine proteinuria<br>9 months | Measured by:<br>Scale: -<br>Based on data from 19 patients in 1 study[3]<br>Follow up 9 months | **31**<br>Mean<br><br>**80**<br>Mean<br><br>Difference: **MD 49 higher**<br>(95% CI: 3.09 higher - 94.91 higher) | **Low**<br>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 S60.**
Population: Children 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)<br>Based on data from 56 patients in 1 study[1]<br>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<br>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)<br>Based on data from 56 patients in 1 study[3]<br>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<br><br>Difference: **35 more per 1000** (95% CI: 175 fewer - 390 more) | **Low**<br>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)<br>Based on data from 56 patients in 1 study[6]<br>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<br><br>Difference: **34 fewer per 1000** (95% CI: 180 fewer - 312 more) | **Low**<br>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:<br>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 S61.**
Population: Adults 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)<br>Based on data from 54 patients in 1 study[1]<br>Follow up 12 months | **207** per 1000 | **39** per 1000<br>Difference: **168 fewer per 1000** (95% CI: 203 fewer - 104 more) | **Low**<br>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)<br>Based on data from 54 patients in 1 study[3]<br>Follow up 12 months | **34** per 1000 | **40** per 1000<br>Difference: **6 more per 1000** (95% CI: 32 fewer - 635 more) | **Low**<br>Due to very serious imprecision[4] | Cyclophosphamide plus glucocorticoids 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 | Relative risk: 0.81 (95% CI: 0.36 - 1.81)<br>Based on data from 54 patients in 1 study[5]<br>Follow up 12 months | **345** per 1000 | **279** per 1000<br>Difference: **66 fewer per 1000** (95% CI: 221 fewer - 279 more) | **Low**<br>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<br>Difference: **2 fewer per 1000** (95% CI: 149 fewer - 378 more) | **Low**<br>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 per 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 eGFR <60 ml/min per 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 S62.**
Population: Children with IgA vasculitis
Intervention: Tacrolimus 0.05 mg/kg orally twice daily
Comparator: Cyclophosphamide 10 mg/kg intravenously × 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 |
| 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 |

| **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 S63.**
Population: Children with IgA vasculitis
Intervention: Tacrolimus 0.05 mg/kg orally twice daily
Comparator: Mycophenolate mofetil 10–15 mg/kg orally twice daily

| **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 |
| 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 |

| **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 S64.**
Population: Children with IgA vasculitis
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 S65.**
Population: Children with IgA vasculitis
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 |
| 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 |

| **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]