DATA SUPPLEMENT

Appendix A. Search strategies

Table S1. Search strategies for systematic review topics

Search dates: May 2018; updated search July 7, 2022; updated search April 25, 2023.

The updated searches conducted in 2023 included both lupus nephritis and ANCA and combined all subtopics (antimalarials, immunosuppressive treatments of both proliferative and non-proliferative lupus nephritis)

Database	Search strategy
PubMed	(wegener* OR systemic vasculitis OR ((renal OR kidney*) AND vasculitis) OR rapidly progressive glomeruloneph* OR (glomerular* AND necrosis) OR (glomerular* AND crescent*) OR anti-neutrophil cytoplasmic antibod* OR antineutrophil cytoplasmic antibod* OR (anca AND vasculitis) OR lupus nephritis OR "lupus glomerulonephritis" OR "Lupus Nephritis"[Mesh]) AND ("Random Allocation"[Mesh] OR "Clinical Trial" [Publication Type] OR "Double-Blind Method"[Mesh] OR "Single-Blind Method"[Mesh] OR random* OR "Placebos"[Mesh] OR placebo OR ((clinical OR controlled) AND trial*) OR ((singl* OR doubl* OR trebl* OR tripl*) AND (blind* OR mask*)) OR rct OR crossover OR cross-over OR cross-over OR "treatment switching" OR "Treatment Switching"[Mesh] OR RCT OR "Randomized Controlled Trial" [Publication Type])
Embase	#1 'vasculitis'/exp OR 'vasculitis' #2 renal OR kidney* #3 #1 AND #2 #4 'rapidly progressive glomerulonephritis' #5 glomerular AND necrosis #6 glomerular* AND crescent* #7 cytoplasmic AND antibod* #8 antineutrophil OR 'anti neutrophil' #9 #7 AND #8 #10 'anca associated vasculitis' #11 'wegener granulomatosis' #12 granulomatosis AND polyangiitis #13 systemic #14 #1 AND #13 #15 wegener* #16 #3 OR #4 OR #5 OR #6 OR #9 OR #10 OR #11 OR #12 OR #14 OR #15 #17 'lupus erythematosus nephritis' #18 'lupus nephritis' #19 'lupus glomerulonephritis' #20 #16 OR #17 OR #18 OR #19 #21 'randomized controlled trial' #22 'crossover procedure' #23 'double blind procedure' #24 'double-blind procedure' #25 'single blind procedure' #26 'single-blind procedure' #27 random* #28 factorial* #29 crossover OR 'cross over'

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

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

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

IOM Standard	Description	Addressed in 2020 KDIGO BP in CKD guideline
Establishing transparency	Clear description on the process of guideline development.	See *Methods for Guideline Development*
Management of conflicts of interests	Disclosure of a comprehensive conflict of interests of the Work Group against a set-criteria and a clear strategy to manage conflicts of interests	See *Work Group Financial Disclosures*
Guideline group composition and guideline development	Appropriate clinical and methodological expertise in the Work Group The processes of guideline development are transparent and allow for involvement of all Work Group Members	For guideline group composition – see *Work Group Membership* For guideline development process see *Methods for Guideline Development*
Establishing evidence foundations for rating strength of recommendations	Rationale is provided for the rating the strength of the recommendation and the transparency for the rating the quality of the evidence.	See *Methods for Guideline Development*
Articulation of recommendations	Clear and standardized wording of recommendations	All recommendations were written to standards of GRADE and were actionable statements. Please see *Methods for Guideline Development*
External review	An external review of relevant experts and stakeholders was conducted. All comments received from external review are considered for finalization of the guideline.	An external public review was undertaken in June 2023.
Updating	An update for the guidelines is planned, with a provisional timeframe provided.	The KDIGO clinical practice guideline will be updated. However, no set timeframe has been provided.

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

Appropriate IOM systematic review standards*	Addressed in 2020 KDIGO diabetes in CKD guideline
Methods	
Include a research protocol with appropriate eligibility criteria (PICO format)	See *Table 4 clinical question and systematic review topics in PICO format*
Include a search strategy	See *Appendix A*
Include a study selection and data extraction process	See guideline development process see *Methods for Guideline Development – Literature searching and article selection, data extraction*
Methods on critical appraisal	See *Methods for Guideline Development – Critical appraisal of studies*
Methods of synthesize of the evidence	See *Methods for Guideline Development – Evidence synthesis and meta-analysis*
Results	
Study selection processes	See *Methods for Guideline Development – Figure MC1 – Search yield and study flow diagram*
Appraisal of individual studies quality	The summary of findings tables in Appendix C & D provide an assessment of risk of bias for all studies in a comparison between intervention and comparator.
Meta-analysis results	See *Appendix C & D* for summary of findings tables for meta-analysis results for all critical and important outcomes
Table and figures	See *Appendix C & D* for summary of findings tables

References

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

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

Table S4.
Population: Patients with ANCA-associated vasculitis and mild-to-moderate CKD
Intervention: Rituximab
Comparator: Cyclophosphamide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Cyclophosphamide	Rituximab	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality 6 months	Relative risk: 1.0 (95% CI: 0.21 - 4.7) Based on data from 241 patients in 2 studies[1] Follow up 21 months (mean)	**28** per 1000	**28** per 1000 Difference: **0 fewer per 1000** (95% CI: 22 fewer - 104 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether rituximab increases or decreases all-cause mortality at 6 months
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection[3]	Relative risk: 0.89 (95% CI: 0.42 - 1.92) Based on data from 241 patients in 2 studies[4] Follow up 21 months (mean)	**92** per 1000	**82** per 1000 Difference: **10 fewer per 1000** (95% CI: 53 fewer - 85 more)	**Moderate** Due to serious imprecision[5]	Rituximab probably made little or no difference on infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission 6 months	Relative risk: 1.02 (95% CI: 0.79 - 1.32) Based on data from 236 patients in 2 studies[6] Follow up 21 months (mean)	**661** per 1000	**674** per 1000 Difference: **13 more per 1000** (95% CI: 139 fewer - 212 more)	**Moderate** Due to serious imprecision[7]	Rituximab probably has little or no difference on complete remission at 6 months
Complete remission - PR3-ANCA 6 months	Relative risk: 1.01 (95% CI: 0.77 - 1.33) Based on data from 114 patients in 1 study[8] Follow up 6 months	**646** per 1000	**652** per 1000 Difference: **6 more per 1000** (95% CI: 149 fewer - 213 more)	**Low** Due to very serious imprecision[9]	Rituximab may have had little or no difference on complete remission in PR3-ANCA at 6 months

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Cyclophosphamide	 Rituximab	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Complete remission - MPO-ANCA 6 months	Relative risk: 0.95 (95% CI: 0.65 - 1.39) Based on data from 114 patients in 1 study[10] Follow up 6 months	**636** per 1000	**604** per 1000 Difference: **32 fewer per 1000** (95% CI: 223 fewer - 248 more)	**Low** Due to very serious imprecision[11]	Rituximab may have had little or no difference on complete remission in MPO-ANCA at 6 months
Relapse 1-6 months	Relative risk: 0.63 (95% CI: 0.35 - 1.14) Based on data from 187 patients in 1 study[12] Follow up 18 months	**242** per 1000	**152** per 1000 Difference: **90 fewer per 1000** (95% CI: 157 fewer - 34 more)	**Moderate** Due to serious imprecision[13]	Rituximab probably has little or no difference on relapse from 1-6 months
Sustained remission 12 months	Relative risk: 0.93 (95% CI: 0.66 - 1.3) Based on data from 44 patients in 1 study[14] Follow up 24 months	**818** per 1000	**761** per 1000 Difference: **57 fewer per 1000** (95% CI: 278 fewer - 245 more)	**Low** Due to very serious imprecision[15]	Rituximab may have little or no difference on sustained remission at 12 months
Serious adverse events	Relative risk: 0.98 (95% CI: 0.89 - 1.09) Based on data from 242 patients in 2 studies[16] Follow up 21 months (mean)	**818** per 1000	**802** per 1000 Difference: **16 fewer per 1000** (95% CI: 90 fewer - 74 more)	**Moderate** Due to serious risk of bias[17]	Rituximab probably has little or no difference on serious adverse events
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [427], [413] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear of outcome assessors, resulting in potential for detection bias in RAVE 2010; **Imprecision: Very Serious.** Wide confidence intervals, due to few events.
3. Serious infection
4. Systematic review [448] with included studies: [413], [427] **Baseline/comparator:** Control arm of reference used for intervention.
5. **Imprecision: Serious.**
6. Systematic review [448] with included studies: [413], [427] **Baseline/comparator:** Control arm of reference used for intervention.
7. **Imprecision: Serious.** Low number of patients.
8. Systematic review [448] with included studies: [427] **Baseline/comparator:** Control arm of reference used for intervention.
9. **Imprecision: Very Serious.** Low number of patients, only data from one study, Wide confidence intervals.
10. Systematic review [448] with included studies: [427] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Imprecision: Very Serious.** Low number of patients, Wide confidence intervals, only data from one study.
12. Systematic review [448] with included studies: [427] **Baseline/comparator:** Control arm of reference used for intervention.
13. **Imprecision: Serious.** Low number of patients, only data from one study.
14. Primary study [413] **Baseline/comparator:** Control arm of reference used for intervention.
15. **Imprecision: Very Serious.** Only data from one study, Low number of patients, Wide confidence intervals.
16. Systematic review [448] with included studies: [427], [413] **Baseline/comparator:** Control arm of reference used for intervention.
17. **Risk of bias: Serious.** Unclear of outcome assessors, resulting in potential for detection bias in RAVE 2010.

References

[413] Jones RB, Tervaert JW, Hauser T., Luqmani R., Morgan MD, Peh CA, et al. Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis. New England Journal of Medicine 2010;363(3):211-220

[427] Stone JH, Merkel PA, Spiera R., Seo P., Langford CA, Hoffman GS, et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. New England Journal of Medicine 2010;363(3):221-232

[448] Walters GD, Willis NS, Cooper TE et al. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews 2020;1 CD003232

Table S5.
Population: Patients with relapsing ANCA-associated vasculitis and mild-to-moderate CKD
Intervention: Rituximab then azathioprine
Comparator: Cyclophosphamide then azathioprine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Cyclophosphamide then azathioprine	Rituximab then azathioprine	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:			No studies were found that reported at all-cause mortality
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
Infection	(95% CI: -)	Difference:			No studies were found that reported at infection
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that reported ≥50% loss of GFR
Malignancy	(95% CI: -)	Difference:			No studies were found that reported malignancy
Complete remission 6 months	Relative risk: 1.59 (95% CI: 1.09 - 2.32) Based on data from 101 patients in 1 study[1] Follow up 18 months	**420** per 1000	**668** per 1000 Difference: **248 more per 1000** (95% CI: 38 more - 554 more)	**Moderate** Due to serious imprecision[2]	Rituximab probably increases complete remission at 6 months
Complete remission 12 months	Relative risk: 2.04 (95% CI: 1.16 - 3.6) Based on data from 101 patients in 1 study[3] Follow up 18 months	**240** per 1000	**490** per 1000 Difference: **250 more per 1000** (95% CI: 38 more - 624 more)	**Moderate** Due to serious imprecision[4]	Rituximab probably increases complete remission at 12 months
Complete remission 18 months	Relative risk: 1.86 (95% CI: 0.96 - 3.6) Based on data from 101 patients in 1 study[5] Follow up 18 months	**200** per 1000	**372** per 1000 Difference: **172 more per 1000** (95% CI: 8 fewer - 520 more)	**Moderate** Due to serious imprecision[6]	Rituximab probably has little or no difference on complete remission at 18 months

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Cyclophosphamide then azathioprine	 Rituximab then azathioprine	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Relapse	Relative risk: 0.31 (95% CI: 0.13 - 0.78) Based on data from 95 patients in 1 study[7] Follow up 18 months	**347** per 1000	**108** per 1000 Difference: **239 fewer per 1000** (95% CI: 302 fewer - 76 fewer)	**Moderate** Due to serious imprecision[8]	Rituximab probably decreases relapse
Major relapse	Relative risk: 0.06 (95% CI: 0.0 - 0.94) Based on data from 95 patients in 1 study[9] Follow up 18 months	**180** per 1000	**11** per 1000 Difference: **169 fewer per 1000** (95% CI: 180 fewer - 11 fewer)	**Moderate** Due to serious imprecision[10]	Rituximab probably decreases major relapse
Serious adverse events	(95% CI: -)	Difference:			No studies were found that reported serious adverse events
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that reported annual GFR loss

1. Systematic review [448] with included studies: [427] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Serious.** Low number of patients, only data from one study.
3. Systematic review [448] with included studies: [427] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Serious.** Low number of patients, only data from one study.
5. Systematic review with included studies: [427] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Serious.** Low number of patients, only data from one study.
7. Systematic review [448] with included studies: [427] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Imprecision: Serious.** Low number of patients, only data from one study.
9. Systematic review [448] with included studies: [427] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Imprecision: Serious.** Low number of patients, only data from one study.

References

[427] Stone JH, Merkel PA, Spiera R., Seo P., Langford CA, Hoffman GS, et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. New England Journal of Medicine 2010;363(3):221-232

[448] Walters GD, Willis NS, Cooper TE et al. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews 2020;1 CD003232

Table S6.
Population: Patients with systemic ANCA-associated vasculitis
Intervention: Pulse cyclophosphamide plus azathioprine
Comparator: Continuous cyclophosphamide plus azathioprine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Continuous cyclophosphamide plus azathioprine	**Absolute effect estimates** Pulse cyclophosphamide plus azathioprine	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.53 (95% CI: 0.19 - 1.52) Based on data from 149 patients in 1 study[1] Follow up 18 months	**123** per 1000	**65** per 1000 Difference: **58 fewer per 1000** (95% CI: 100 fewer - 64 more)	**Low** Due to very serious imprecision[2]	Pulse cyclophosphamide plus azathioprine may have little or no difference on all-cause mortality
All-cause mortality Long-term follow-up	Relative risk: 0.97 (95% CI: 0.48 - 1.96) Based on data from 133 patients in 1 study[3] Follow up Median 4.3 (IQR 2.95, 5.44) years	**191** per 1000	**185** per 1000 Difference: **6 fewer per 1000** (95% CI: 99 fewer - 183 more)	**Low** Due to very serious imprecision[4]	Pulse cyclophosphamide plus azathioprine may have little or no difference on all-cause mortality
End-stage kidney disease	Relative risk: 4.35 (95% CI: 0.52 - 36.13) Based on data from 116 patients in 1 study[5] Follow up 18 months	**19** per 1000	**83** per 1000 Difference: **64 more per 1000** (95% CI: 9 fewer - 667 more)	**Low** Due to very serious imprecision[6]	Pulse cyclophosphamide plus azathioprine may have little or no difference on end-stage kidney disease
End-stage kidney disease Long-term follow-up	Relative risk: 0.84 (95% CI: 0.35 - 1.99) Based on data from 133 patients in 1 study[7] Follow up 4.3 (IQR 2.95, 5.44) years (median)	**147** per 1000	**123** per 1000 Difference: **24 fewer per 1000** (95% CI: 96 fewer - 146 more)	**Low** Due to very serious imprecision[8]	Pulse cyclophosphamide plus azathioprine may have little or no difference on end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection[9]	Relative risk: 0.67 (95% CI: 0.27 - 1.67) Based on data from 149 patients in 1 study[10] Follow up 18 months	**137** per 1000	**92** per 1000 Difference: **45 fewer per 1000** (95% CI: 100 fewer - 92 more)	**Low** Due to very serious imprecision[11]	Pulse cyclophosphamide plus azathioprine may have little or no difference on infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Continuous cyclophosphamide plus azathioprine	 Pulse cyclophosphamide plus azathioprine	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Complete remission 18 months	Relative risk: 0.99 (95% CI: 0.94 - 1.03) Based on data from 116 patients in 1 study[12] Follow up 18 months	**1000** per 1000	**990** per 1000 Difference: **10 fewer per 1000** (95% CI: 60 fewer - 30 more)	**Moderate** Due to serious imprecision[13]	Pulse cyclophosphamide plus azathioprine probably has little or no difference on complete remission
Relapse	Relative risk: 1.89 (95% CI: 0.77 - 4.62) Based on data from 116 patients in 1 study[14] Follow up 18 months	**111** per 1000	**210** per 1000 Difference: **99 more per 1000** (95% CI: 26 fewer - 402 more)	**Low** Due to very serious imprecision[15]	Pulse cyclophosphamide plus azathioprine may increase relapse
Relapse Long-term follow-up	Relative risk: 1.57 (95% CI: 0.76 - 3.24) Based on data from 133 patients in 1 study[16] Follow up 4.3 (IQR 2.95, 5.44) years (median)	**147** per 1000	**231** per 1000 Difference: **84 more per 1000** (95% CI: 35 fewer - 329 more)	**Low** Due to very serious imprecision[17]	Pulse cyclophosphamide plus azathioprine may increase relapse
Leukopenia	Relative risk: 0.58 (95% CI: 0.36 - 0.92) Based on data from 149 patients in 1 study[18] Follow up 18 months	**452** per 1000	**262** per 1000 Difference: **190 fewer per 1000** (95% CI: 289 fewer - 36 fewer)	**Moderate** Due to serious imprecision[19]	Pulse cyclophosphamide plus azathioprine probably decreases leukopenia
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [432] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
3. Systematic review [448] with included studies: [432] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: No serious.** due to long-term follow-up study with post-randomization. However, with good attrition rate; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
5. Systematic review [448] with included studies: [432] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Very Serious.** due to few events, only data from one study, Wide confidence intervals.
7. Systematic review [448] with included studies: [432] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Imprecision: Very Serious.** due to few events, only data from one study, Wide confidence intervals.
9. Serious infections
10. Systematic review [448] with included studies: [432] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
12. Systematic review [448] with included studies: [432] **Baseline/comparator:** Control arm of reference used for intervention.
13. **Imprecision: Serious.** Only data from one study, Low number of patients, Wide confidence intervals.
14. Systematic review [448] with included studies: [432] **Baseline/comparator:** Control arm of reference used for intervention.
15. **Imprecision: Very Serious.** due to few events, Wide confidence intervals, only data from one study.
16. Systematic review [448] with included studies: [432] **Baseline/comparator:** Control arm of reference used for intervention.
17. **Imprecision: Very Serious.** due to few events, Wide confidence intervals, only data from one study.
18. Systematic review [448] with included studies: [432] **Baseline/comparator:** Control arm of reference used for intervention.
19. **Imprecision: Serious.** Only data from one study.

References

[432] de Groot K, Harper L, Jayne DRW, Flores Suarez LF, Gregorini G, Gross WL, Luqmani R, Pusey CD, Rasmussen N, Sinico RA, Tesar V, Vanhille P, Westman K, Savage COS. Pulse versus daily oral cyclophosphamide for induction of remission in antineutrophil cytoplasmic antibody-associated vasculitis: a randomized trial. Annals of Internal Medicine 2009;150(10):670-80

[448] Walters GD, Willis NS, Cooper TE et al. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews 2020;1 CD003232

Table S7.
Population: Patients with ANCA-associated vasculitis
Intervention: Mycophenolate mofetil
Comparator: Cyclophosphamide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Cyclophosphamide	Mycophenolate mofetil	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 1.4 (95% CI: 0.46 - 4.3) Based on data from 224 patients in 2 studies[1] Follow up 33 months (mean)	**45** per 1000	**63** per 1000 Difference: **18 more per 1000** (95% CI: 24 fewer - 149 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Mycophenolate mofetil may have little or no difference on all-cause mortality
End-stage kidney disease	Relative risk: 1.0 (95% CI: 0.14 - 6.9) Based on data from 140 patients in 1 study[3] Follow up 18 months	**29** per 1000	**29** per 1000 Difference: **0 fewer per 1000** (95% CI: 25 fewer - 171 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether mycophenolate mofetil increases or decreases end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.3 (95% CI: 0.81 - 2.06) Based on data from 290 patients in 4 studies[5] Follow up 20 months (mean)	**175** per 1000	**228** per 1000 Difference: **53 more per 1000** (95% CI: 33 fewer - 186 more)	**Moderate** Due to serious risk of bias[6]	Mycophenolate mofetil probably has little or no difference on infection
Malignancy	Relative risk: 1.04 (95% CI: 0.27 - 3.98) Based on data from 224 patients in 2 studies[7] Follow up 33 months (mean)	**36** per 1000	**37** per 1000 Difference: **1 more per 1000** (95% CI: 26 fewer - 107 more)	**Low** Due to serious risk of bias, Due to serious imprecision[8]	Mycophenolate mofetil may have little or no difference on malignancy
Complete remission 6 months	Relative risk: 1.09 (95% CI: 0.84 - 1.41) Based on data from 216 patients in 3 studies[9] Follow up 6 months	**658** per 1000	**717** per 1000 Difference: **59 more per 1000** (95% CI: 105 fewer - 270 more)	**Moderate** Due to serious risk of bias[10]	Mycophenolate mofetil probably makes little or no difference to remission
Relapse	Relative risk: 1.36 (95% CI: 0.8 - 2.31) Based on data from 189 patients in 2 studies[11] Follow up 33 months (mean)	**293** per 1000	**398** per 1000 Difference: **105 more per 1000** (95% CI: 59 fewer - 384 more)	**Moderate** Due to serious risk of bias,[12]	Mycophenolate mofetil probably has little or no difference on relapse

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Cyclophosphamide	Mycophenolate mofetil	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Major relapse	Relative risk: 1.32 (95% CI: 0.57 - 3.02) Based on data from 189 patients in 2 studies[13] Follow up 33 months (mean)	**91** per 1000	**120** per 1000 Difference: **29 more per 1000** (95% CI: 39 fewer - 184 more)	**Low** Due to serious risk of bias, Due to serious imprecision[14]	Mycophenolate mofetil may have little or no difference on relapse
Serious adverse events	Relative risk: 1.25 (95% CI: 0.86 - 1.81) Based on data from 140 patients in 1 study[15] Follow up 18 months	**400** per 1000	**500** per 1000 Difference: **100 more per 1000** (95% CI: 56 fewer - 324 more)	**Low** Due to serious risk of bias, Due to serious imprecision[16]	Mycophenolate mofetil may have little or no difference on serious adverse events
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [443], [444] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Wide confidence intervals.
3. Systematic review [448] with included studies: [444] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** Unclear of blinding of outcome assessors, resulting in potential for detection bias, due to inclusion of abstract only publication; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
5. Systematic review [448] with included studies: [404], [407], [412], [443] **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.
7. Systematic review [448] with included studies: [444], [443] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Wide confidence intervals.
9. Systematic review [448] with included studies: [444], [443], [404], [407] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias.
11. Systematic review [448] with included studies: [443], [444] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Unclear blinding of outcome assessors.
13. Systematic review [448] with included studies: [443], [444] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Risk of bias: Serious.** Unclear blinding of outcome assessors; **Imprecision: Serious.** Wide confidence intervals.
15. Systematic review [448] with included studies: [412] **Baseline/comparator:** Control arm of reference used for intervention.
16. **Risk of bias: Serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias, due to inclusion of MYCYC 2007 is an abstract and a full study report has not been published; **Imprecision: Serious.** Only data from one study, Low number of patients.

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Table S8.
Population: Patients with ANCA-associated vasculitis
Intervention: Methotrexate
Comparator: Cyclophosphamide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Cyclophosphamide	Methotrexate	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality 18 months	Relative risk: 0.94 (95% CI: 0.14 - 6.39) Based on data from 95 patients in 1 study[1] Follow up 18 months	**43** per 1000	**40** per 1000 Difference: **3 fewer per 1000** (95% CI: 37 fewer - 232 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether methotrexate increases or decreases all-cause mortality
End-stage kidney disease Long-term follow-up	Relative risk: 2.82 (95% CI: 0.12 - 67.52) Based on data from 95 patients in 1 study[3] Follow up 6 (0.1 - 10.8) years (median)	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI: 0 fewer - 0 fewer)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether methotrexate increases or decreases end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection Long-term follow-up	Relative risk: 1.56 (95% CI: 0.62 - 3.96) Based on data from 95 patients in 1 study[5] Follow up Median 6 (0.1 - 10.8) years	**174** per 1000	**271** per 1000 Difference: **97 more per 1000** (95% CI: 66 fewer - 515 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether methotrexate increases or decreases infection
Malignancy Long-term follow-up	Relative risk: 1.17 (95% CI: 0.34 - 4.1) Based on data from 95 patients in 1 study[7] Follow up 6 (0.1 - 10.8) years (median)	**65** per 1000	**76** per 1000 Difference: **11 more per 1000** (95% CI: 43 fewer - 202 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[8]	We are uncertain whether methotrexate increases or decreases malignancy
Complete remission 6 months	Relative risk: 0.96 (95% CI: 0.85 - 1.08) Based on data from 95 patients in 1 study[9] Follow up 18 months	**935** per 1000	**898** per 1000 Difference: **37 fewer per 1000** (95% CI: 140 fewer - 75 more)	**Low** Due to serious risk of bias, Due to serious imprecision[10]	Methotrexate may have little or no difference on complete remission
Relapse	Relative risk: 1.5 (95% CI: 1.03 - 2.17) Based on data from 89 patients in 1 study[11] Follow up 18 months	**465** per 1000	**698** per 1000 Difference: **233 more per 1000** (95% CI: 14 more - 544 more)	**Low** Due to serious risk of bias, Due to serious imprecision[12]	Methotrexate may increase relapse
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [433] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear 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 [448] with included studies: [433] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Unclear 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.
5. Systematic review [448] with included studies: [433] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
7. Systematic review [448] with included studies: [433] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
9. Systematic review [448] with included studies: [433] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study, Low number of patients.
11. Systematic review [448] with included studies: [433] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study, Low number of patients.

References

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[448] Walters GD, Willis NS, Cooper TE et al. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews 2020;1 CD003232

Table S9.
Population: Patients with systemic ANCA-associated vasculitis
Intervention: Pulse cyclophosphamide
Comparator: Continuous cyclophosphamide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Continuous cyclophosphamide	Pulse cyclophosphamide	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality At the end of follow-up	Relative risk: 0.87 (95% CI: 0.42 - 1.8) Based on data from 129 patients in 3 studies[1] Follow up 23 months (mean)	**294** per 1000	**256** per 1000 Difference: **38 fewer per 1000** (95% CI: 171 fewer - 235 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Pulse cyclophosphamide may have little or no difference on all-cause mortality
End-stage kidney disease At the end of the study	Relative risk: 1.7 (95% CI: 0.78 - 3.67) Based on data from 129 patients in 3 studies[3] Follow up 23 months (mean)	**118** per 1000	**201** per 1000 Difference: **83 more per 1000** (95% CI: 26 fewer - 315 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Pulse cyclophosphamide may have little or no difference on end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection[5]	Relative risk: 0.71 (95% CI: 0.32 - 1.58) Based on data from 129 patients in 3 studies[6] Follow up 23 months (mean)	**574** per 1000	**247** per 1000 Difference: **101 fewer per 1000** (95% CI: 216 fewer - 115 more)	**Low** Due to serious risk of bias, Due to serious imprecision[7]	Pulse cyclophosphamide may have little or no difference on infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	Relative risk: 1.17 (95% CI: 1.0 - 1.35) Based on data from 97 patients in 2 studies[8] Follow up 18 months	**813** per 1000	**951** per 1000 Difference: **138 more per 1000** (95% CI: 0 fewer - 285 more)	**Moderate** Due to serious risk of bias[9]	Pulse cyclophosphamide probably increases complete remission slightly
Relapse	Relative risk: 1.75 (95% CI: 1.0 - 3.05) Based on data from 119 patients in 3 studies[10] Follow up 23 months (mean)	**242** per 1000	**424** per 1000 Difference: **182 more per 1000** (95% CI: 0 fewer - 496 more)	**Low** Due to serious risk of bias, Due to serious imprecision[11]	Pulse cyclophosphamide may increase relapse

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Continuous cyclophosphamide	 Pulse cyclophosphamide	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Leukopenia	Relative risk: 0.43 (95% CI: 0.22 - 0.84) Based on data from 129 patients in 3 studies[12] Follow up 23 months (mean)	**382** per 1000 Difference: **218 fewer per 1000** (95% CI: 298 fewer - 61 fewer)	**164** per 1000	**Moderate** Due to serious risk of bias[13]	Pulse cyclophosphamide probably decreases leukopenia
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [405], [402], [396] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up in one study Haubitz 1998, studies were terminated early in two studies Gullerin 1997 and Haubitz 1998 due to differences between the groups.; **Imprecision: Serious.** Wide confidence intervals.
3. Systematic review [448] with included studies: [405], [402], [396] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up in one study Haubitz 1998, studies were terminated early in two studies Gullerin 1997 and Haubitz 1998 due to differences between the groups.; **Imprecision: Serious.** due to few events.
5. Serious infections
6. Systematic review [448] with included studies: [402], [396], [405] **Baseline/comparator:** Control arm of reference used for intervention.
7. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up in one study Haubitz 1998, studies were terminated early in two studies Gullerin 1997 and Haubitz 1998 due to differences between the groups.; **Imprecision: Serious.** Wide confidence intervals.
8. Systematic review [448] with included studies: [405], [402] **Baseline/comparator:** Control arm of reference used for intervention.
9. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up in one study Haubitz 1998, studies were terminated early in two studies Gullerin 1997 and Haubitz 1998 due to differences between the groups.
10. Systematic review [448] with included studies: [396], [402], [405] **Baseline/comparator:** Control arm of reference used for intervention.
11. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up in one study Haubitz 1998, studies were terminated early in two studies Gullerin 1997 and Haubitz 1998 due to differences between the groups., Incomplete data and/or large loss to follow up, due to [reason]; **Imprecision: Serious.** due to few events.
12. Systematic review [448] with included studies: [402], [396], [405] **Baseline/comparator:** Control arm of reference used for intervention.
13. **Risk of bias: Serious.** Incomplete data and/or large loss to follow up in one study Haubitz 1998, studies were terminated early in two studies Gullerin 1997 and Haubitz 1998 due to differences between the groups.

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[448] Walters GD, Willis NS, Cooper TE et al. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews 2020;1 CD003232

Table S10.
Population: Patients with ANCA-associated vasculitis and severe kidney disease
Intervention: Reduced-dose oral glucocorticoid
Comparator: Standard-dose oral glucocorticoid

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Reduced-dose oral glucocorticoid	**Absolute effect estimates** Standard-dose oral glucocorticoid	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.85 (95% CI: 0.60 - 1.22) Based on data from 838 patients in 2 studies[1] Follow up 6 months or median 2.9 years	**109** per 1000	**130** per 1000 Difference: **20 fewer per 1000** (95% CI: 52 fewer - 29 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Reduced-dose glucocorticoids may have little or no difference on all-cause mortality
End-stage kidney disease	Relative risk: 1.01 (95% CI: 0.75 – 1.36) Based on data from 838 patients in 2 studies[1] Follow up 6 months or median 2.9 years	**146** per 1000	**155** per 1000 Difference: **2 more per 1000** (95% CI: 39 fewer - 56 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Reduced-dose glucocorticoids may have little or no difference on end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection, serious	Relative risk: 0.57 (95% CI: 0.23 - 1.37) Based on data from 838 patients in 2 studies[1] Follow up 6 to 12 months	**239** per 1000	**326** per 1000 Difference: **140 fewer per 1000** (95% CI: 251 fewer - 121 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Reduced-dose glucocorticoids may have little or no difference on serious infection
Malignancy	Relative risk: 0.94 (95% CI: 0.06 – 14.75) Based on data from 134 patients in 1 study[3] Follow up 6 months	**14** per 1000	**15** per 1000 Difference: **1 fewer per 1000** (95% CI: 14 fewer - 206 more)	**Very low** Due to very serious imprecision and sparseness[4]	We are uncertain whether reduced dose glucocorticoids increases or decreases malignancy
Sustained remission	Relative risk: 1.04 (95% CI: 0.93 - 1.17) Based on data from 838 patients in 2 studies[1] Follow up 6 months or median 2.9 years	**600** per 1000	**573** per 1000 Difference: **23 more per 1000** (95% CI: 40 fewer - 97 more)	**Moderate** Due to serious risk of bias[5]	Reduced-dose glucocorticoids probably has little or no difference on sustained remission

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Reduced-dose oral glucocorticoid	 Standard-dose oral glucocorticoid	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Relapse	Relative risk: 6.60 (95% CI: 0.35 – 125.35) Based on data from 134 patients in 1 study[3] Follow up 6 months.	**43** per 1000	**0** per 1000 Difference: **43 more per 1000** (95% CI: 12 fewer - 99 more)	**Very low** Due to very serious imprecision and sparseness[4]	We are uncertain whether reduced dose glucocorticoids increases or decreases relapse
Adverse events, serious	Relative risk: 0.73 (95% CI: 0.34 – 1.57) Based on data from 838 patients in 2 studies[1] Follow up 6 months or median 2.9 years	**598** per 1000	**623** per 1000 Difference: **168 fewer per 1000** (95% CI: 411 fewer - 355 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Reduced-dose glucocorticoids may have little or no difference on serious adverse events
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Included studies: [LoVAS 2021], [449].
2. **Risk of bias: Serious.** Unblinded studies; **Imprecision: Serious.** Wide confidence intervals.
3. Included study: [LoVAS 2021].
4. **Risk of bias: Serious.** Unblinded studies; **Imprecision: Very Serious.** Very wide confidence intervals. **Other: Serious.** Single study only.
5. **Risk of bias: Serious.** Unblinded studies.

Commented [EB1]: Here and elsewhere, references need to be updated.

References

[LoVAS 2021] Furuta S, Nakagomi D, Kobayashi Y, et al. Effect of Reduced-Dose vs High-Dose Glucocorticoids Added to Rituximab on Remission Induction in ANCA-Associated Vasculitis: A Randomized Clinical Trial. JAMA. 2021 Jun 1;325(21):2178-2187. doi: 10.1001/jama.2021.6615. PMID: 34061144.

[449] Walsh M, Merkel PA, Peh CA, Szpirt WM, Puéchal X, Fujimoto S, Hawley CM, Khalidi N, Floßmann O, Wald R, et al.. Plasma Exchange and Glucocorticoids in Severe ANCA-Associated Vasculitis. New England Journal of Medicine 2020;382(622-631):622-631.

Table S11.
Population: Patients with ANCA-associated vasculitis and severe kidney disease
Intervention: Avacopan
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Avacopan	Placebo	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.99 (95% CI: 0.14 – 6.93) Based on data from 372 patients in 2 studies[1] Follow up 3 to 12 months	**6** per 1000	**2** per 1000 Difference: **0 fewer per 1000** (95% CI: 2 fewer - 11 more)	**Very low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether avacopan increases or decreases mortality
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 0.91 (95% CI: 0.79 – 1.04) Based on data from 372 patients in 2 studies[1] Follow up 3 to 12 months	**618** per 1000	**722** per 1000 Difference: **65 fewer per 1000** (95% CI: 152 fewer - 29 more)	**Low** Due to serious risk of bias, Due to serious imprecision[3]	Avacopan may make little or no difference in serious infections
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Remission, sustained[4]	Relative risk: 1.18 (95% CI: 1.00 – 1.40) Based on 372 patients in 2 studies[1] Follow up 3 to 12 months	**645** per 1000	**549** per 1000 Difference: **99 more per 1000** (95% CI: 0 fewer - 220 more)	**Moderate** Due to serious risk of bias[5]	Avacopan probably leads to increased remission

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Avacopan Placebo	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Relapse[6]	Relative risk: 0.48 (95% CI: 0.28 – 0.84) Based on data from 315 patients in 1 study[1] Follow up 12 months	**101** per 1000 **157** per 1000 Difference: **82 fewer per 1000** (95% CI: 113 fewer – 25 fewer)	**Very low** Due to serious risk of bias, Due to sparse data[7]	We are uncertain whether avacopan increases or decreases relapse
Adverse events, severe	Relative risk: 0.75 (95% CI: 0.61 – 0.94) Based on 372 patients in 2 studies[1] Follow up 3 to 12 months	**386** per 1000 **542** per 1000 Difference: **136 fewer per 1000** (95% CI: 211 fewer - 33 fewer)	**Moderate** Due to serious risk of bias[4]	Avacopan probably leads to fewer severe adverse events
Discontinuation due to adverse events	Relative risk: 0.89 (95% CI: 0.56 – 1.41) Based on 372 patients in 2 studies[1] Follow up 3 to 12 months	**150** per 1000 **166** per 1000 Difference: **18 fewer per 1000** (95% CI: 73 fewer – 68 more)	**Low** Due to serious risk of bias, Due to serious imprecision[3]	Avacopan may make little or no difference on adverse events leading to discontinuation
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:		No studies were found that looked at annual loss of GFR

1. Included studies: [Jayne 2021] [Merkel 2020].
2. **Risk of bias: Serious.** One of two studies with high loss to follow-up and change in primary outcome [Merkel 2020]; **Imprecision: Very serious.** Very wide confidence intervals. **Other: Serious.** Relative risk based on a single study since one study had no events [Merkel 2020]
3. **Risk of bias: Serious.** One of two studies with high loss to follow-up and change in primary outcome [Merkel 2020]; **Imprecision: Serious.** Wide confidence intervals.
4. Defined as BVAS = 0.
5. **Risk of bias: Serious.** One of two studies with high loss to follow-up and change in primary outcome [Merkel 2020].
6. Worsening of disease after previous BVAS=0.
7. **Risk of bias: Serious.** One of two studies with high loss to follow-up and change in primary outcome [Merkel 2020]; **Other: Very serious.** Sparse: single study only.

References

[Jayne 2021] Jayne DRW, Merkel PA, Schall TJ, Bekker P; ADVOCATE Study Group. Avacopan for the Treatment of ANCA-Associated Vasculitis. N Engl J Med. 2021 Feb 18;384(7):599-609. doi: 10.1056/NEJMoa2023386. PMID: 33596356

[Merkel 2020] Merkel PA, Niles J, Jimenez R, Spiera RF, Rovin BH, Bomback A, Pagnoux C, Potarca A, Schall TJ, Bekker P; CLASSIC Investigators. Adjunctive Treatment With Avacopan, an Oral C5a Receptor Inhibitor, in Patients With Antineutrophil Cytoplasmic Antibody-Associated Vasculitis. ACR Open Rheumatol. 2020 Nov;2(11):662-671. doi: 10.1002/acr2.11185. Epub 2020 Oct 31. PMID: 33128347

Table S12.
Population: Patients with ANCA-associated vasculitis and severe kidney disease
Intervention: Avacopan low dose (10 mg 2x/day)
Comparator: Avacopan high dose (30 mg 2x/day)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Avacopan low dose	Avacopan high dose	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: not calculable (0 events) Based on data from 29 patients in 1 study[1] Follow up 3 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI: 126 fewer – 126 more)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to sparse data[2]	We are uncertain whether lower-dose avacopan increases or decreases mortality
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection, serious	(95% CI: -)	Difference:			No studies were found that looked at serious infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Remission, sustained	Relative risk: 1.43 (95% CI: 0.73 – 2.80) Based on data from 29 patients in 1 study[1] Follow up 3 months	**200** per 1000	**573** per 1000 Difference: **23 more per 1000** (95% CI: 167 fewer - 567 more)	**Very low** Due to serious imprecision, Due to sparse data[3]	Avacopan probably leads to increased remission
Relapse	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Adverse events, severe	(95% CI: -)	Difference:			No studies were found that looked at severe adverse events
Discontinuation due to adverse events	(95% CI: -)	Difference:			No studies were found that looked at severe adverse events

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Avacopan low dose	Avacopan high dose	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Annual GFR loss (≥3 year follow-up)	(95% CI: -)	Difference:			No studies were found that looked at annual loss of GFR

1. Included study: [Merkel 2020].
2. **Risk of bias: Serious.** High loss to follow-up and change in primary outcome [Merkel_2020_33128347]; **Imprecision: Very serious.** No events. **Other: Serious.** Single study only.
3. **Risk of bias: Serious.** High loss to follow-up and change in primary outcome [Merkel_2020_33128347]; **Imprecision: Serious.** Wide confidence interval. **Other: Serious.** Single study only.

References

[Merkel 2020] Merkel PA, Niles J, Jimenez R, Spiera RF, Rovin BH, Bomback A, Pagnoux C, Potarca A, Schall TJ, Bekker P; CLASSIC Investigators. Adjunctive Treatment With Avacopan, an Oral C5a Receptor Inhibitor, in Patients With Antineutrophil Cytoplasmic Antibody-Associated Vasculitis. ACR Open Rheumatol. 2020 Nov;2(11):662-671. doi: 10.1002/acr2.11185. Epub 2020 Oct 31. PMID: 33128347

Table S13.
Population: Patients with ANCA-associated vasculitis and severe kidney disease
Intervention: Plasma exchange as adjunctive therapy
Comparator: Control (usual care)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Control (usual care)	Plasma exchange as adjunctive therapy	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Serious adverse events	Relative risk: 1.0 (95% CI: 0.89 - 1.11) Based on data from 841 patients in 2 studies[1] Follow up unclear	**613** per 1000	**613** per 1000 Difference: **0 fewer per 1000** (95% CI: 67 fewer - 67 more)	**Low** Due to very serious risk of bias[2]	Plasma exchange may have little or no difference on serious adverse events
All-cause mortality	Relative risk: 1.02 (95% CI: 0.78 - 1.33) Based on data from 989 patients in 7 studies[3] Follow up 30 months (mean)	**172** per 1000	**175** per 1000 Difference: **3 more per 1000** (95% CI: 38 fewer - 57 more)	**Low** Due to very serious risk of bias[4]	Plasma exchange may have little or no difference on all-cause mortality
All-cause mortality *Studies with newer plasma exchange regimens only*	Relative risk: 1.01 (95% CI: 0.78 - 1.33) Based on data from 925 patients in 4 studies[5] Follow up 30 months (mean)	**180** per 1000	**182** per 1000 Difference: **2 more per 1000** (95% CI: 40 fewer - 59 more)	**Moderate** Due to serious risk of bias[6]	Plasma exchange probably has little or no difference on all-cause mortality
End-stage kidney disease 3 months	Relative risk: 0.43 (95% CI: 0.23 - 0.78) Based on data from 147 patients in 2 studies[7] Follow up 3 months (mean)	**375** per 1000	**161** per 1000 Difference: **214 fewer per 1000** (95% CI: 289 fewer - 82 fewer)	**Moderate** Due to serious risk of bias[8]	Plasma exchange probably decreases end-stage kidney disease at 3 months
End-stage kidney disease 12 months	Relative risk: 0.45 (95% CI: 0.29 - 0.72) Based on data from 235 patients in 6 studies[9] Follow up 36 months (mean)	**376** per 1000	**169** per 1000 Difference: **207 fewer per 1000** (95% CI: 267 fewer - 105 fewer)	**Moderate** Due to serious risk of bias[10]	Plasma exchange probably decreases end-stage kidney disease
End-stage kidney disease 12 months *Studies with newer plasma exchange regimens only*	Relative risk: 0.44 (95% CI: 0.24 - 0.81) Based on data from 172 patients in 3 studies[11] Follow up 56 months (mean)	**376** per 1000	**165** per 1000 Difference: **211 fewer per 1000** (95% CI: 286 fewer - 71 fewer)	**Moderate** Due to serious risk of bias[12]	Plasma exchange probably decreases end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Control (usual care)	 Plasma exchange as adjunctive therapy	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Infection[13]	Relative risk: 1.26 (95% CI: 1.03 - 1.54) Based on data from 956 patients in 5 studies[14] Follow up 25 months (mean)	**253** per 1000	**319** per 1000 Difference: **66 more per 1000** (95% CI: 8 more - 137 more)	**Low** Due to very serious risk of bias[15]	Plasma exchange may increase infection
Infection[16] *Studies with newer plasma exchange regimens only*	Relative risk: 1.26 (95% CI: 1.02 - 1.55) Based on data from 893 patients in 3 studies[17] Follow up 36 months (mean)	**257** per 1000	**324** per 1000 Difference: **67 more per 1000** (95% CI: 5 more - 141 more)	**Low** Due to very serious risk of bias[18]	Plasma exchange may increase infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Sustained complete remission	Relative risk: 1.02 (95% CI: 0.89 - 1.16) Based on data from 704 patients in 1 study[19] Follow up unclear	**560** per 1000	**571** per 1000 Difference: **11 more per 1000** (95% CI: 62 fewer - 90 more)	**Very Low** Due to very serious risk of bias, Due to serious imprecision[20]	Plasma exchange may have little or no difference on complete remission
Relapse	Relative risk: 0.62 (95% CI: 0.3 - 1.26) Based on data from 137 patients in 1 study[21] Follow up 3.5 years (median)	**235** per 1000	**146** per 1000 Difference: **89 fewer per 1000** (95% CI: 164 fewer - 61 more)	**Moderate** Due to serious imprecision[22]	Plasma exchange probably has little or no difference on relapse
Annual GFR loss 3 years	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [411], [413] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Very Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to inclusion of abstract only study PEXIVAS.
3. Systematic review [448] with included studies: [400], [398], [428], [411], [422], [421], [413] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Very Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to one trial taking over 10 years and resulting in change in equipoise due to changing physicians, also one study allowed for cross-over one month after therapy, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to inclusion of abstract only study PEXIVAS that has a large weight in the meta-analysis; **Imprecision: No serious.**
5. Systematic review [448] with included studies: [413], [421], [428], [411] **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, due to inclusion of abstract only study PEXIVAS that has a large weight in the meta-analysis.

7. Systematic review [448] with included studies: [411], [428] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Serious.** Unclear lack of blinding of outcome assessors, resulting in potential for detection bias.
9. Systematic review [448] with included studies: [421], [416], [428], [411], [422], [398] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to one trial taking over 10 years and resulting in change in equipoise due to changing physicians, Incomplete data and/or large loss to follow up in Mauri 1985.
11. Systematic review [448] with included studies: [428], [421], [411] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to one trial taking over 10 years and resulting in change in equipoise due to changing physician.
13. Serious infections
14. Systematic review [448] with included studies: [398], [442], [421], [400], [411] **Baseline/comparator:** Control arm of reference used for intervention.
15. **Risk of bias: Very Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to one trial taking over 10 years and resulting in change in equipoise due to changing physicians, also one study allowed for cross-over one month after therapy, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to inclusion of abstract only study PEXIVAS that has a large weight in the meta-analysis.
16. Serious infections
17. Systematic review [448] with included studies: [411], [413], [421] **Baseline/comparator:** Control arm of reference used for intervention.
18. **Risk of bias: Very Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to one trial taking over 10 years and resulting in change in equipoise due to changing physicians, also one study allowed for cross-over one month after therapy, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to inclusion of abstract only study PEXIVAS that has a large weight in the meta-analysis.
19. Systematic review [448] with included studies: [442] **Baseline/comparator:** Control arm of reference used for intervention.
20. **Risk of bias: Very Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, due to inclusion of abstract only study PEXIVAS; **Imprecision: Serious.** Only data from one study.
21. Systematic review [448] with included studies: [411] **Baseline/comparator:** Control arm of reference used for intervention.
22. **Imprecision: Serious.** Only data from one study.

References

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Table S14.
Population: Patients with ANCA-associated vasculitis
Intervention: Maintenance therapy: Azathioprine
Comparator: Maintenance therapy: Cyclophosphamide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Cyclophosphamide	Azathioprine	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality Long-term follow-up	Relative risk: 0.77 (95% CI: 0.35 - 1.72) Based on data from 144 patients in 1 study[1] Follow up 8.5 years (median)	**164** per 1000	**126** per 1000 Difference: **38 fewer per 1000** (95% CI: 107 fewer - 118 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Azathioprine may have little or no difference on all-cause mortality
End-stage kidney disease Long-term follow-up	Relative risk: 1.65 (95% CI: 0.57 - 4.79) Based on data from 144 patients in 1 study[3] Follow up 8.5 years (median)	**68** per 1000	**112** per 1000 Difference: **44 more per 1000** (95% CI: 29 fewer - 258 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether azathioprine increases or decreases end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.03 (95% CI: 0.51 - 2.06) Based on data from 144 patients in 1 study[5] Follow up 18 months	**178** per 1000	**183** per 1000 Difference: **5 more per 1000** (95% CI: 87 fewer - 189 more)	**Moderate** Due to serious imprecision[6]	Azathioprine probably has little or no difference on infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Relapse 18 months	Relative risk: 1.13 (95% CI: 0.51 - 2.5) Based on data from 144 patients in 1 study[7] Follow up 18 months	**137** per 1000	**155** per 1000 Difference: **18 more per 1000** (95% CI: 67 fewer - 206 more)	**Moderate** Due to serious imprecision[8]	Azathioprine probably has little or no difference on relapse
Relapse Long-term follow-up	Relative risk: 1.46 (95% CI: 1.0 - 2.14) Based on data from 144 patients in 1 study[9] Follow up 8.5 years (median)	**360** per 1000	**526** per 1000 Difference: **166 more per 1000** (95% CI: 0 fewer - 410 more)	**Moderate** Due to serious imprecision[10]	Azathioprine may have no effect or slightly increase relapse in long-term follow-up

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Cyclophosphamide	 Azathioprine	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Leukopenia	Relative risk: 0.65 (95% CI: 0.42 - 0.99) Based on data from 144 patients in 1 study[11] Follow up 18 months	**479** per 1000	**311** per 1000 Difference: **168 fewer per 1000** (95% CI: 278 fewer - 5 fewer)	**Moderate** Due to serious imprecision[12]	Azathioprine may decrease leukopenia
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [408] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** due to long-term follow-up study post randomization but with a good attrition rate, due to [reason]; **Imprecision: Serious.** Only data from one study, Low number of patients, only data from one study, Low number of patients, Wide confidence intervals.
3. Systematic review [448] with included studies: [408] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** due to long-term follow-up study post randomization but with a good attrition rate. **Imprecision: Very Serious.** Only data from one study, Low number of patients, Wide confidence intervals.
5. Systematic review [448] with included studies: [408] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Serious.** Only data from one study, Low number of patients.
7. Systematic review [448] with included studies: [408] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Imprecision: Serious.** Only data from one study, Low number of patients.
9. Systematic review [448] with included studies: [408] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Risk of bias: No serious.** due to long-term follow-up study post randomization but with a good attrition rate; **Imprecision: Serious.** Only data from one study, Low number of patients.
11. Systematic review [448] with included studies: [408] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Imprecision: Serious.** Only data from one study, Low number of patients.

References

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[448] Walters GD, Willis NS, Cooper TE, et al. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews 2020;1 CD003232

Table S15.
Population: Patients with ANCA-associated vasculitis
Intervention: Maintenance therapy: Mycophenolate mofetil
Comparator: Maintenance therapy: Azathioprine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Azathioprine	Mycophenolate mofetil	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Infection	Relative risk: 0.39 (95% CI: 0.11 - 1.43) Based on data from 156 patients in 1 study[1] Follow up 4 years	**100** per 1000	**39** per 1000 Difference: **61 fewer per 1000** (95% CI: 89 fewer - 43 more)	**Low** Due to very serious imprecision[2]	Mycophenolate mofetil may have little or no difference on infection
Relapse	Relative risk: 1.47 (95% CI: 1.04 - 2.09) Based on data from 156 patients in 1 study[3] Follow up 4 years	**375** per 1000	**551** per 1000 Difference: **176 more per 1000** (95% CI: 15 more - 409 more)	**Moderate** Due to serious imprecision[4]	Mycophenolate mofetil probably increases relapse
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [406] **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 [448] with included studies: [406] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Serious.** Only data from one study, Low number of patients.

References

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[448] Walters GD, Willis NS, Cooper TE, et al. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews 2020;1 CD003232

Table S16.
Population: Patients with ANCA-associated vasculitis
Intervention: Maintenance therapy: Azathioprine
Comparator: Maintenance therapy: Methotrexate

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Methotrexate	Azathioprine	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality Long-term follow-up	Relative risk: 1.25 (95% CI: 0.64 - 2.45) Based on data from 126 patients in 1 study[1] Follow up 10 years	**190** per 1000	**238** per 1000 Difference: **48 more per 1000** (95% CI: 68 fewer - 276 more)	**Low** Due to very serious imprecision[2]	Azathioprine may have little or no difference on all-cause mortality
End-stage kidney disease Long-term follow-up	Relative risk: 0.88 (95% CI: 0.34 - 2.27) Based on data from 126 patients in 1 study[3] Follow up 10 years	**111** per 1000	**98** per 1000 Difference: **13 fewer per 1000** (95% CI: 73 fewer - 141 more)	**Low** Due to very serious imprecision[4]	Azathioprine may have little or no difference on end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection Long-term follow-up	Relative risk: 0.73 (95% CI: 0.46 - 1.25) Based on data from 126 patients in 1 study[5] Follow up 10 years	**349** per 1000	**255** per 1000 Difference: **94 fewer per 1000** (95% CI: 188 fewer - 87 more)	**Moderate** Due to serious imprecision[6]	Azathioprine probably has little or no difference on infection
Malignancy Long-term follow-up	Relative risk: 1.1 (95% CI: 0.5 - 2.4) Based on data from 126 patients in 1 study[7] Follow up 10 years	**159** per 1000	**175** per 1000 Difference: **16 more per 1000** (95% CI: 79 fewer - 223 more)	**Low** Due to very serious imprecision[8]	Azathioprine may have little or no difference on malignancy
Relapse 3 years	Relative risk: 1.1 (95% CI: 0.68 - 1.77) Based on data from 126 patients in 1 study[9] Follow up 3 years	**333** per 1000	**366** per 1000 Difference: **33 more per 1000** (95% CI: 107 fewer - 256 more)	**Moderate** Due to serious imprecision[10]	Azathioprine may have little or no difference on relapse at 3 years
Relapse Long-term follow-up	Relative risk: 1.12 (95% CI: 0.83 - 1.51) Based on data from 126 patients in 1 study[11] Follow up 10 years	**540** per 1000	**605** per 1000 Difference: **65 more per 1000** (95% CI: 92 fewer - 275 more)	**Moderate** Due to serious imprecision[12]	Azathioprine may have little or no difference on relapse at 10 years

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Methotrexate Azathioprine	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Adverse event	Relative risk: 0.58 (95% CI: 0.25 - 1.38) Based on data from 126 patients in 1 study[13] Follow up 3 years	**190** per 1000 **110** per 1000 Difference: **80 fewer per 1000** (95% CI: 142 fewer - 72 more)	**Moderate** Due to serious imprecision[14]	Azathioprine probably has little or no difference on adverse events resulting in death or drug discontinuation
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [418] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
3. Systematic review [448] with included studies: [418] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
5. Systematic review [448] with included studies: [418] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Serious.** Only data from one study.
7. Systematic review [448] with included studies: [418] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
9. Systematic review [448] with included studies: [418] **Baseline/comparator:** Control arm of reference used for intervention.
10. **Imprecision: Serious.** Wide confidence intervals, only data from one study, Low number of patients.
11. Systematic review [448] with included studies: [418] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Imprecision: Serious.** Wide confidence intervals, only data from one study, Low number of patients.
13. Systematic review [448] with included studies: [418] **Baseline/comparator:** Control arm of reference used for intervention.
14. **Imprecision: Serious.** Only data from one study, Low number of patients.

References

[418] Pagnoux C, Mahr A, Hamidou MA, Boffa JJ, Ruivard M, Ducroix JP, et al. Azathioprine or methotrexate maintenance for ANCA-associated vasculitis. New England Journal of Medicine 2008;359(26):2790-2803
[448] Walters GD, Willis NS, Cooper TE, et al. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews 2020;1 CD003232

Table S17.
Population: Patients with ANCA-associated vasculitis
Intervention: Maintenance therapy: Extended azathioprine
Comparator: Maintenance therapy: Standard azathioprine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard azathioprine	Extended azathioprine	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 2.81 (95% CI: 0.69 - 11.5) Based on data from 162 patients in 2 studies[1] Follow up 48 months (mean)	**25** per 1000	**70** per 1000 Difference: **45 more per 1000** (95% CI: 8 fewer - 263 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether extended or standard azathioprine increases or decreases all-cause mortality
End-stage kidney disease	Relative risk: 0.1 (95% CI: 0.01 - 1.86) Based on data from 117 patients in 1 study[3] Follow up 48 months	**71** per 1000	**7** per 1000 Difference: **64 fewer per 1000** (95% CI: 70 fewer - 61 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether extended or standard azathioprine increases or decreases end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection[5]	Relative risk: 1.14 (95% CI: 0.38 - 3.41) Based on data from 45 patients in 1 study[6] Follow up 48 months	**208** per 1000	**237** per 1000 Difference: **29 more per 1000** (95% CI: 129 fewer - 501 more)	**Very Low** Due to very serious risk of bias, Due to very serious imprecision[7]	We are uncertain whether extended or standard azathioprine increases or decreases infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Relapse	Relative risk: 0.41 (95% CI: 0.26 - 0.64) Based on data from 162 patients in 2 studies[8] Follow up 48 months (mean)	**538** per 1000	**221** per 1000 Difference: **317 fewer per 1000** (95% CI: 398 fewer - 194 fewer)	**Moderate** Due to serious risk of bias[9]	Extended azathioprine probably decreases relapse
Major relapse	Relative risk: 0.41 (95% CI: 0.19 - 0.86) Based on data from 117 patients in 1 study[10] Follow up 48 months	**321** per 1000	**132** per 1000 Difference: **189 fewer per 1000** (95% CI: 260 fewer - 45 fewer)	**Low** Due to serious risk of bias, Due to serious imprecision[11]	Extended azathioprine may decrease major relapse

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard azathioprine	Extended azathioprine	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Serious adverse events	Relative risk: 2.75 (95% CI: 0.78 - 9.66) Based on data from 117 patients in 1 study[12] Follow up 48 months	**54** per 1000	**149** per 1000 Difference: **95 more per 1000** (95% CI: 12 fewer - 468 more)	**Low** Due to serious risk of bias, Due to serious imprecision[13]	We are uncertain whether extended or standard azathioprine increases or decreases serious adverse events
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [414], [423] **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, due to early termination of the AZA-ANCA due to poor recruitment.; **Imprecision: Very Serious.** Wide confidence intervals, due to few events.
3. Systematic review [448] with included studies: [414] **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, Low number of patients, Wide confidence intervals.
5. Serious Infections
6. Systematic review [448] with included studies: [423] **Baseline/comparator:** Control arm of reference used for intervention.
7. **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, due to early termination of the AZA-ANCA due to poor recruitment.; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study, Low number of patients.
8. Systematic review [448] with included studies: [423], [414] **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, due to early termination of the AZA-ANCA due to poor recruitment.
10. Systematic review [448] with included studies: [414] **Baseline/comparator:** Control arm of reference used for intervention.
11. **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: Serious.** Only data from one study, Low number of patients.
12. Systematic review [448] with included studies: [414] **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, Low number of patients.

References

[414] Karras A, Pagnoux C, Haubitz M, Groot K, Puechal X, Tervaert JWC, et al. Randomised controlled trial of prolonged treatment in the remission phase of ANCA-associated vasculitis. Annals of the Rheumatic Diseases 2017;76(10):1662-1668
[423] Sanders JF, de Joode AA, DeSevaux RG, Broekroelofs J., Voskuyl AE, van Paassen P., et al. Extended versus standard azathioprine maintenance therapy in newly diagnosed proteinase-3 anti-neutrophil cytoplasmic antibody-associated vasculitis patients who remain cytoplasmic anti-neutrophil cytoplasmic antibody-positive after induction of remission: a randomized clinical trial. Nephrology Dialysis Transplantation 2016;31(9):1453-1459
[448] Walters GD, Willis NS, Cooper TE et al. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews 2020;1 CD003232

Table S18.
Population: Patients with ANCA-associated vasculitis
Intervention: Maintenance therapy: Tailored rituximab therapy
Comparator: Maintenance therapy: Fixed-schedule rituximab therapy

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Fixed-schedule rituximab therapy	Tailored rituximab therapy	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.33 (95% CI: 0.04 - 3.14) Based on data from 162 patients in 1 study[1] Follow up 28 months	**37** per 1000	**12** per 1000 Difference: **25 fewer per 1000** (95% CI: 36 fewer - 79 more)	**Low** Due to very serious imprecision[2]	Tailored rituximab therapy may have little or no difference on all-cause mortality
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.0 (95% CI: 0.56 - 1.78) Based on data from 162 patients in 1 study[3] Follow up 28 months	**222** per 1000	**222** per 1000 Difference: **0 fewer per 1000** (95% CI: 98 fewer - 173 more)	**Low** Due to very serious imprecision[4]	Tailored rituximab therapy may have little or no difference on infection
Malignancy	Relative risk: 0.33 (95% CI: 0.04 - 3.14) Based on data from 162 patients in 1 study[5] Follow up 28 months	**37.0**	**12.0** Difference: **25.0 fewer** (95% CI: 36.0 fewer - 79.0 more)	**Low** Due to very serious imprecision[6]	Tailored rituximab therapy may have little or no difference on malignancy
Relapse[7]	Relative risk: 1.63 (95% CI: 0.71 - 3.71) Based on data from 162 patients in 1 study[8] Follow up 28 months	**99** per 1000	**161** per 1000 Difference: **62 more per 1000** (95% CI: 29 fewer - 268 more)	**Low** Due to very serious imprecision[9]	Tailored rituximab therapy may have little or no difference on relapse
Relapse[10] in relapsing disease	Relative risk: 2.0 (95% CI: 0.55 - 7.22) Based on data from 56 patients in 1 study[11] Follow up 28 months	**111** per 1000	**222** per 1000 Difference: **111 more per 1000** (95% CI: 50 fewer - 690 more)	**Low** Due to very serious imprecision[12]	Tailored rituximab therapy may have little or no difference on relapse in patients with relapsing disease
Major relapse[13]	Relative risk: 2.0 (95% CI: 0.52 - 7.72) Based on data from 162 patients in 1 study[14] Follow up 28 months	**37** per 1000	**74** per 1000 Difference: **37 more per 1000** (95% CI: 18 fewer - 249 more)	**Low** Due to very serious imprecision[15]	Tailored rituximab therapy may have little or no difference on major relapse

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Fixed-schedule rituximab therapy	 Tailored rituximab therapy	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Major relapse[16] in relapsing disease	Relative risk: 4.0 (95% CI: 0.48 - 33.58) Based on data from 56 patients in 1 study[17] Follow up 28 months	**40** per 1000	**160** per 1000 Difference: **120 more per 1000** (95% CI: 21 fewer - 1303 more)	**Low** Due to very serious imprecision[18]	Tailored rituximab therapy may have little or no difference on major relapse in patients with relapsing disease
Serious adverse events	Relative risk: 0.84 (95% CI: 0.55 - 1.28) Based on data from 162 patients in 1 study[19] Follow up 28 months	**383** per 1000	**322** per 1000 Difference: **61 fewer per 1000** (95% CI: 172 fewer - 107 more)	**Low** Due to very serious imprecision[20]	Tailored rituximab therapy may have little or no difference on serious adverse events
Annual GFR loss	Measured by: Scale: - Lower better	Mean	Mean Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [435] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: No serious.** Not all pre-specified outcomes were reported in this study, i.e., quality of life; **Imprecision: Very Serious.** Only data from one study, Wide confidence intervals.
3. Systematic review [448] with included studies: [435] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
5. Systematic review [448] with included studies: [435] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
7. reappearance or worsening of AAV symptoms, that is, BVAS>0.
8. Systematic review [448] with included studies: [435] **Baseline/comparator:** Control arm of reference used for intervention.
9. **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
10. reappearance or worsening of AAV symptoms, that is, BVAS>0.
11. Systematic review [448] with included studies: [435] **Baseline/comparator:** Control arm of reference used for intervention.
12. **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
13. defined as life-threatening or involving at least one major organ
14. Systematic review [448] with included studies: [435] **Baseline/comparator:** Control arm of reference used for intervention.
15. **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
16. defined as life-threatening or involving at least one major organ
17. Systematic review [448] with included studies: [435] **Baseline/comparator:** Control arm of reference used for intervention.
18. **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.
19. Systematic review [448] with included studies: [435] **Baseline/comparator:** Control arm of reference used for intervention.
20. **Imprecision: Very Serious.** Wide confidence intervals, only data from one study.

References

[435] Charles P, Terrier B, Perrodeau É, Cohen P, Faguer S, Huart A, Hamidou M, Agard C, Bonnotte B, Samson M, Karras A, Jourde-Chiche N, Lifermann F, Gobert P, Hanrotel-Saliou C, Godmer P, Martin-Silva N, Pugnet G, Matignon M, Aumaitre O, Viallard J-F, Maurier F, Meaux-Ruault N, Rivière S, Sibilia J, Puéchal X, Ravaud P, Mouthon L, Guillevin L. Comparison of individually tailored versus fixed-schedule rituximab regimen to maintain ANCA-associated vasculitis remission: results of a multicentre, randomised controlled, phase III trial (MAINRITSAN2). Annals of the Rheumatic Diseases 2018;77(8):1143-1149

[448] Walters GD, Willis NS, Cooper TE, et al. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews 2020;1 CD003232

Table S19.
Population: Patients with ANCA-associated vasculitis and relapsing disease
Intervention: Maintenance therapy: Rituximab
Comparator: Maintenance therapy: Azathioprine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Azathioprine	Rituximab	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.95 (95% CI: 0.07 – 13.1) Based on data from 285 patients in 2 studies[1] Follow up 28-48 months	**16** per 1000	**17** per 1000 Difference: **3 fewer per 1000** (95% CI: 58 fewer - 53 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether rituximab increases or decreases all-cause mortality
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection[3]	Relative risk: 0.98 (95% CI: 0.57 – 1.68) Based on data from 285 patients in 2 studies[4] Follow up 28-48 months	**181** per 1000	**183** per 1000 Difference: **1 more per 1000** (95% CI: 101 fewer - 99 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[5]	We are uncertain whether rituximab increases or decreases infection
Malignancy	Relative risk: 0.77 (95% CI: 0.57 – 1.05) Based on data from 170 patients in 1 study[6] Follow up 48 months	**565** per 1000	**435** per 1000 Difference: **129 fewer per 1000** (95% CI: 278 fewer - 20 more):	**Low** Due to serious risk of bias, Due to serious imprecision[7]	Rituximab may have lower risk of malignancy
Major relapse	Relative risk: 0.59 (95% CI: 0.45 – 0.77) Based on data from 285 patients in 2 studies[8] Follow up 28-48 months	**501** per 1000	**247** per 1000 Difference: **249 fewer per 1000** (95% CI: 345 fewer - 152 fewer)	**Moderate** Due to serious risk of bias[9]	Rituximab probably decreases major relapse
Major relapse in relapsing disease	Relative risk: 0.08 (95% CI: 0.01 - 1.36) Based on data from 115 patients in 1 study[10] Follow up 28 months	**450** per 1000	**36** per 1000 Difference: **414 fewer per 1000** (95% CI: 445 fewer - 162 more)	**Low** Due to serious risk of bias, Due to serious imprecision[11]	Rituximab in patients with relapsing disease may have little or no difference on major relapse

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Azathioprine Rituximab	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [403] [Smith 2023] **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. Serious infections
4. Systematic review [448] with included studies: [403] [Smith 2023] **Baseline/comparator:** Control arm of reference used for intervention.
5. **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.
6. Systematic review [448] with included studies: [Smith 2023] **Baseline/comparator:** Control arm of reference used for intervention.
7. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: Serious.** Only data from one study.
8. Systematic review [448] with included studies: [403] [Smith 2023] **Baseline/comparator:** Control arm of reference used for intervention.
9. **Risk of bias: Serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias.
10. Systematic review [448] with included studies: [403] **Baseline/comparator:** Control arm of reference used for intervention.
11. **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.

References

[403] Guillevin L, Pagnoux C, Karras A, Khouatra C, Aumaitre O, Cohen P., et al. Rituximab versus azathioprine for maintenance in ANCA-associated vasculitis. New England Journal of Medicine 2014;371(19):1771-1780
[Smith 2023] Smith RM, Jones RB, Specks U, Bond S, Nodale M, Al-Jayyousi R, et al. Rituximab versus azathioprine for maintenance of remission for patients with ANCA-associated vasculitis and relapsing disease: an international randomised controlled trial. Annals of Rheumatic Diseases 2023;82(7):937-944
[448] Walters GD, Willis NS, Cooper TE, et al. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews 2020;1 CD003232

Table S20.
Population: Patients with ANCA-associated vasculitis and relapsing disease
Intervention: Maintenance therapy: Rituximab
Comparator: Maintenance therapy: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Rituximab maintenance	Placebo maintenance	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: not calculable (0 events) Based on data from 97 patients in 1 study[1] Follow up 28 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI: 39 fewer – 39 more)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to sparse data[2]	We are uncertain whether maintenance rituximab increases or decreases mortality
End-stage kidney disease	Relative risk: not calculable (0 events) Based on data from 97 patients in 1 study[1] Follow up 28 months	**0** per 1000	**0** per 1000 Difference: **0 fewer per 1000** (95% CI: 39 fewer – 39 more)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to sparse data[2]	We are uncertain whether maintenance rituximab increases or decreases ESKD
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.41 (95% CI: 0.42 – 4.69) Based on data from 97 patients in 1 study[1] Follow up 28 months	**120** per 1000	**85** per 1000 Difference: **35 more per 1000** (95% CI: 85 fewer - 155 more)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to sparse data[2]	We are uncertain whether maintenance rituximab increases or decreases infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Remission	(95% CI: -)	Difference:			No studies were found that looked at remission
Relapse	Relative risk: 0.16 (95% CI: 0.04 - 0.66) Based on data from 97 patients in 1 study[1] Follow up 28 months	**40** per 1000	**255** per 1000 Difference: **215 fewer per 1000** (95% CI: 351 fewer - 79 fewer)	**Low** Due to serious risk of bias, Due to sparse data, Strong effect [3]	Maintenance rituximab may decrease relapse
Annual GFR loss	(95% CI: -)	Difference:		No studies were found that looked at remission	(95% CI: -)

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Rituximab maintenance	 Placebo maintenance	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Adverse events, severe	Relative risk: 1.10 (95% CI: 0.67 – 1.79) Based on data from 97 patients in 1 study[1] Follow up 28 months	**420** per 1000	**383** per 1000 Difference: **37 more per 1000** (95% CI: 158 fewer - 232 more)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to sparse data[2]	We are uncertain whether maintenance rituximab increases or decreases severe adverse events
Discontinuation due to adverse events	Relative risk: 3.76 (95% CI: 0.44 – 32.44) Based on data from 97 patients in 1 study[1] Follow up 28 months	**80** per 1000	**21** per 1000 Difference: **59 more per 1000** (95% CI: 27 fewer - 144 more)	**Very low** Due to serious risk of bias, Due to serious imprecision, Due to sparse data[2]	We are uncertain whether maintenance rituximab increases or decreases discontinuation due to adverse events

1. Included study: [Charles_2020_32479166].
2. **Risk of bias: Serious.** Selective reporting (primary outcome omitted); **Imprecision: Serious.** No events; **Other: Serious** Only data from one study.
3. **Risk of bias: Serious.** Selective reporting (primary outcome omitted); **Other: Serious** Only data from one study; upgraded due to strong effect (RR = 0.16).

References

Charles P, Perrodeau É, Samson M, et al. Long-Term Rituximab Use to Maintain Remission of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis: A Randomized Trial. Ann Intern Med. 2020 Aug 4;173(3):179-187. doi: 10.7326/M19-3827. Epub 2020 Jun 2. PMID: 32479166

Table S21.
Population: Patients with ANCA-associated vasculitis
Intervention: Maintenance therapy: Antibiotics (trimethoprim-sulfamethoxazole)
Comparator: Maintenance therapy: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	Antibiotics	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality 6 months	Relative risk: 0.33 (95% CI: 0.01 - 7.76) Based on data from 81 patients in 1 study[1] Follow up 6 months	**25** per 1000	**8** per 1000 Difference: **17 fewer per 1000** (95% CI: 25 fewer - 169 more)	**Low** Due to very serious imprecision[2]	Antibiotics may have little or no difference on all-cause mortality at 6 months
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥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 1 year	Relative risk: 1.14 (95% CI: 0.98 - 1.33) Based on data from 111 patients in 2 studies[3] Follow up 12 months (mean)	**796** per 1000	**907** per 1000 Difference: **111 more per 1000** (95% CI: 16 fewer - 263 more)	**Low** Due to serious risk of bias, Due to serious imprecision[4]	Antibiotics may have little or no difference on complete remission at 1 year
Complete remission 2 years	Relative risk: 1.28 (95% CI: 0.94 - 1.76) Based on data from 80 patients in 1 study[5] Follow up 24 months	**590** per 1000	**755** per 1000 Difference: **165 more per 1000** (95% CI: 35 fewer - 448 more)	**Low** Due to serious imprecision, Due to serious risk of bias[6]	Antibiotics probably has little or no difference on complete remission at 2 years
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [425] **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 [448] with included studies: [431], [425] **Baseline/comparator:** Control arm of reference used for intervention.

4. **Risk of bias: Serious.** In Zycinska 2009 the groups were not balanced. Patients in the placebo group were older, had worse kidney function and a higher mean BVAS score at baseline; **Imprecision: Serious.** Low number of patients.
5. Systematic review [448] with included studies: [425] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: Serious. Imprecision: Serious.** Only data from one study, Low number of patients.

References

[425] Stegeman CA, Cohen TJ, de Jong PE, Kallenberg CG. Trimethoprim-sulfamethoxazole (co-trimoxazole) for the prevention of relapses of Wegener's granulomatosis. Dutch Co-Trimoxazole Wegener Study Group. New England Journal of Medicine 1996;335(1):16-20

[431] Zycinska K, Wardyn KA, Zielonka TM, Krupa R, Lukas W. Co-trimoxazole and prevention of relapses of PR3-ANCA positive vasculitis with pulmonary involvement. European Journal of Medical Research 2009;14 Suppl 4 265-267

[448] Walters GD, Willis NS, Cooper TE, et al. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews 2020;1 CD003232

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

Table S22.
Population: Patients with ANCA-associated vasculitis
Intervention: Intravenous immunoglobulin
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	Intravenous immunoglobulin	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Relapse	Relative risk: 1.17 (95% CI: 0.39 - 3.56) Based on data from 31 patients in 1 study[1] Follow up 12 months	**267** per 1000	**312** per 1000 Difference: **45 more per 1000** (95% CI: 163 fewer - 684 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether intravenous immunoglobulin increases or decreases relapse
All-cause mortality	Relative risk: 0.2 (95% CI: 0.01 - 3.88) Based on data from 34 patients in 1 study[3] Follow up 12 months	**118** per 1000	**24** per 1000 Difference: **94 fewer per 1000** (95% CI: 117 fewer - 340 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether intravenous immunoglobulin increases or decreases all-cause mortality
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥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
Treatment response[5] 3 months	Relative risk: 2.33 (95% CI: 1.18 - 4.61)	**353** per 1000	**822** per 1000 Difference: **469 more per 1000**	**Moderate** Due to serious risk of bias, Due to serious imprecision,	Intravenous immunoglobulin probably increases treatment response

	Based on data from 34 patients in 1 study[6] Follow up 12 months	(95% CI: 64 more - 1274 more)	Upgraded due to Large magnitude of effect[7]	
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Primary study [413] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias and pharmaceutical sponsor involved in random sequence generation; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study, Low number of patients
3. Primary study [413] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: Serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias and pharmaceutical sponsor involved in random sequence generation; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study, Low number of patients
5. Treatment response - BVAS reduction of 50% between entry
6. Primary study [413] **Baseline/comparator:** Control arm of reference used for intervention.
7. **Risk of bias: Serious.** Unclear blinding of outcome assessors, resulting in potential for detection bias and pharmaceutical sponsor involved in random sequence generation; **Imprecision: Serious.** Only data from one study, Low number of patients; **Upgrade: Large magnitude of effect.**

References

[413] Jayne DR, Chapel H., Adu D., Misbah S., O'Donoghue D., Scott D., et al. Intravenous immunoglobulin for ANCA-associated systemic vasculitis with persistent disease activity. Qjm 2000;93(7):433-439
[448] Walters GD, Willis NS, Cooper TE, Craig JC. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews. 2020;1 CD003232

Table S23.
Population: Patients with ANCA-associated vasculitis
Intervention: Plasma exchange
Comparator: Immunoadsorption

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Immunoadsorption	Plasma exchange	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality 6 months	Relative risk: 1.64 (95% CI: 0.3 - 8.89) Based on data from 44 patients in 1 study[1] Follow up 6 months	**87** per 1000	**143** per 1000 Difference: **56 more per 1000** (95% CI: 61 fewer - 686 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision, Due to serious indirectness[2]	We are uncertain whether plasma exchange increases or decreases all-cause mortality
End-stage kidney disease 6 months	Relative risk: 0.58 (95% CI: 0.12 - 2.82) Based on data from 39 patients in 1 study[3] Follow up 6 months	**190** per 1000	**110** per 1000 Difference: **80 fewer per 1000** (95% CI: 167 fewer - 346 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision, Due to serious indirectness[4]	We are uncertain whether plasma exchange increases or decreases end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Primary study [429] **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; **Indirectness: Serious.** Differences between the population of interest and those studied, study included patients with Goodpasture's syndrome and 87% of patients without Goodpasture's syndrome had ANCA antibodies; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study, Low number of patients
3. Primary study [429] **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; **Indirectness: Serious.** Differences between the population of interest and those studied, study included patients with Goodpasture's syndrome and 87% of patients without Goodpasture's syndrome had ANCA antibodies; **Imprecision: Very Serious.** Wide confidence intervals, only data from one study, Low number of patients

References

[429] Stegmayr BG, Almroth G., Berlin G., Fehrman I., Kurkus J., Norda R., et al. Plasma exchange or immunoadsorption in patients with rapidly progressive crescentic glomerulonephritis. A Swedish multi-center study. International Journal of Artificial Organs 1999;22(2):81-87

[448] Walters GD, Willis NS, Cooper TE, Craig JC. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews. 2020;1 CD003232

Table S24.
Population: Patients with ANCA-associated vasculitis
Intervention: Etanercept
Comparator: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Placebo	Etanercept	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
Infection	Relative risk: 1.0 (95% CI: 0.74 - 1.35) Based on data from 174 patients in 1 study[1] Follow up 22 months (median)	**494** per 1000	**494** per 1000 Difference: **0 fewer per 1000** (95% CI: 128 fewer - 173 more)	**Low** Due to serious risk of bias, Due to serious imprecision[2]	Etanercept may have little or no difference on infection
Malignancy	Relative risk: 12.42 (95% CI: 0.71 - 217.18) Based on data from 174 patients in 1 study[3] Follow up 22 months (median)	**0** per 1000	per 1000 Difference: **fewer per 1000**	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	There were too few who experienced the malignancy, to determine whether etanercept made a difference
Complete remission - Sustained	Relative risk: 0.93 (95% CI: 0.77 - 1.11) Based on data from 174 patients in 1 study[4] Follow up 22 months (median)	**753** per 1000	**700** per 1000 Difference: **53 fewer per 1000** (95% CI: 173 fewer - 83 more)	**Low** Due to serious risk of bias, Due to serious imprecision[5]	Etanercept may have little or no difference on sustained remission
Relapse	Relative risk: 0.93 (95% CI: 0.56 - 1.56) Based on data from 126 patients in 1 study[6] Follow up 22 months (median)	**328** per 1000	**305** per 1000 Difference: **23 fewer per 1000** (95% CI: 144 fewer - 184 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[7]	Etanercept may have little or no difference on relapse
All-cause mortality	Relative risk: 1.91 (95% CI: 0.36 - 10.16) Based on data from 174 patients in 1 studies[8] Follow up Median 22 months	**24** per 1000	**46** per 1000 Difference: **22 more per 1000** (95% CI: 15 fewer - 220 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[9]	We are uncertain whether etanercept increases or decreases all-cause mortality
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥50% loss of GFR	(95% CI: -)				No studies were found that looked

		Difference:		at ≥50% loss of GFR
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Primary study [437] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study, Low number of patients
3. Primary study [437] **Baseline/comparator:** Control arm of reference used for intervention.
4. Primary study [437] **Baseline/comparator:** Control arm of reference used for intervention.
5. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Serious.** Only data from one study, Low number of patients
6. Primary study [437] **Baseline/comparator:** Control arm of reference used for intervention.
7. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
8. Primary study [437] **Baseline/comparator:** Control arm of reference used for intervention.
9. **Risk of bias: Serious.** Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[437] Wegener's Granulomatosis Etanercept Trial (WGET) Research Group. Etanercept plus standard therapy for Wegener's granulomatosis. The New England journal of medicine 2005;352(4):351-61
[448] Walters GD, Willis NS, Cooper TE, Craig JC. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews. 2020;1 CD003232

Table S25.
Population: Patients with ANCA-associated vasculitis
Intervention: Lymphocytapheresis
Comparator: Standard of care – intravenous methylprednisone, glucocorticoids, and cyclophosphamide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard of care	Lymphocytapheresis	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality 6 months	Relative risk: 0.4 (95% CI: 0.1 - 1.67) Based on data from 24 patients in 1 study[1] Follow up 6 months	**417** per 1000	**167** per 1000 Difference: **250 fewer per 1000** (95% CI: 375 fewer - 279 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether lymphocytapheresis increases or decreases all-cause mortality
End-stage kidney disease 6 months	Relative risk: 0.33 (95% CI: 0.04 - 2.77) Based on data from 24 patients in 1 study[3] Follow up 6 months	**250** per 1000	**83** per 1000 Difference: **167 fewer per 1000** (95% CI: 240 fewer - 443 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether lymphocytapheresis increases or decreases end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Complete remission	(95% CI: -)	Difference:			No studies were found that looked at complete remission
Annual GFR loss	Measured by: Scale: - Lower better	Difference			No studies were found that looked at annual GFR loss

1. Primary study [402] **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, 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, 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, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients
3. Primary study [402] **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, Selective outcome reporting; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[402] Furuta T., Hotta O., Yusa N., Horigome I., Chiba S., Taguma Y. Lymphocytapheresis to treat rapidly progressive glomerulonephritis: a randomised comparison with steroid-pulse treatment. Lancet 1998;352(9123):203-204
[448] Walters GD, Willis NS, Cooper TE, Craig JC. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews. 2020;1 CD003232

Table S26.
Population: Patients with ANCA-associated vasculitis
Intervention: Maintenance therapy: Leflunomide
Comparator: Maintenance therapy: Methotrexate

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Maintenance therapy: methotrexate	Maintenance therapy: leflunomide	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.17 (95% CI: 0.66 - 2.07) Based on data from 54 patients in 1 study[1] Follow up 24 months	**429** per 1000	**502** per 1000 Difference: **73 more per 1000** (95% CI: 146 fewer - 459 more)	**Moderate** Due to serious imprecision[2]	We are uncertain whether leflunomide as maintenance therapy increases or decreases infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Relapse	Relative risk: 0.52 (95% CI: 0.22 - 1.11) Based on data from 54 patients in 1 study[3] Follow up 24 months	**464** per 1000	**241** per 1000 Difference: **223 fewer per 1000** (95% CI: 362 fewer - 51 more)	**Moderate** Due to serious imprecision[4]	We are uncertain whether leflunomide as maintenance therapy increases or decreases relapse
Major relapse	Relative risk: 0.15 (95% CI: 0.02 - 1.17) Based on data from 54 patients in 1 study[5] Follow up 24 months	**250** per 1000	**38** per 1000 Difference: **212 fewer per 1000** (95% CI: 245 fewer - 43 more)	**Moderate** Due to serious imprecision[6]	We are uncertain whether leflunomide as maintenance therapy increases or decreases major relapse
Serious adverse events	Relative risk: 11.81	**0** per 1000	**0** per 1000	**Very Low**	There were too few who experienced

	(95% CI: 0.69 - 203.68) Based on data from 54 patients in 1 study[7] Follow up 24 months	Difference: **0 fewer per 1000** (95% CI: 0 fewer - 0 fewer)	Due to very serious risk of bias, Due to very serious imprecision[8]	the serious adverse events, to determine whether leflunomide as maintenance therapy made a difference
Annual GFR loss	Measured by: Scale: - Lower better	Difference:		No studies were found that looked at annual GFR loss

1. Primary study [420] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Risk of bias: No serious.** Study terminated early due to high rate of relapses in control group; **Imprecision: Serious.** Only data from one study, Low number of patients
3. Primary study [420] **Baseline/comparator:** Control arm of reference used for intervention.
4. **Risk of bias: No serious.** Study terminated early due to high rate of relapses in control group; **Imprecision: Serious.** Only data from one study, Low number of patients, Only data from one study, Low number of patients, Only data from one study, Low number of patients
5. Primary study [420] **Baseline/comparator:** Control arm of reference used for intervention.
6. **Risk of bias: No serious.** Study terminated early due to high rate of relapses in control group; **Imprecision: Serious.** Only data from one study, Low number of patients
7. Primary study [420] **Baseline/comparator:** Control arm of reference used for intervention.
8. **Risk of bias: Very Serious.** Study terminated early due to high rate of relapses in control group; **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study, Low number of patients

References

[420] Metzler C., Miehle N., Manger K., Iking-Konert C., de Groot K., Hellmich B., et AL: Elevated relapse rate under oral methotrexate versus leflunomide for maintenance of remission in Wegener's granulomatosis. Rheumatology 2007;46(7):1087-1091

[448] Walters GD, Willis NS, Cooper TE, Craig JC: Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews. 2020;1 CD003232

Table S27.
Population: Patients with ANCA-associated vasculitis who have undergone plasma exchange adjunctive therapy or usual care
Intervention: Maintenance therapy: Cyclosporine
Comparator: Maintenance therapy: Cyclophosphamide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Maintenance therapy: cyclophosphamide	Maintenance therapy: cyclosporine	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥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
Relapse	Relative risk: 1.38 (95% CI: 0.82 - 2.33) Based on data from 64 patients in 1 study[1] Follow up 5 years	**406** per 1000	**560** per 1000 Difference: **154 more per 1000** (95% CI: 73 fewer - 540 more)	**Moderate** Due to serious imprecision[2]	Cyclosporine as maintenance therapy probably has little or no difference on relapse
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Primary study [431] **Baseline/comparator:** Control arm of reference used for intervention.
2. **Imprecision: Serious.** Low number of patients, Only data from one study

References
[431] Szpirt WM, Heaf JG, Petersen J. Plasma exchange for induction and cyclosporine A for maintenance of remission in Wegener's granulomatosis--a clinical randomized controlled trial. Nephrology Dialysis Transplantation 2011;26(1):206-213
[448] Walters GD, Willis NS, Cooper TE, Craig JC. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews. 2020;1 CD003232

Table S28.
Population: Patients with ANCA-associated vasculitis
Intervention: Maintenance therapy: Preemptive therapy for relapse
Comparator: Maintenance therapy: Standard of care

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard of care	Maintenance therapy: pre-emptive therapy for relapse	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at all-cause mortality
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	(95% CI: -)	Difference:			No studies were found that looked at infection
Relapse	Relative risk: 0.23 (95% CI: 0.03 - 1.59) Based on data from 60 patients in 2 studies[1] Follow up 9 months (mean)	**677** per 1000	**156** per 1000 Difference: **521 fewer per 1000** (95% CI: 657 fewer - 399 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether pre-emptive therapy for relapse for maintenance therapy increases or decreases relapse
Annual GFR loss	Measured by: Scale: - Lower better	Mean	Mean Difference:		No studies were found that looked at annual GFR loss

1. Systematic review [448] with included studies: [400], [432] **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 of Tervaert 1990 and Boomsma 2003 is an abstract only; **Imprecision: Very Serious.** Low number of patients, Wide confidence intervals.

References

[400] Boomsma MM, Stegeman CA, Hermans J., Kallenberg CGM, Hene RJ, Limburg PC, et al. Prevention of relapses in PR3 anti-neutrophil cytoplasmic antibody associated vasculitis by treatment with azathioprine and corticosteroids: a multi-center, randomized study [abstract no: T208]. Nephrology Dialysis Transplantation 2003;18(Suppl 4):347-348
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[448] Walters GD, Willis NS, Cooper TE, Craig JC. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews. 2020;1 CD003232

Table S29.
Population: Patients with ANCA-associated vasculitis
Intervention: Maintenance therapy: Methotrexate
Comparator: Maintenance therapy: Cyclophosphamide

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Maintenance therapy: cyclophosphamide	Maintenance therapy: methotrexate	**Certainty of the evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 0.44 (95% CI: 0.04 - 4.67) Based on data from 68 patients in 1 study[1] Follow up 24 months	**63** per 1000	**28** per 1000 Difference: **35 fewer per 1000** (95% CI: 60 fewer - 231 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether methotrexate as maintenance therapy increases or decreases all-cause mortality
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥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
Relapse	Relative risk: 1.14 (95% CI: 0.48 - 2.72) Based on data from 68 patients in 1 study[3] Follow up 24 months	**219** per 1000	**250** per 1000 Difference: **31 more per 1000** (95% CI: 114 fewer - 377 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether methotrexate as maintenance therapy increases or decreases relapse
Annual GFR loss	Measured by: Scale: - Lower better	Difference:			No studies were found that looked at annual GFR loss

1. Primary study [418] **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, 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. Primary study [418] **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 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

References

[418] Maritati F., Alberici F., Oliva E., Urban ML, Palmisano A., Santarsia F., et al. Methotrexate versus cyclophosphamide for remission maintenance in ANCA-associated vasculitis: A randomised trial. PLoS ONE [Electronic Resource] 2017;12(10): e0185880-e0185880

[448] Walters GD, Willis NS, Cooper TE, Craig JC. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews. 2020;1 CD003232

Table S30.
Population: Patients with ANCA-associated vasculitis
Intervention: Maintenance therapy: Belimumab plus azathioprine
Comparator: Maintenance therapy: Placebo plus azathioprine

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Maintenance therapy: Placebo + azathioprine	Maintenance therapy: Belimumab + azathioprine	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk: 2.94 (95% CI: 0.12 - 70.67) Based on data from 105 patients in 1 study[1] Follow up 12 months	per 1000	per 1000 Difference: **fewer per 1000**	**Very Low** Due to very serious imprecision, Due to serious publication bias[2]	There were too few who experienced the all-cause mortality to determine whether belimumab made a difference
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 0.98 (95% CI: 0.26 - 3.72) Based on data from 105 patients in 1 study[3] Follow up 12 months	**77** per 1000	**75** per 1000 Difference: **2 fewer per 1000** (95% CI: 57 fewer - 209 more)	**Very Low** Due to very serious imprecision, Due to serious publication bias[4]	There were too few who experienced the infection to determine whether belimumab made a difference
Malignancy	Relative risk: 8.83 (95% CI: 0.49 - 160.07) Based on data from 105 patients in 1 study[5] Follow up 12 months	per 1000	per 1000 Difference: **fewer per 1000**	**Very Low** Due to very serious imprecision, Due to serious publication bias[6]	There were too few who experienced the infection to determine whether belimumab made a difference
Major relapse	Relative risk: 2.94 (95% CI: 0.12 - 70.67) Based on data from 105 patients in 1 study[7] Follow up 12 months	per 1000	per 1000 Difference: **fewer per 1000**	**Very Low** Due to very serious imprecision, Due to serious publication bias[8]	There were too few who experienced the major relapse to determine whether belimumab made a difference
Serious adverse events	Relative risk: 0.74	**347** per 1000	**257** per 1000	**Low**	Belimumab may have little or no

	(95% CI: 0.27 - 1.97) Based on data from 105 patients in 1 study[9] Follow up 12 months	Difference: **90 fewer per 1000** (95% CI: 253 fewer - 337 more)	Due to serious imprecision, Due to serious publication bias[10]	difference on serious adverse events
Vasculitis relapse	Relative risk: 0.74 (95% CI: 0.27 - 1.97) Based on data from 105 patients in 1 study[11] Follow up 12 months	**154** per 1000 **114** per 1000 Difference: **40 fewer per 1000** (95% CI: 112 fewer - 149 more)	**Low** Due to serious imprecision, Due to serious publication bias[12]	Belimumab may have little or no difference on vasculitis relapse

1. Systematic review with included studies: [553] **Baseline/comparator** Control arm of reference used for intervention.
2. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study; **Publication bias: Serious.** Mostly commercially funded studies.
3. Systematic review with included studies: [553] **Baseline/comparator** Control arm of reference used for intervention.
4. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study; **Publication bias: Serious.** Mostly commercially funded studies.
5. Systematic review with included studies: [553] **Baseline/comparator** Control arm of reference used for intervention.
6. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study; **Publication bias: Serious.** Mostly commercially funded studies.
7. Systematic review with included studies: [553] **Baseline/comparator** Control arm of reference used for intervention.
8. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study; **Publication bias: Serious.** Mostly commercially funded studies.
9. Systematic review with included studies: [553] **Baseline/comparator** Control arm of reference used for intervention.
10. **Imprecision: Serious.** Only data from one study; **Publication bias: Serious.** Mostly commercially funded studies.
11. Systematic review with included studies: [553] **Baseline/comparator** Control arm of reference used for intervention.
12. **Imprecision: Serious.** Only data from one study; **Publication bias: Serious.** Mostly commercially funded studies.

References

[448] Walters GD, Willis NS, Cooper TE, Craig JC: Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews. 2020;1 CD003232

[553] Jayne D, Blockmans D, Luqmani R, Moiseev S, Ji B, Green Y, Hall L, Roth D, Henderson RB, Merkel PA. Efficacy and Safety of Belimumab and Azathioprine for Maintenance of Remission in Antineutrophil Cytoplasmic Antibody-Associated Vasculitis: A Randomized Controlled Study. Arthritis & Rheumatology 2019;71(6):952-963

Table S31.
Population: Patients with ANCA-associated vasculitis
Intervention: Maintenance therapy: Rituximab
Comparator: Maintenance therapy: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Maintenance therapy: Placebo	Maintenance therapy: Rituximab	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	Relative risk (95% CI: -) Based on data from 97 patients in 1 study[1] Follow up 28 months	per 1000	per 1000 Difference: **fewer per 1000**	**Low** Due to very serious imprecision[2]	There were too few who experienced the all-cause mortality to determine whether maintenance therapy: rituximab made a difference
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.41 (95% CI: 0.42 - 4.69) Based on data from 97 patients in 1 study[3] Follow up 12 months	**86** per 1000	**121** per 1000 Difference: **35 more per 1000** (95% CI: 50 fewer - 317 more)	**Low** Due to very serious imprecision[4]	Maintenance therapy: rituximab may have little or no difference on infection
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Relapse	Relative risk: 0.16 (95% CI: 0.04 - 0.66) Based on data from 97 patients in 1 study[5] Follow up 28 months	**256** per 1000	**41** per 1000 Difference: **215 fewer per 1000** (95% CI: 246 fewer - 87 fewer)	**Moderate** Due to serious imprecision[6]	Maintenance therapy: rituximab probably decreases relapse
Serious adverse events	Relative risk: 0.81 (95% CI: 0.42 - 1.56) Based on data from 97 patients in 1 study[7] Follow up 28 months	**298** per 1000	**241** per 1000 Difference: **57 fewer per 1000** (95% CI: 173 fewer - 167 more)	**Low** Due to very serious imprecision[8]	Maintenance therapy: rituximab may have little or no difference on serious adverse events

1. Systematic review with included studies: [554] **Baseline/comparator** Control arm of reference used for intervention.
2. **Imprecision: Very Serious.** Only data from one study, Low number of patients.
3. Systematic review with included studies: [554] **Baseline/comparator** Control arm of reference used for intervention.
4. **Imprecision: Very Serious.** Wide confidence intervals, Only data from one study.
5. Systematic review with included studies: [554] **Baseline/comparator** Control arm of reference used for intervention.
6. **Imprecision: Serious.** Only data from one study.
7. Systematic review with included studies: [554] **Baseline/comparator** Control arm of reference used for intervention.
8. **Imprecision: Very Serious.** Only data from one study.

References

[448] Walters GD, Willis NS, Cooper TE, Craig JC. Interventions for renal vasculitis in adults. The Cochrane Database of Systematic Reviews. 2020;1 CD003232

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Table S32.
Population: Patients with ANCA-associated vasculitis
Intervention: Maintenance therapy: Mizoribine
Comparator: Maintenance therapy: Placebo

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Maintenance therapy: Placebo	Maintenance therapy: Mizoribine	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
All-cause mortality	(95% CI: -)	Difference:			No studies were found that looked at mortality
End-stage kidney disease	(95% CI: -)	Difference:			No studies were found that looked at end-stage kidney disease
≥50% loss of GFR	(95% CI: -)	Difference:			No studies were found that looked at ≥50% loss of GFR
Infection	Relative risk: 1.12 (95% CI: 0.25 – 5.05) Based on data from 53 patients in 1 study[1] Follow up 12 months	**107** per 1000	**120** per 1000 Difference: **13 more per 1000** (95% CI: 158 fewer - 184 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[2]	We are uncertain whether mizoribine increases or decreases infections
Malignancy	(95% CI: -)	Difference:			No studies were found that looked at malignancy
Relapse	Relative risk: 1.68 (95% CI: 0.53 – 5.28) Based on data from 53 patients in 1 study[3] Follow up 12 months	**143** per 1000	**240** per 1000 Difference: **97 more per 1000** (95% CI: 115 fewer - 309 fewer)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[4]	We are uncertain whether mizoribine increases or decreases replapse
Serious adverse events	Relative risk: 5.37 (95% CI: 0.27 – 106.88) Based on data from 53 patients in 1 study[5] Follow up 12 months	**0** per 1000	**77** per 1000 Difference: **77 more per 1000** (95% CI: 44 fewer - 195 more)	**Very Low** Due to serious risk of bias, Due to very serious imprecision[6]	We are uncertain whether mizoribine increases or decreases serious adverse events

1. Systematic review with included studies: [Mase 2022] **Baseline/comparator** Control arm of reference used for intervention.
2. **Imprecision: Very Serious.** Only data from one study, Low number of patients.
3. Systematic review with included studies: [Mase 2022] **Baseline/comparator** Control arm of reference used for intervention.
4. **Imprecision: Very Serious.** Only data from one study, Low number of patients.

5. Systematic review with included studies: [Mase 2022] **Baseline/comparator** Control arm of reference used for intervention.
6. **Imprecision: Very Serious.** Only data from one study, Low number of patients.

References

[Mase 2022] Mase K, Saito C, Usui J, Arimura Y, Nitta K, Wada T. The efficacy and safety of mizoribine for maintenance therapy in patients with myeloperoxidase anti-neutrophil cytoplasmic antibody (MPO-ANCA)-associated vasculitis: the usefulness of serum mizoribine monitoring. Clin Exp Nephrol 2022;26(11):1092-1099.