Appendix 4 GRADE summary of findings on the use of reduced-dose regimen versus standard-dose regimen of glucocorticoids in patients with ANCA-associated vasculitis

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Standard-dose regimen of glucocorticoids / Reduced-dose regimen of glucocorticoids	**Certainty of the Evidence** (Quality of evidence)	**Plain text summary**
Death	Based on data from 838 patients in 2 study Follow up: 6 months to 2.9 years	Two RCTs reported death from any cause. In Walsh et al's trial, death occurred in 46 of 353 patients (13.0%) in the reduced-dose GC therapy group and in 53 of 351 patients (15.1%) in the standard-dose GC therapy group (Risk difference, -2.1%; 95% confidence interval, -6% to 3.6%). In Furuta et al's trial, death occurred in 2 of 69 patients (2.9%) in the reduced-dose GC treatment group and in 3 of 65 patients (4.6%) in the high-dose GC treatment group (Risk difference, -1.7%; 95% confidence interval, -4.7% to 8.2%).	**Low** Due to very serious imprecision[1]	Reduced dose of glucocorticoids may reduce death at follow-up of 6 months to 2.9 years
End-stage kidney disease	Based on data from 838 patients in 2 study Follow up: 6 months to 2.9 years	Two RCTs reported end-stage kidney disease. In Walsh et al's trial, end-stage kidney disease occurred in 70 of 353 patients (19.8%) in the reduced-dose GC therapy group and in 68 of 351 patients (19.4%) in the standard-dose GC therapy group (Risk difference, 0.4%; 95% confidence interval, -4.7%	**Moderate** Due to serious imprecision[2]	Reduced dose of glucocorticoids probably has little or no effect on end-stage kidney disease at follow-up of 6 months to 2.9 years

		to 7.4%). In Furuta et al's trial, end-stage kidney disease occurred in none of 69 patients (0%) in the reduced-dose GC treatment group and in 1 of 65 patients (1.5%) in the high-dose GC treatment group (Risk difference, -1.5; 95% confidence interval, -4.5 to 1.5).		
Remission	Based on data from 838 patients in 2 study Follow up: 6 months to 2.9 years	Two RCTs reported remission rate. In Walsh et al's trial, remission was analyzed in the two GC groups with the use of Cox proportional-hazards models resulting a hazard ratio of 1.04 (95% confidence interval, 0.81 to 1.33). In Furuta et al's trial, remission occurred in 49 of 69 patients (71.0%) in the reduced-dose GC treatment group and in 45 of 65 patients (69.2%) in the high-dose GC treatment group (Risk difference, 1.8%; 97.5% confidence interval, -13% to ∞).	**Moderate** Due to serious imprecision[1]	Reduced dose of glucocorticoids probably has little or no effect on disease remission at follow-up of 6 months to 2.9 years
Relapse	Based on data from 838 patients in 2 study Follow up: 6 months to 2.9 years	Two RCTs reported remission rate. In Walsh et al's trial, relapse occurred in 32 of 353 patients (9.1%) in the reduced-dose GC therapy group and in 23 of 351 patients (6.6%) in the standard-dose GC therapy group (Risk difference, 2.5%; 95% confidence interval, -1.45% to 6.47%). In Furuta et al's trial, relapse occurred in 3	**Moderate** Due to serious imprecision[3]	Reduced dose of glucocorticoids probably has little or no effect on relapse in patients at follow-up of 6 months to 2.9 years

		of 69 patients (4.3%) in the reduced-dose GC treatment group and in none of 65 patients (0%) in the high-dose GC treatment group (Risk difference, 4.4%; 95% confidence interval, -0.5% to 9.2%).		
Serious adverse events	Based on data from 838 patients in 2 study Follow up: 6 months to 1 year	Two RCTs reported serious adverse events. In Walsh et al's trial, serious adverse events occurred in 230 of 353 patients (65.2%) in the reduced-dose GC therapy group and in 218 of 351 patients (62.1%) in the standard-dose GC therapy group (Risk difference, 3.1%; 95% confidence interval, -3.7% to 11.2%). In Furuta et al's trial, serious adverse events occurred in 13 of 69 patients (18.8%) in the reduced-dose GC treatment group and in 24 of 65 patients (36.9%) in the high-dose GC treatment group (Risk difference, -18.1%; 95% confidence interval, -33.0% to -3.2%).	**Very Low** Due to serious imprecision[4] Due to very serious inconsistency	We are uncertain whether reduced dose of glucocorticoids increases or reduce the risk of serious adverse events at 6 months to 1 year
Serious infections	Based on data from 838 patients in 2 study Follow up: 6 months to 1 year	Two RCTs reported serious infections. In Walsh et al's trial, serious infections occurred in 230 of 353 patients (27.1%) in the reduced-dose GC therapy group and in 218 of 351 patients (33.0%) in the standard-dose GC therapy group (Risk difference, -5.9%;	**Moderate** Due to serious imprecision[3]	Reduced dose of glucocorticoids probably reduces the risk of serious infections at 6 months to 1 year

		95% confidence interval, -11.2% to 1.0%). In Furuta et al's trial, serious infections occurred in 5 of 69 patients (7.2%) in the reduced-dose GC treatment group and in 13 of 65 patients (20.0%) in the high-dose GC treatment group (Risk difference, -12.8%; 95% confidence interval, -24.2% to -1.3%).		
Health related quality of life (SF-36 PCS)	Measured by: SF-36 PCS Scale: - High better Based on data from 838 patients in 2 study Follow up: 6 months to 1 years	Two RCTs reported health related quality of life assessed by SF-36 PCS. Walsh et al's trial reported that the mean score of health related quality of life measured by SF-36PCS was 39.13 in the reduced-dose GC therapy group and 37.84 in the standard-dose GC therapy group (Mean difference, 1.29 higher; 95% confidence interval, 0.26 lower to 2.84 higher). Furuta et al's trial reported that the median score of health related quality of life measured by SF-36PCS was 38.3 (IQR : 21.1 to 47.4) in the reduced-dose GC treatment group and 31.7 (IQR : 22.0 to 49.4) in the high-dose GC treatment group (Mean difference, 6.3 higher; 95% confidence interval, 2.6 lower to 15.2 higher).	**Moderate** Due to serious imprecision	Reduced dose of glucocorticoids probably has little or no effect on health related quality of life (SF-36PCS) at 6 months to 1 years

Health related quality of life (SF-36 MCS)	Measured by: SF-36 MCS Scale: - High better Based on data from 838 patients in 2 study Follow up: 6 months to 1 years	Two RCTs reported health related quality of life assessed by SF-36 MCS. Walsh et al's trial reported that the mean score of health related quality of life measured by SF-36MCS was 52.16 in the reduced-dose GC therapy group and 51.19 in the standard-dose GC therapy group (Mean difference, 0.97 higher; 95% confidence interval, 0.24 lower to 2.18 higher). Furuta et al's trial reported that the median score of health related quality of life measured by SF-36MCS was 49.8 (IQR : 45.1 to 56.6) in the reduced-dose GC treatment group and 50.4 (IQR : 46.3 to 57.2) in the high-dose GC treatment group (Mean difference, 0.4 lower; 95% confidence interval, 4.7 lower to 4.0 higher).	**High**	Reduced dose of glucocorticoids has little or no effect on health related quality of life (SF-36MCS) at 6 months to 1 years
Health related quality of life (EQ-5D Index) at 1 year	Measured by: EQ-5D Index Scale: - High better Based on data from 704 patients in 1 study Follow up at 1 year	**0.77** Mean **0.79** Mean Difference: **MD 0.02 higher** (CI 95% 0.01 lower - 0.05 higher)	**Moderate** Due to serious imprecision[5]	Reduced dose of glucocorticoids probably has little or no effect on health related quality of life (EQ-5D) at 1 year
Health related quality of life (EQ-5D Thermometer) at 1 year	Measured by: EQ-5D Thermometer Scale: - High better Based on data from 704 patients in 1 study Follow up at 1 year	**71.07** Mean **72.11** Mean Difference: **MD 1.04 higher** (CI 95% 1.09 lower - 3.17 higher)	**High**	Reduced dose of glucocorticoids has little or no effect on health related quality of life (EQ-5D Thermometer) at 1 year

1. **Imprecision: Very serious.** Because the 95% CI includes both the minimally important difference for benefit (20 fewer death in 1000 patients) and minimally important difference for harm (20 more death in 1000 patients, we rated down two levels for imprecision;

2. **Imprecision: Serious.** The 95% CI crosses the minimally important difference for benefit (30 fewer ESKD in 1000 patients) and minimally important difference for harm (30 more ESKD in 1000 patients) ;

3. **Imprecision: Serious.** The 95% CI crosses the minimally important difference (50 fewer serious infections in 1000 patients);

4. **Imprecision: Serious.** The 95% CI includes an increase in serious adverse event over 10%;

5. **Imprecision: Serious.** The 95% CI crosses the minimally important difference for benefit and the minimally important difference for harm (0.03 reduction or increase in EQ-5D Index) ;

ESKD: end-stage kidney disease; SF-36 = short form 36; PCS = physical component score; MCS = mental component score; EQ = EuroQol; RR: relative risk; MD: mean difference; CI: confidence interval. IQR = interquartile range