Additional file 11. GRADE summary of evidence

Certainty of evidence for the ten principal comparisons, given separately for each comparison and outcome, using the RoB 2 judgements in Additional file 10. Certainty starts at high for randomized evidence, and **the reported grade equals high minus the deductions listed in that row**, so every row can be recomputed from its own ledger. Domains not listed for a row were not deducted.

Why four comparisons were added. MAIN, the STOP-IgAN 10-year follow-up, the DAPA-CKD IgA subgroup and the EMPA-KIDNEY IgA subgroup carry treatment-level statements in this review — on additional immunosuppression and on SGLT2 inhibition — and were therefore assessed rather than left unrated. No effect estimate was recalculated when they were added.

Scope. GRADE covers the 23 outcomes from the ten principal comparisons. Additional RoB 2 assessments do not automatically receive a GRADE rating. Other results are listed in section 3 without a grade. The exploratory calculation in Additional file 4 and candidate results from the three unresolved-eligibility entries are outside the graded clinical synthesis.

What this table does not do. It does not apply a second, automatic deduction to results that are read as evidence about kidney failure: where the outcome is an eGFR quantity or a composite containing an eGFR-threshold component, the limits of that reading are given as an interpretation note under the row and are not converted into a second grade. It does not deduct for a design or reporting label: being eGFR-based, subgroup-derived, secondary-endpoint, open-label or small-sample was not by itself a ground for a deduction. Two distinctions follow from that and are applied to the four comparisons added here. **Being a subgroup does not deduct; having been defined post hoc does, when its effect on the specific row cannot be excluded** — the EMPA-KIDNEY IgA row is deducted once for exactly that, while both subgroup rows whose comparison was pre-specified (DAPA-CKD, FIND-CKD) are not deducted for being subgroups. **Being open-label does not deduct; a recorded concern that plausibly bears on this result does** — MAIN and the STOP-IgAN 10-year follow-up are deducted because the allocation process itself is not documented in the material: neither report states how the sequence was concealed from those enrolling participants, and for MAIN it is not stated how the sequence was generated either. That deduction rests on the allocation process alone. It is not supported by the fact that the trials were open-label, and it is not supported by the possibility that clinicians who knew the assignment decided when to start kidney replacement therapy: that is a question about how the outcome was ascertained, it is asked under domain 4 in Additional file 10, and in MAIN the report's blinded adjudicating committee answers it. A concern is therefore only carried into this table under the domain to which it belongs. And it does not convert a risk-of-bias concern into a deduction automatically: where Additional file 10 records a concern, the row states what that concern is and whether it was judged to affect **this** result.

1. Scales and thresholds used for imprecision

Judging imprecision requires a stated scale, and two are used, one for each kind of quantity in the table.

1. **Outcomes reported as a ratio (hazard ratio or relative risk).** The anchor is a 25% relative reduction, which is 0.75 on the scale the row reports. A hazard ratio is a ratio of hazard rates over the follow-up actually observed, and a relative risk is a ratio of cumulative risk; these are different quantities and are not treated as interchangeable. The anchor is applied **within** a row, and is never used to compare one row with another.
2. **Annualized eGFR slope differences.** The anchor is 1.0 mL/min/1.73 m² per year. MAIN reports trial-phase annual decline rates of 1.2 (0.6) and 3.8 (0.6), P<0.001, and specifies a linear mixed-effects model for the treatment effect. The model-based contrast interval is not reported. The arithmetic rate difference is 2.6. The 0.6 printed beside

each arm mean is not identified as a between-patient SD, and it cannot be used as one: an SD of 0.6 at a mean annual decline of 3.8 could not coexist with the 32.9% of supportive-care participants that the trial reports above 5 mL/min/1.73 m²/year. The figure therefore gives no precision for the between-group comparison, no interval was reconstructed from it, and the row is downgraded once for imprecision because the report states P<0.001 only and no contrast interval.

Both are this review's interpretive choices. They were selected **after the results of these comparisons were known** and are disclosed as post hoc interpretive thresholds, not as pre-registered hypotheses; they are not presented as validated minimum important differences. A value below a threshold is described as being below that threshold, not as clinically negligible.

A quantity that is neither of these. Two rows report a difference in mL/min/1.73 m² that is not an annual rate: the ALIGN week-136 eGFR change, and the NefIgArd two-year time-weighted average. Neither anchor applies to them, because a rate and a level are not the same quantity. For these rows imprecision was judged only from whether the interval excluded no difference, and the row states that no minimum important difference in these units is available, so its certainty speaks to the **existence and direction** of a difference rather than to its clinical importance. No deduction was applied for the absence of a threshold, and none was applied by borrowing a threshold from another quantity.

An assumption in a power calculation is not a clinical threshold. The NefIgArd power calculation assumed "a difference in mean eGFR of 2·24 mL/min per 1·73 m² at 2 years". That is the design assumption for the quantity that calculation addressed — a difference in mean eGFR **at** two years — and the endpoint rated here is the time-weighted average **over** two years. Equal units do not make them the same estimand, and the material does not establish that the assumed figure corresponds to the time-weighted average. The figure is therefore recorded as design background only and is **not** used as this row's threshold.

No required number of events was calculated. No number of events or participants needed for a given power was computed for these comparisons, so no row claims that such a number was reached or exceeded. Participants and events are recorded only where the source reports them; where a source reports arm percentages only, no count is stated.

Deduction rule for imprecision. Imprecision was deducted by one where the interval did not exclude an effect smaller than the anchor for that row, or where it included no difference. A limit that lands exactly on the anchor is recorded as reaching the threshold and is **not** treated as a mechanical trigger for a deduction.

2. Certainty per comparison and outcome

Comparison	Outcome	Effect as reported	RoB	Indirectness	Imprecision	Certainty	Interpretation note
TESTING	Composite: 40% eGFR decline, kidney failure or kidney death	HR 0.53 (0.39–0.72); 180 events (74 vs 106) / 503	0	0	0 (the whole interval lies below 0.75, the ratio corresponding to the anchored 25% relative reduction)	**High**	The composite contains a ≥40% eGFR-decline component, so a reduction in the composite is not identical to a reduction in kidney failure; the kidney-failure component was also reported separately (50/257 vs 67/246; HR 0.59, 0.40–0.87; 117 events)

Comparison	Outcome	Effect as reported	RoB	Indirectness	Imprecision	Certainty	Interpretation note
TESTING	eGFR slope	Difference 2.46 (0.94–3.99)	0	0	**−1** (lower bound 0.94 is below the 1.0 mL/min/1.73 m² per year anchor, so an effect below the chosen threshold is not excluded)	**Moderate**	A slope over the trial period, not a fixed-time difference; effects below the threshold are not thereby negligible
NefIgArd	Composite: confirmed ≥30% eGFR decline or kidney failure	HR 0.45 (0.26–0.75); 60 events (21 vs 39) / 364	0	0	0 (the reported upper limit reaches the chosen threshold of 0.75; the rounded limit is recorded as reaching the anchor and is not used as a mechanical trigger for a deduction)	**High**	The composite is mainly confirmed ≥30% eGFR decline
NefIgArd	2-year eGFR time-weighted average	Difference 5.05 (3.24–7.38); 364	0	0	0 (the interval excludes no difference; no minimum important difference is available in these units — see section 1)	**High**	A time-weighted average is not a slope and cannot be read as an annual rate. Certainty concerns the existence and direction of the difference, not its clinical importance, for which no threshold is available. The 2.24 mL/min/1.73 m² assumed in the trial's power calculation is recorded as design background only
APPLAUSE-IgAN	Composite kidney-failure endpoint (secondary, within the multiplicity-controlled sequence)	HR 0.57 (0.40–0.81); full analysis population 477; the source reports arm percentages (21.4% vs 33.5%) and no event count	**−1** (D3: the participant flow, and therefore censoring before 24 months, is in a supplementary figure not in the material available)	0	**−1** (the upper bound 0.81 exceeds 0.75, the anchored ratio, so the interval does not exclude a reduction smaller than 25%)	**Low**	The composite contains a sustained ≥30% eGFR-decline component. No event count is stated because the source gives percentages only. Two independent limitations apply, and the row should be revisited if the supplement is obtained
APPLAUSE-IgAN	24-month annualized total slope	Difference 3.02 (2.02–4.01); 477	**−1** (D3: completeness of the slope data is not documented and no analysis in the material varies the missing-data assumption; the extent to which the estimate depends on that assumption cannot be bounded)	0	0 (lower bound 2.02 is above the 1.0 anchor)	**Moderate**	A total slope includes the initial period, in which a haemodynamic effect is expected

Comparison	Outcome	Effect as reported	RoB	Indirectness	Imprecision	Certainty	Interpretation note
ALIGN	Total slope to week 136 (supportive analysis)	Difference 1.4 (0.5–2.3); 340	**−1** (D3: the number with missing eGFR values by arm is not reported, and the reported sensitivity analyses vary the handling of intercurrent events rather than the missing-data assumption)	0	**−1** (lower bound 0.5 is below the anchor)	**Low**	Not part of the multiplicity-controlled sequence; the analysis is reported in full
ALIGN	Week-136 eGFR change (key secondary)	Difference 2.4 (−0.1 to 4.8); 340	**−1** (D3, as above)	0	**−1** (the interval includes no difference)	**Low**	A fixed-time difference, not a slope; no same-unit anchor is stated for a week-136 change, so only the exclusion of no difference is used
ALIGN	Composite kidney outcome (30% eGFR decline, kidney failure or all-cause death)	HR 0.64 (0.39–1.05); 63 events / 340	0 (D3 is at some concerns, but the row is **not** deducted: the numbers leaving the study are documented by arm and reason, with loss to follow-up of 2 of 170 and 4 of 170, so the extent of censoring is bounded and the concern is recorded as a limitation rather than applied to this result)	0	**−1** (the interval includes both no difference and reductions smaller than the anchored 25%)	**Moderate**	The composite contains a 30% eGFR-decline component
FIND-CKD (IgA subgroup)	Chronic slope	Difference 1.17 (0.43–1.91); 416	**−1** (D3: the subgroup's missing outcome data are not documented in the material available, so the proportion missing cannot be bounded)	0 (the subgroup is the target population; randomization is preserved within it)	**−1** (lower bound 0.43 is below the anchor)	**Low**	The subgroup analysis was pre-specified and is reported as exploratory with descriptive P values
FIND-CKD (IgA subgroup)	Total slope	Difference 0.61 (−0.14 to 1.36); 416	**−1** (D3, as above)	0	**−1** (the interval includes no difference)	**Low**	As above
FIND-CKD (IgA subgroup)	Composite: kidney failure or ≥40% eGFR decline	HR 0.82 (0.56–1.21); 103 events / 416	**−1** (D3, as above)	0	**−1** (the interval includes no difference and reductions smaller than the anchored 25%)	**Low**	Contains a ≥40% eGFR-decline component

Comparison	Outcome	Effect as reported	RoB	Indirectness	Imprecision	Certainty	Interpretation note
PROTECT	Chronic slope (weeks 6–110)	Difference 1.1 (0.1–2.1); 404	**−1** (D3: the number with observed values by outcome is not reported and the reported sensitivity analyses vary the analysis set and intercurrent-event handling, not the missing-at-random assumption on which the imputation rests)	0	**−1** (lower bound 0.1 is below the 1.0 anchor)	**Low**	A chronic slope excludes the initial period. The trial's own power calculation assumed 3.15 mL/min/1.73 m² per year for this endpoint; the interval lies entirely below that figure as well
PROTECT	Total slope (day 1 to week 110)	Difference 1.0 (−0.03 to 1.94); 404	**−1** (D3, as above)	0	**−1** (the interval includes no difference)	**Low**	As above; total and chronic slopes are different quantities
PROTECT	Composite kidney endpoint (confirmed 40% eGFR reduction, ESKD or all-cause death)	RR 0.70 (0.40–1.20); 44 events / 404	0 (D3 is at some concerns, but the row is **not** deducted: discontinuations are documented by arm and reason and the number at risk is shown throughout follow-up, so the extent of censoring is bounded)	0	**−1** (the interval includes no difference and reductions smaller than the anchored 25%)	**Moderate**	Contains a confirmed ≥40% eGFR-reduction component. This row reports a relative risk, a cumulative-risk ratio, and is not compared with the hazard-ratio rows

Comparison	Outcome	Effect as reported	RoB	Indirectness	Imprecision	Certainty	Interpretation note
MAIN	Composite: creatinine doubling, kidney failure or death from a kidney or cardiovascular cause	Adjusted HR 0.23 (0.09–0.63); 24 events (6 vs 18) / 170 randomised within the trial; the report also gives the unadjusted HR 0.31 (0.12–0.78)	**−1** (D1: the report states that participants "were randomly assigned at a 1:1 ratio" and that "randomization was carried out via phone call", and says nothing further about the process — neither how the sequence was generated nor that it was kept out of the reach of those assigning participants — so the concealment question is unresolved in the material. The deduction concerns the allocation process alone: whether the sequence was random and whether it could be foreseen. The separate question of whether knowledge of the open-label assignment could have influenced ascertainment of the kidney-replacement-therapy component is assessed under domain 4 in Additional file 10, where the report's blinded adjudicating committee answers it, and it is not used to support this deduction)	0 (the comparator is optimized supportive care, which is the relevant alternative rather than a surrogate for it)	0 (the whole interval lies below 0.75, the anchored ratio: the upper limit 0.63 excludes a reduction smaller than 25%)	**Moderate**	The reviewed estimate is the covariate-adjusted hazard ratio, adjusted for age, sex, body mass index, systolic blood pressure, baseline eGFR, urinary protein excretion and the individual Oxford MEST-C scores, over 24 events; the unadjusted estimate is in the same direction. Certainty therefore concerns whether the reduction is at least of the anchored size, not whether a difference exists. Two limits are not deducted: the report's own significance threshold was $P < 0.025$ because it specifies two primary outcomes, and its intervals were not adjusted for multiplicity; and the report describes the trial as single-centre while the registration lists several facilities, which restricts where the result applies rather than what it shows

Comparison	Outcome	Effect as reported	RoB	Indirectness	Imprecision	Certainty	Interpretation note
MAIN	Annual rate of eGFR decline over the 3-year trial phase	Published annual decline: 1.2 (0.6) vs 3.8 (0.6) mL/min/1.73 m²/year, P<0.001. Linear mixed-effects treatment-effect model specified; no interval for its trial-phase contrast. Arithmetic rate difference 2.6; no reconstructed CI.	**−1 (D1, as in the row above: the report states** neither how the sequence was generated nor **how it was held, so 1.2 is NI and the domain follows the tool's path for that answer)**	0 (an annual rate over the trial phase, which is the estimand used here)	−1 (The report gives no model-based contrast and no interval for the trial-phase slope, only P<0.001. The 0.6 printed beside each arm mean is not identified as a between-patient SD and cannot substitute for the missing interval: at a mean of 3.8 an SD of 0.6 could not produce the 32.9% of supportive-care participants reported above 5 mL/min/1.73 m²/year. Precision against the 1.0 mL/min/1.73 m²/year anchor therefore cannot be established, and no interval was reconstructed.)	Low	Graded Low: one deduction for risk of bias (allocation reporting) and one for imprecision (no contrast interval). This is the trial-phase annual decline, kept separate from post-trial follow-up and from the composite, which is a different row graded Moderate; that grade does not apply to this result. The published arm means and the stated mixed-effects method are retained; no model-based contrast or interval was reconstructed.

Comparison	Outcome	Effect as reported	RoB	Indirectness	Imprecision	Certainty	Interpretation note
STOP-IgAN (10-year follow-up)	Composite: all-cause death, end-stage kidney disease or >40% eGFR decline	HR 1.20 (0.75–1.92), reported with supportive care as the reference category; 71 events (35 of 77 with added immunosuppression, 36 of 72 with supportive care) / 149 analysed of 162 randomised	**−1** (D1: the allocation is that of the original trial, and the original trial report [27] was consulted rather than relying on the long-term report alone. It states that "randomization codes that were used to assign patients in a 1:1 ratio were generated by means of covariate adaptive randomization" with respect to baseline eGFR and proteinuria, so the generation of the sequence is described; neither that report nor the long-term report states how the codes were held or concealed from those enrolling participants, so the concealment question remains unresolved. The comparison also rests on 149 of 162 participants followed observationally for a median of 7.4 years, during which post-trial treatment was neither standardized nor shown to be comparable between the groups. Two concerns that belong to other domains are not used here: whether knowledge of the original allocation influenced recognition of end-stage kidney disease is assessed under domain 4, and whether the missing long-term data biased the comparison under domain 3, where the report's best- and worst-case analyses answer it)	0 (the randomised groups are the target comparison, analysed as randomised over a median of 7.4 years)	**−1** (the interval includes no difference and includes relative effects from 0.75 to 1.92, so neither a 25% reduction nor appreciable harm is excluded)	**Low**	A null result with a wide interval: it limits rather than establishes, in the specific sense that a benefit of the anchored size or larger is not excluded. The report's multivariate analysis found the trial-phase regimen not predictive of the endpoint, and the authors record that they could not test histology-defined subsets because MEST-C scores could not be assessed retrospectively. Because 149 of the 162 randomised participants contributed, the result applies to those followed and not to all randomized patients

Comparison	Outcome	Effect as reported	RoB	Indirectness	Imprecision	Certainty	Interpretation note
DAPA-CKD (IgA subgroup)	Composite: sustained ≥50% eGFR decline, end-stage kidney disease or death from a kidney or cardiovascular cause	HR 0.29 (0.12–0.73); 26 events (6 vs 20) / 270; median follow-up 2.1 years	**−1** (D3: within the subgroup the material does not document how many participants lacked the data needed to ascertain the composite. The reported sensitivity analysis restricted to biopsy-proven cases varies the population, not the missing-data assumption, and no analysis in the material varies that assumption)	0 (the subgroup is the target population and the analysis was pre-specified; the diagnose rests on biopsy in 254 of 270)	0 (the upper limit 0.73 lies below 0.75, the anchored ratio, so the interval excludes a reduction smaller than 25%)	**Moderate**	Twenty-six events over a median of 2.1 years is the reason the row should be read with its interval rather than its point estimate; the limitations on this are those of precision in small numbers, which the interval already carries. The parent trial stopped early on its monitoring committee's recommendation, which limits the number of events rather than the comparability of the groups. The composite contains a ≥50% eGFR-decline component, so a reduction in it is not identical to a reduction in kidney failure
DAPA-CKD (IgA subgroup)	Total eGFR slope to end of treatment	Difference 1.2 mL/min/1.73 m² per year (−0.12 to 2.51); 137 vs 133	**−1** (D3: **as in the composite row, completeness within the subgroup is not documented in the material available, and no analysis in it varies the missing-data** assumption)	0 (the subgroup is the target population and randomization is preserved within it)	−1 (the interval includes no difference)	**Low**	The total slope includes the initial period. This quantity crosses zero while the chronic slope from the same subgroup does not, so the two are reported separately and are not interchangeable
DAPA-CKD (IgA subgroup)	Chronic eGFR slope from week 2	Difference 2.4 mL/min/1.73 m² per year (1.08 to 3.71)	**−1 (D3, as above)**	0	0 (lower bound 1.08 is above the 1.0 mL/min/1.73 m² per year anchor)	**Moderate**	A chronic slope excludes the initial period, so it is not the total slope from the same subgroup and the two are not compared

Comparison	Outcome	Effect as reported	RoB	Indirectness	Imprecision	Certainty	Interpretation note
EMPA-KIDNEY (IgA subgroup)	Kidney disease progression (sustained ≥40% eGFR decline, end-stage kidney disease, sustained eGFR <10, or death from kidney failure)	HR 0.67 (0.46–0.97); 118 events (51 vs 67) / 817; median follow-up 2.0 years	**−1** (two concerns, deducted once. D3: completeness within the IgA group is not documented. D5: the report states that the glomerular disease subgroup "was further split post hoc", so this comparison had no pre-specified analysis plan finalised before outcome data were available; the report gives a stated external reason for the split and presents all three glomerular categories together, which is why the concern is not read as evidence that this result was selected, but what would have been reported under a different split cannot be established)	0 (the IgA group is the target population; allocation is preserved within a grouping recorded at randomisation)	**−1** (the upper limit 0.97 exceeds 0.75, so the interval does not exclude a reduction smaller than the anchored 25%)	**Low**	The row's estimate is on the boundary in another sense too: the interval barely excludes no difference, so this row supports a reduction without establishing its size

Comparison	Outcome	Effect as reported	RoB	Indirectness	Imprecision	Certainty	Interpretation note
EMPA-KIDNEY (IgA subgroup)	Chronic eGFR slope (2 months to final follow-up)	Relative reduction 43% (95% CI 27 to 59); absolute group values are not reported for this subgroup	**−1** (as in the row above: D3 for undocumented completeness within the group, and D5 for the post hoc definition of the split)	0	**0** (no deduction is made for imprecision, and none is assumed away; the reason is given in the note)	**Moderate**	This row reports a **relative** difference in slope, and the material gives no absolute chronic-slope difference for the IgA group, so **neither of the two anchors in this file applies to it and none is borrowed** : the 1.0 mL/min/1.73 m² per year anchor is an absolute annualized quantity that cannot be reached from a percentage, and the 25% ratio anchor was defined for event hazards and does not describe a slope, so the earlier comparison between the two has been removed. The estimate is therefore judged on what it is: the interval excludes no difference and spans relative reductions from 27% to 59%, which is a wide range of magnitudes even though it does not include zero. Whether the underlying effect exceeds 1.0 mL/min/1.73 m² per year cannot be determined from what is reported, and that is recorded as a limit of what this result can establish rather than as grounds for a deduction or a reason to withhold one. The grade is what the ledger gives — high less the single deduction for risk of bias — and is not fixed in advance

Summary of grades. High: the NefIgArd two-year time-weighted average and composite and the TESTING composite (3 rows). Moderate: the APPLAUSE-IgAN 24-month total slope, the TESTING eGFR slope, the ALIGN and PROTECT composite kidney endpoints, the MAIN composite, the **DAPA-CKD IgA composite and chronic slope and the EMPA-KIDNEY IgA chronic slope (8** rows). Low: the APPLAUSE-IgAN composite, both ALIGN eGFR outcomes, both PROTECT slope outcomes, all three FIND-CKD outcomes, the STOP-IgAN 10-year **composite, the MAIN annual eGFR rate, the DAPA-CKD IgA total slope and the EMPA-KIDNEY IgA progression composite (12** rows). No result was rated very low, and no result was deducted for its design or reporting label. These grades describe the certainty of the evidence; they are not a restatement of the risk-of-bias summary in Figure 5, which reports 4 of the **23 assessed results at low risk, 19** at some concerns and 0 at high risk. The two tables measure different properties

and their distributions differ: a result can be at low risk of bias and still be graded low for imprecision, and every row's grade can be recomputed from the deductions stated for it. Within MAIN, the annual eGFR rate is the row graded Low and the composite is the separate row graded Moderate.

What the deductions mean. Of the **twenty-three rows, three are at high certainty, eight at moderate and twelve at low. Seventeen** rows carry a deduction for risk of bias. **Fourteen of those seventeen** rest partly or wholly on what the source reports about the completeness of the outcome data; **three of them, the MAIN composite, the MAIN annual eGFR rate and the STOP-IgAN 10-year composite,** rest instead on what the source reports about the allocation process: neither report states how the sequence was concealed from those enrolling participants, and for MAIN it does not state how the sequence was generated, whereas for STOP-IgAN the generation is described in the original trial report [27] and the missing part is the account of concealment. **None of those three** deductions draws on anything about how the outcome was ascertained, which is asked under a different domain in Additional file 10 and answered low there; and the two EMPA-KIDNEY rows additionally carry the post hoc definition of the comparison. Two further rows carry a D3 concern recorded in Additional file 10 without a deduction — the ALIGN and PROTECT composite kidney endpoints — because the material documents the numbers leaving the study by arm and reason and the extent of censoring is therefore bounded. In no row does the deduction follow from the size, direction or statistical significance of the reported effect. The practical consequence is stated in the manuscript: the long-term effects are supported but their certainty is limited partly by what the sources report about completeness and partly by the width of the intervals, and this applies to eGFR quantities and progression composites alike.

3. Results that were not rated

Result	Why it is not rated
All included results other than the twenty-three rows above	Not formally GRADE-rated. Result-specific RoB 2 coverage, including unassessed results and the additional assessments, is mapped in Additional file 10.
The exploratory pooled MMF calculation (Additional file 4)	A post hoc interval-method illustration that is excluded from the clinical synthesis; grading it would give a formal status to a calculation the review does not use.
The safety summary of systemic glucocorticoid regimens (Additional file 5)	Definitions, observation windows and denominators are not comparable between trials; a descriptive summary only, with no pooled estimate.
Proteinuria-related results	Proteinuria is not an eligible outcome of this review.
"New" relative to previous syntheses	A question of literature coverage, not a body of evidence.

4. Cross-row disciplines

1. No two rows may be combined into a statement that one drug class is better than another. Populations, background therapy, endpoint definitions and follow-up differ, and progression events, fixed-time changes, total slopes and chronic slopes are not interchangeable.
2. A certainty grade is not a statement about the size of an effect, and the interpretation notes in the right-hand column are not grades.
3. A result may not be converted into a number of kidney-failure events avoided.

4. **Arithmetic self-check:** for every row in section 2, high minus the deductions in that row equals the grade stated. **Twenty-three** rows were recomputed row by row when this file was rebuilt, including the five added for MAIN, STOP-IgAN, DAPA-CKD and **EMPA-KIDNEY and the three added in the revision of 26 October 2026 for the MAIN annual eGFR rate and the two DAPA-CKD slopes.**
5. Where an estimate could not be extracted, no grade is assigned; the row is listed in section 3 instead.
6. Rows that report a hazard ratio and rows that report a relative risk are on different scales; both were judged against the same relative-reduction anchor but are not compared with one another.
7. A risk-of-bias concern and a certainty deduction are not the same thing. Each row that carries a concern states whether the concern was judged to affect that result; in two rows it was not, and the reason is given in the row.
8. A comparison's being added later to the appraisal did not change any effect estimate it contributes, and did not change any count of included entries: the four comparisons added here were already included entries in this review. What changed is that their results now carry a domain assessment and a grade.