Additional file 14. Verification against previous syntheses, document by document

What each comparison synthesis covers, separating the formal final report from the trial, with the search cut-off date of each document. Referred to in the Results and the Discussion.

Executed 30 September 2026 (updated 7 October 2026 to add two further syntheses). The comparison documents available in full text were obtained as open-access full text from Europe PMC and searched document by document for the trials and outcomes concerned: Jeyabalan 2025 (PMC12151485), Chen B 2025 (PMC12213760), Chen R 2026 (PMC13267211) and Kim 2025 (PMC12708380). The Alharbi preprint (Research Square) is not indexed in PMC and is recorded from the scope stated in its abstract. Two further syntheses were added on 7 October 2026 and were checked against the publisher page and the article text: the 37-trial network meta-analysis of Wu et al. 2026 (BMC Nephrol 27(1):255) and the complement-targeted systematic review of Li et al. 2026 (Front Med 13:1933632).

1. Search cut-off dates (the facts first)

Comparison document	Search cut-off	Size	Outcomes analysed
Jeyabalan 2025 (PLoS One 20(6):e0323530)	**December 2023**	76 RCTs / 100 reports	proteinuria, eGFR, **kidney failure, safety**
Chen B 2025 (Front Med 12:1515723)	**20 February 2025**	57 RCTs / 5123 participants / 19 interventions	remission, **ESKD or kidney damage** , adverse events, 24-h proteinuria
Chen R 2026 (BMC Nephrol 27(1):359)	**March 2025**	17 RCTs	serious adverse events, **eGFR slope** , proteinuria, haematuria
Kim 2025 (CJASN 20(12):1753-66)	**21 May 2025**	14 multicentre phase 2b/3 RCTs	**proteinuria (6–12 month relative change) and eGFR slope (≥12 months) only** ; progression events not analysed
Alharbi et al. (preprint, Research Square)	**24 June 2026**	10 comparisons / 2036 participants	geometric mean ratio of UPCR at 26–39 weeks
Wu et al. 2026 (BMC Nephrol 27(1):255)	**15 November 2024**	37 RCTs, 15 therapies	proteinuria, serum-creatinine doubling, ESRD, adverse events; **eGFR slope not analysed**
Li et al. 2026 (Front Med 13:1933632)	**24 June 2026**	complement-targeted agents	eGFR slope and composite kidney-failure endpoint for iptacopan; **atrasentan and finerenone not covered**

2. Document-by-document verification (whether the report appears in that document's text or tables)

Our report	Jeyabalan 2025	Chen B 2025	Chen R 2026	Kim 2025
iptacopan	**Present** (phase 2 trial NCT03373461, in the safety table)	**Present** (17 mentions; deriving from the 2023 phase 2 report)	**Present** (one of the included agents, with eGFR slope among the outcomes)	**Present** (phase 2)
atrasentan / ALIGN	Only in its **table of ongoing trials** (NCT04573478, phase 3, planned completion 2025-12-01), **no results**	**Absent**	**Absent**	**Present** (ALIGN week-36 proteinuria primary analysis)
finerenone / FIND-CKD	**Absent**	**Absent**	**Absent**	**Absent**
calcitriol (Joo 2026)	**Absent**	**Absent**	**Absent**	**Absent**
felzartamab / IGNAZ	Only in its **table of ongoing trials** (NCT05065970, phase 2, planned completion 2024-01-01), **no results**	**Absent**	**Absent**	**Absent**
HR19042	**Absent**	**Absent**	**Absent**	**Absent**
sparsentan / PROTECT	Present (56 mentions)	Present (29 mentions)	Absent	Present
NefIgArd / Nefecon	Present (27 mentions)	Present (18 mentions)	Present (included)	Present
ENVISION / sibeprenlimab	Present (21 mentions, including a table of kidney-failure and death counts)	Present (13 mentions)	Present (included)	Present
ORIGIN / atacicept	Present (8 mentions)	Present (11 mentions)	**Explicitly not included** (the text states that atacicept, telitacicept, zigakibart and similar agents were not included because no mature phase 3 data were available)	Present
MAIN / MMF	Present (17 mentions; its table lists Han et al.'s MMF-plus-steroid trial)	Present (16 mentions)	Present (MMF included)	**Explicitly excluded** (the text states: "we excluded trials evaluating mycophenolate mofetil, leflunomide, hydroxychloroquine, fostamatinib and tonsillectomy because of insufficient trial size and duration")

Our report	Jeyabalan 2025	Chen B 2025	Chen R 2026	Kim 2025
STOP-IgAN	Present (5 references)	Absent	Absent	Present (post hoc analysis)

For Wu et al. 2026 and Li et al. 2026, the document-by-document result is reported in Table 4 of the manuscript: Wu et al. 2026 did not analyse eGFR slope, and its endothelin-receptor-antagonist node draws on the PROTECT two-year report and the ALIGN interim report while its iptacopan node draws on the phase 2 trial; Li et al. 2026 reports the APPLAUSE-IgAN 24-month eGFR slope and the composite kidney-failure endpoint but does not cover atrasentan or finerenone.

3. Key finding: a search cut-off date cannot by itself establish that a result was not covered

The text of Kim 2025 states explicitly:"Unpublished data were obtained for three of these trials through collaborative efforts (TESTING, DAPA-CKD and Telitacicept). Additional data for two of these trials were obtained through other sources: Post hoc analysis of the STOP-IgAN trial and updated Phase 3 data from the ORIGIN trial obtained from a webcast presentation on the sponsor website **delivered after the date of the literature search**."

>"Two additional studies were included in the meta-analysis through other sources: a prespecified secondary analysis of the EMPA-KIDNEY trial and **prespecified interim analyses of the ongoing VISIONARY trial, which reported data after the date of the literature search**."

The inference "a report was published after that document's cut-off, therefore it cannot have been included" does not hold: a synthesis may add data obtained after its search (Kim 2025 added five). A cut-off date describes only what the search string could retrieve before that date; **it is not a substitute for actually reading the other document's text, tables and supplementary material.**

4. Separating three different questions

For each of our reports, three questions are answered separately: **Q1. was this formal final report covered? Q2. was the same trial already covered (as an interim or other report)? Q3. which specific outcomes or follow-up data are added here?**

Our report	Q1. Formal final report covered?	Q2. Same trial already covered?	Q3. Specific data added here
APPLAUSE-IgAN 24-month final report (29 March 2026)	**No** for the four earlier syntheses; **yes** for Li et al. 2026, which reports the 24-month eGFR slope and the composite kidney-failure endpoint	**Yes** — the iptacopan phase 2 trial is included by Jeyabalan (safety table), Chen B, Chen R and Kim; the Wu et al. 2026 node also draws on the phase 2 trial	**24-month annualised total eGFR slope difference 3.02 (2.02–4.01)** ; **composite kidney-failure endpoint 21.4% vs 33.5%, HR 0.57 (0.40–0.81)** (secondary endpoint)
ALIGN 2.5-year final report (4 June 2026)	**No**	**Yes** — ALIGN appears in Jeyabalan's table of ongoing trials (no results); **Kim 2025 included the ALIGN week-36 proteinuria primary analysis**	**Week-136 eGFR change difference 2.4 (−0.1 to 4.8, P=0.057, not significant)** ; **total slope difference 1.4 (0.5–2.3)** ; **composite kidney endpoint 15% vs 22%, HR 0.64 (0.39–1.05, not significant) — the non-significant results included**

Our report	Q1. Formal final report covered?	Q2. Same trial already covered?	Q3. Specific data added here
FIND-CKD IgA subgroup (1 July 2026)	**No**	**No** — finerenone **does not appear** in any of the six syntheses	IgA subgroup of a non-immunosuppressive (non-steroidal MRA) trial: **total slope 0.61 (−0.14 to 1.36)** , **chronic slope 1.17 (0.43 to 1.91)** , composite endpoint 52/226 vs 51/190 (23.0% vs 26.8%), HR 0.82 (0.56–1.21)
calcitriol (online September 2025)	**No**	**No** — absent from all six	**Annual eGFR decline over 12 months −0.32 (−2.54 to 1.99) vs −3.64 (−5.70 to −1.58), P=0.02** ; no progression events
IGNAZ (felzartamab) (26 June 2025)	**No**	**No** — Jeyabalan lists it only among ongoing trials, with no results; absent from the others	**Month-24 change in eGFR from baseline, about 8.1 mL/min/1.73 m² versus placebo (95% CI −3.5 to 19.7)** ; 35 evaluable at month 24; no progression events
HR19042 (WCN'26 abstract, 2026)	**No**	**No** — absent from all six	**Month-12 eGFR change difference 3.30 (0.50–6.10) / 5.22 (2.44–7.99)** ; no progression events; abstract-level
ENVISION (sibeprenlimab phase 2) (2 November 2023)	**Cannot be determined** — the trial is listed in the text, but whether the month-12 eGFR change was extracted depends on that document's supplementary material, which was not obtained	**Yes**	Month-12 eGFR change; **no novelty claimed**
JANUS (atacicept phase 2) (26 May 2022)	**Cannot be determined** (atacicept/ORIGIN is covered by Jeyabalan and Kim; whether JANUS was listed separately cannot be judged from the text)	**Yes** (as part of the atacicept programme)	72-week renal function; **no novelty claimed**
MAIN (1 February 2023)	**Cannot be determined** — Jeyabalan and Chen B both include MMF trials; **Kim explicitly excluded MMF trials because of insufficient size and duration**	**Yes**	Progression-event evidence (composite 6/85 vs 18/85); **no novelty claimed**
STOP-IgAN 10-year (22 May 2020)	**Probably already covered** — STOP-IgAN is included by Jeyabalan (five references) and by Kim (post hoc analysis)	**Yes**	10-year composite; **no novelty claimed**
DAPA-CKD, IgA subgroup (Wheeler et al.)	**Cannot be determined** — Kim 2025 states that "unpublished data were obtained for three of these trials through collaborative efforts (TESTING, DAPA-CKD and Telitacicept)", but its text and tables do not show whether the IgA-specific result was among them; no other document reports the IgA subgroup	**Yes, as the parent trial** — DAPA-CKD is a trial in broader chronic kidney disease populations, used by the syntheses for other purposes	Composite of sustained ≥50% eGFR decline, end-stage kidney disease or renal or cardiovascular death: 6/137 vs 20/133, HR 0.29 (0.12–0.73); **no novelty claimed for the subgroup result**

Our report	Q1. Formal final report covered?	Q2. Same trial already covered?	Q3. Specific data added here
EMPA-KIDNEY, IgA subgroup (EMPA-KIDNEY Collaborative Group)	**Cannot be determined** — Kim 2025 states that "two additional studies were included in the meta-analysis through other sources: a prespecified secondary analysis of the EMPA-KIDNEY trial and prespecified interim analyses of the ongoing VISIONARY trial"; whether the IgA-specific split, which the source report describes as post hoc, was extracted cannot be judged from the text	**Yes, as the parent trial** — EMPA-KIDNEY is a trial in broader chronic kidney disease populations	Kidney disease progression 51/413 vs 67/404, HR 0.67 (0.46–0.97); chronic slope reduced by 43% (95% CI 27–59); **no novelty claimed for the subgroup result**

5. Conclusions (as written into the manuscript)

• **Can be claimed:** the APPLAUSE-IgAN 24-month final report, the ALIGN 2.5-year final report, the FIND-CKD IgA subgroup, the calcitriol trial and the IGNAZ 24-month data **do not appear** in the comparison documents verified here — with the exception that Li et al. 2026 does report the APPLAUSE-IgAN 24-month result. **This is a statement about the documents examined, not about the literature as a whole.**

• **Cannot be claimed:** "these trials are new, therefore they are this review's addition" — **the same trials were already covered in part by several comparison documents** (the iptacopan phase 2 trial by four of them; ALIGN by Kim 2025; STOP-IgAN and MAIN by several).

• **Cannot be claimed:** "because a report was published after another document's cut-off, that document cannot have included it" — Kim 2025 demonstrates that a synthesis can add data obtained after its search. **Date comparison is used only to describe search windows, never to infer what a synthesis included.**

• **Uncertainty that must be retained:** whether the supplementary material of a comparison document actually extracted ENVISION, JANUS, MAIN, the STOP-IgAN 10-year data, the DAPA-CKD IgA subgroup or the EMPA-KIDNEY IgA subgroup **cannot be determined here**, so **no novelty is claimed** for any of them. For the two SGLT2 subgroups this is a stronger uncertainty than for the others: Kim 2025 states on its face that it obtained data for DAPA-CKD and included a prespecified analysis of EMPA-KIDNEY, so the trials were covered; what cannot be judged is whether the IgA-specific estimates reached its text or tables, and whether a post hoc split such as EMPA-KIDNEY's IgA group would have been used at all.