Abstract Code: IUC26699-97

Topic: Real-world evidence

Who Gets Left Out? The Real-World Eligibility Gap in Landmark Metastatic Renal Cell Carcinoma Trials

Jehan Zeb | University Hospital Birmingham - United Kingdom

Background

Pivotal trials in metastatic renal cell carcinoma (mRCC) often enrol selected, relatively fit patients. This may limit how well trial findings reflect routine clinical practice.

Objective

To assess how many real-world patients with advanced or metastatic renal cell carcinoma would have been ineligible for landmark systemic therapy trials, and whether eligibility was associated with clinical outcomes.

Methods

- Systematic review of observational studies.
- Two complementary PubMed searches from database inception to 17 July 2026.
- Included adults with advanced or metastatic renal cell carcinoma treated in routine practice.
- Studies applied eligibility criteria from pivotal phase II or III systemic therapy trials.
- Overlapping cohorts reviewed; largest or most informative report retained.
- Trial-ineligibility proportions pooled using a random-effects logit model.
- Survival and treatment outcomes synthesised narratively because therapies, criteria and effect measures varied.
- Risk of bias assessed using the Joanna Briggs Institute cohort appraisal framework.

10
unique cohorts

6,146
patients

Search and synthesis summary

Key Results

46.9%
trial-ineligible

95% CI 36.2–57.9; I^2 = 98.4%

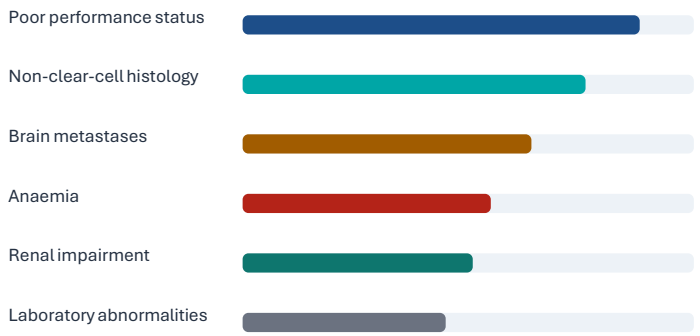
41.6%
after sensitivity analysis

Excluding PRINCIPAL; 95% CI 34.9–48.7; I^2 = 95.7%

Real-world eligibility gap

≈ 2 in 5 patients would not have qualified

Common reasons for exclusion



Bar lengths are illustrative to aid readability; reasons are reported qualitatively across included cohorts.

Clinical outcomes: Six of seven comparative cohorts reported poorer survival among trial-ineligible patients; one prospective cohort found broadly comparable treatment outcomes.

Interpretation

Conclusion

Approximately two in five patients treated for metastatic renal cell carcinoma in routine practice would not have qualified for the landmark trials that established current standards of care. Trial-ineligible patients generally had poorer outcomes, although substantial heterogeneity and residual confounding limit causal interpretation.

Clinical implications

- Landmark trials may under-represent routine clinical populations.
- Broader eligibility criteria may improve generalisability.
- Outcomes for commonly excluded patient groups should be reported consistently.
- Trial design should better reflect real-world practice where clinically appropriate.

Risk of bias

Moderate: 7 studies High: 3 studies

Key Message

Nearly half of real-world patients with metastatic renal cell carcinoma would have been excluded from landmark trials, raising important concerns about generalisability.

Future trials should justify restrictive criteria, broaden eligibility where safe, and report outcomes for commonly excluded groups.

Abbreviations: CI, confidence interval; I^2, heterogeneity statistic; mRCC, metastatic renal cell carcinoma.