**PICO**

**Question:**

What is the effectiveness exerted by the lenvantinib and everolimus combination in metastatic renal cell carcinoma (mRCC) after progression on an immune-checkpoint inhibitor (ICI)-based regimen?

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* The primary objective of this review is to determine the effectiveness of lenvatinib and everolimus combination.
* The secondary objective of this review is to determine safety and toxicity profile of lenvatinib and everolimus combination.

**P (Population/patient):**

* Inclusion Criteria:
  + Patients affected by mRCC
  + Lenvatinib and everolimus combination treatment
  + Previous treatment with ICI-based regimen
  + Prospective and retrospective studies
  + Studies published between 2020 and 2025
* Exclusion criteria
  + Meta-analysis
  + Systematic review
  + Case-control studies
  + Editorials
  + Commentaries

**I (intervention):**

Lenvatinib and everolimus combination as second or further lines treatment.

**C (Comparison):**

No other treatment regimen for comparison.

**O (Outcome):**

* Primary outcomes:
  + Median overall survival
  + Median progressive free survival
  + Objective response rate
* Secondary outcome:
  + Treatment related adverse events

**GRADE**

**High certainty level**

We are **very confident** that the true effect lies close to that of the estimate of the effect.

* Evidence from well-conducted randomized studies without major limitations.
* Further research is unlikely to change the estimate.

**Moderate certainty level**

We are **moderately confident** in the effect estimate: the true effect is likely to be close to the estimate, but there is a possibility it is substantially different.

* Some methodological limitations, inconsistency, or imprecision.
* Further studies may have a significant impact on our confidence and the estimate.

**Low certainty level**

Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate.

* Evidence from observational studies or from RCTs with serious limitations.
* It is likely that further research will change the estimate.

**Very low certainty level**

We have **very little confidence** in the effect estimate: the true effect is likely to be substantially different from the estimate.

* Very indirect, imprecise, or substantially biased evidence.
* The estimate is very uncertain.