

This is a provisional PDF only. Copyedited and fully formatted version will be made available soon.

# REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY

ISSN: 1507-1367

e-ISSN: 2083-4640

## **Immune combinations and complete response: a new hope for metastatic renal cell carcinoma**

**Authors:** Martina Catalano, Gabriella Nesi, Giandomenico Roviello

**DOI:** 10.5603/RPOR.a2022.0119

**Article type:** Letter to the Editor

**Published online:** 2022-11-02

This article has been peer reviewed and published immediately upon acceptance. It is an open access article, which means that it can be downloaded, printed, and distributed freely, provided the work is properly cited.

## **Immune combinations and complete response: a new hope for metastatic renal cell carcinoma**

**Running title:** ICI+TKI and RC

10.5603/RPOR.a2022.0119

Martina Catalano, Gabriella Nesi, Giandomenico Roviello

*Department of Health Sciences, University of Florence, Florence, Italy*

**Address for correspondence:** Giandomenico Roviello MD PhD, Department of Health Sciences, University of Florence, viale Pieraccini 6, 50139, Florence, Italy; e-mail: giandomenicoroviello@hotmail.it

**Keywords:** sunitinib; immunotherapy; angiogenesis; immune checkpoint inhibitors; tyrosine kinase inhibitors

Dear Editor,

According to Response Evaluation Criteria in Solid Tumours (RECIST), complete response is defined as “disappearance of all target lesions” [1]. Any pathological lymph nodes (whether target or non-target) must reduce to < 10 mm along the short axis. In all probability, patients who achieve complete response will have a better prognosis than those who do not.

Recently, several phase III studies have shown that immune combinations have greater efficacy than TKI monotherapy for primary treatment of metastatic renal cell carcinoma (mRCC) [2–7]. We performed a pooled analysis of pivotal phase III studies investigating immune combinations versus sunitinib administered to treatment-naïve mRCC patients, and compared the pooled risk of complete response of combination therapy with monotherapy. Pooled analysis with a fixed-effects model revealed that the incidence of complete response was higher in patients receiving immune combinations than in those treated with sunitinib alone [risk ratio (RR) = 2.41, 95% CI: 1.92–3.02;  $p \leq 0.01$   $I^2 = 81\%$ ; Fig. 1].

Significant limitations of our evaluation should be disclosed, namely meta-analysis based on literature data rather than on individual patient data, as well as substantial heterogeneity among experimental arm combinations. Nevertheless, our results point to higher complete response rates

with immune combinations than with monotherapy, underlining the relevance of this approach in mRCC.

### ***Conflict of interest***

The other authors declare no conflict of interest.

### ***Funding***

No funding.

### ***Ethical approval***

Not necessary.

### ***Contributorship***

G.R. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: G.R., M.C. Acquisition of data: G.R. Analysis and interpretation of data: G.R. Drafting of the manuscript: G.R. Critical revision of the manuscript for important intellectual content: G.N. Statistical analysis: G.R. Supervision: G.N.

### ***Acknowledgements***

None declared.

## **References**

1. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer*. 2009; 45(2): 228–247, doi: [10.1016/j.ejca.2008.10.026](https://doi.org/10.1016/j.ejca.2008.10.026), indexed in Pubmed: [19097774](https://pubmed.ncbi.nlm.nih.gov/19097774/).
2. Motzer RJ, Penkov K, Haanen J, et al. Avelumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2019; 380(12): 1103–1115, doi: [10.1056/NEJMoa1816047](https://doi.org/10.1056/NEJMoa1816047), indexed in Pubmed: [30779531](https://pubmed.ncbi.nlm.nih.gov/30779531/).
3. Rini BI, Plimack ER, Stus V, et al. KEYNOTE-426 Investigators. Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2019; 380(12): 1116–1127, doi: [10.1056/NEJMoa1816714](https://doi.org/10.1056/NEJMoa1816714), indexed in Pubmed: [30779529](https://pubmed.ncbi.nlm.nih.gov/30779529/).
4. Motzer R, Porta C, Alekseev B, et al. CLEAR Trial Investigators. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. *N Engl J Med*. 2021; 384(14): 1289–1300, doi: [10.1056/NEJMoa2035716](https://doi.org/10.1056/NEJMoa2035716), indexed in Pubmed: [33616314](https://pubmed.ncbi.nlm.nih.gov/33616314/).
5. Choueiri TK, Powles T, Burotto M, et al. CheckMate 9ER Investigators. Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2021; 384(9): 829–841, doi: [10.1056/NEJMoa2026982](https://doi.org/10.1056/NEJMoa2026982), indexed in Pubmed: [33657295](https://pubmed.ncbi.nlm.nih.gov/33657295/).
6. Motzer R, Tannir N, McDermott D, et al. Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2018; 378(14): 1277–1290, doi: [10.1056/nejmoa1712126](https://doi.org/10.1056/nejmoa1712126), indexed in Pubmed: [29562145](https://pubmed.ncbi.nlm.nih.gov/29562145/).
7. Rini B, Powles T, Atkins M, et al. Atezolizumab plus bevacizumab versus sunitinib in patients with previously untreated metastatic renal cell carcinoma (IMmotion151): a multicentre, open-label, phase 3, randomised controlled trial. *Lancet*. 2019; 393(10189): 2404–2415, doi: [10.1016/s0140-6736\(19\)30723-8](https://doi.org/10.1016/s0140-6736(19)30723-8), indexed in Pubmed: [31079938](https://pubmed.ncbi.nlm.nih.gov/31079938/).

**Figure 1.** Forest plots of risk ratio (RR) for complete response comparing immune combinations with sunitinib

