

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

LETTER TO THE EDITOR

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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% confidence interval (CI): 1.92–3.02; p  $\leq$  0.01 I<sup>2</sup> = 81%; Fig. 1].

Significant limitations of our evaluation should be disclosed, namely meta-analysis based on literature data rather than on individual patient data,

	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Check-Mate 214	59	550	14	546	14.4%	4.18 [2.36, 7.40]	
CheckMate 9ER	40	323	17	328	17.3%	2.39 [1.38, 4.13]	
CLEAR	57	355	35	357	35.7%	1.64 [1.10, 2.43]	
IMmotion151	24	454	10	461	10.1%	2.44 [1.18, 5.04]	
JAVELIN Renal101	17	442	9	444	9.2%	1.90 [0.86, 4.21]	
KEYNOTE-426	38	432	13	429	13.3%	2.90 [1.57, 5.37]	
Total (95% CI)		2556		2565	100.0%	2.41 [1.92, 3.02]	•
Total events	235		98				
Heterogeneity: Chi <sup>2</sup> =	7.97, df =	5 (P = 0	.16); I <sup>2</sup> = 3	37%			
Test for overall effect	Z=7.56 (F	< 0.00	001)				0.01 0.1 1 10 10 Envoure (control) Envoure (concrimental)

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

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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.

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#### 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.

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