

Peer Review File

Article Information: <https://dx.doi.org/10.21037/tcr-23-846>

Reviewer A

Comment 1: Ref 32 is outdated. Authors should cite the pivotal trials regarding immune-oncology and TKI combinations as first line in mRCC.

Reply 1: We have modified our text as advised.

Changes in the text: Page 8, line 260-261; Page 9, line 340-341.

Comment 2: I suggest authors to cite the paper by Simonetti et al (PMID 36104102) that report on a similar sample size the prognostic and potentially predictive role of RANKL one mRCC patients treated with nivolumab. Furthermore, the paper by Fotia et al gives an interesting view regarding prognostic score in mRCC (PMID 37000341)

Reply 2: We have modified our text as advised.

Changes in the text: Page 8, line 262-264; Page 10, line 346-250.

Comment 3: Authors should explain the limits of their study such as the small sample size that was not calculated a priori and the heterogeneity of patients. By the way, authors should describe the characteristics of subjects included as the lack of informations regarding the sample should be another limit.

Reply 3: We have modified our text as advised.

Changes in the text: Page 8, line 266, 268; Page 6, 179-180; Page 11, line 355-356.

Comment 4: Overall, this interesting study should be defined by authors as an hypothesis generating and exploratory. Conclusion of the abstract, which state that they validate NR3C2 as prognostic should be reconsidered.

Reply 4: We have modified our text as advised.

Changes in the text: Page 2, line 40-41.

Comment 5: In lines 144 and 145 KIRC and KIRP have the same words component.

Reply 5: We have modified our text.

Changes in the text: Page 5, line 145-146.

Reviewer B

Comment 1: The background of the changing scenario of medical treatment in renal cell carcinoma should be better discussed, and some recent papers regarding this topic should be included (PMID: 36414800; PMID: 36633661; PMID: 35031442; PMID: 33880963)

Reply 1: We have modified our text as advised.

Changes in the text: Page 7, line 257-258; Page 8, line 259-260; Page 8, line 236-234; Page 9, line 332-339; Page 10, line 351-352.

Comment 2: Discussion: Very interesting and timely discussion. Of note, the authors should expand the Discussion section, including a more personal perspective to reflect on. For example, they could answer the following questions – in order to facilitate the understanding of this complex topic to readers: what potential does this study hold? What are the knowledge gaps and how do researchers tackle them? How do you see this area unfolding in the next 5 years? We think it would be extremely interesting for the readers.

Reply 2: We have modified our text as advised.

Changes in the text: Page 8, line 265-268.