Author's response to reviews

Title: Prolonged survival after sequential multimodality treatment in metastatic renal cell carcinoma: case report of two patients and a short literature review.

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Author's response to reviews: see over
Dear Sirs,

Please find enclosed the revised version of our article entitled “Prolonged survival after sequential multimodality treatment in metastatic renal cell carcinoma: case report of two patients and a short literature review”. We appreciate the careful review and thoughtful comments from the editorial board and the reviewers.

We have given careful consideration to each specific point raised by the reviewers and modified our manuscript accordingly. All the corrections have been highlighted with yellow in the amended manuscript. We hope that our work will now be considered suitable for publication in JMCR.

Reviewer Dr Vasilios Karavasilis:

1. The lack of established guidelines by the time we treated the patients of the study made us adopt the sequential strategy treatment as eventually more effective. We alternated the TKI’s and mTOR inhibitors that we had at our disposal each time, based on the shaping literature.

2. Regarding the sequential therapy in mRCC, we stressed the importance of following the pace of the disease growth and we amended our manuscript by adding a paragraph in the discussion section referring to the Kirchner et al. study. We also added the citation of this study (Kirchner H, et al.: Patient-based strategy for systemic treatment of metastatic renal cell carcinoma. Expert Rev Anticancer Ther, 10(4):585-596).

3. The rationale of using combination and sequential treatment is still being under evaluation. It is believed that the combination of two antiangiogenic agents may help overcome the resistance to anti-VEGF therapy. We amended the discussion section by adding a paragraph referring to resistance to anti-VEGF therapy in order to provide a rationale of using combination and sequential treatment. A citation was also added (Moreno Garcia V et al.: Combining Antiangiogenics to Overcome Resistance: rationale and clinical experience. Clin Cancer Res).

Reviewer Dr Panagiotis Vlachostergios

1. We amended the discussion section by adding a paragraph referring to the adverse effects of the drugs used.

2. We added a paragraph referring to the management of the toxicities and clinical symptoms that the patients of the study experienced.

3. The best supportive care provided is described in the cases presentation and discussion section and further highlighted throughout the manuscript according to the reviewer’s suggestion.

Yours sincerely,

John Syrios, MD