Reviewer’s report

Title: Survival of patients receiving systematic therapy for metachronous or synchronous metastatic renal cell carcinoma: a retrospective analysis

Version: 0 Date: 03 Apr 2018

Reviewer: Jeanette Eckel-Passow

Reviewer's report:

Summary

The major concern with the paper is the lack of utilization of appropriate statistical analysis methods for retrospective designs that compare treatment modalities. Particularly, when comparing treatment modalities using a retrospective design, the analysis must account for the underlying probability of being treated with a particular modality. For example, these might consist of the variables described in Table 1 that are significantly different between patients treated with TT vs. IT. One way to do this is via a propensity score adjustment; other approaches are also available. Additionally, the analyses described in Figures 3 and 4 are inappropriate. Specifically, it is not appropriate to look forward in time to classify patients as TFI<1 vs TFI>1 and then go backwards in time and use these in the survival analyses.

Major Comments

* When comparing survival across treatment groups using a retrospective design, the analysis must correct for the probability of receiving a particular treatment (e.g., propensity score adjustment).

* Introduction states that TT has cancer-specific survival rates of 1316 months; assuming this is a typo?

* There is no justification for using TFI<1 year. Also, what if a patient was censored prior to the 1 year threshold?

* Methods: Patients were excluded if they had incomplete medical records; incomplete with respect to what? Similarly, the methods states that patients were excluded if they had disease progression, yet progression free survival was analyzed. Additionally, were none of the patients predicted to be low risk by the Heng criteria?

* Table 1 and Table 2: Sex is the correct term to use vs gender? Overall survival is not the same as cancer specific survival, which did the authors use? Incorrect to state how many patients "survived" as this does not account for censoring. However, appropriate to state how
many events there were and likewise, follow-up duration for patients who have not experienced an event.

* Figures 3 and 4: Not appropriate to look ahead in time (aka, use TFI) to group patients and then go back and look at survival.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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