Author's response to reviews

Title: Prognostic Stratification Of Patients With Advanced Renal Cell Carcinoma Treated With Sunitinib. Comparison With The Memorial Sloan-Kettering Prognostic Factors Model.

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

On behalf of all authors I would like to express my gratitude for giving us the opportunity to submit a revised version of our manuscript titled **PROGNOSTIC STRATIFICATION OF PATIENTS WITH ADVANCED RENAL CELL CARCINOMA TREATED WITH SUNITINIB. COMPARISON WITH THE MEMORIAL SLOAN-KETTERING PROGNOSTIC FACTORS MODEL.** for publication in your journal.

We are grateful to you and the Reviewers for your time to improve our manuscript. Below you will find a list with a point-to-point description of the changes made according to the Reviewers’ comments and the editorial points. The changes are underlined in the revised manuscript.

We hope that our manuscript is now suitable for publication in your journal.

Regardless of your decision, we remain grateful for your time and effort.

Yours sincerely,

Aristotle Bamias MD, PhD

Corresponding Author
LIST WITH ANSWERS TO THE REVIEWERS’ COMMENTS AND THE EDITORIAL POINTS

Reviewer #1

It is nice retrospective analysis on prognostic factors in mRCC treated with anti-angiogenics (sunitinib) in six greek oncology centers. The authors found that only three prognostic factors could be relevant for OS evaluation. Stratification into two groups result in distinctly different OS. This classification is easier to use than the MSKCC (Motzer classification) since no biological parameter need to be taken into account. Some biais are noted but the authors spoke about that in the discussion and concluded that this classification need to be validate.

We thank the Reviewer for his very supportive comments.

Reviewer #2

The patients included in this analysis included patients entered into a prospective database as of January 2008 - however, patients prior to this data were retrieved by their medical records and entered retrospectively. How were these patients identified - were all patients who received sunitinib during this time period included?

As mentioned by the reviewer, patients treated prior to January 2008 were retrieved by their medical records. All centers which contributed to this analysis have a detailed database of new patients from which these patients were identified. We are, therefore, confident that most patients receiving sunitinib have been entered into HECOG’s RCC database.

The final model consisted of two risk groups with statistically significantly different clinical outcomes. However, selection of this as the “best” model is largely the result of the small sample size and given the heterogeneity of patients with RCC, models that separate patients into more groups with disparate outcomes may be more helpful in clinical practice and for clinical trial stratification. The utility of the two-group model compared with models separating patients into additional risk groups should be discussed further and the small sample size contributing the selection of the final model should be discussed as a “limitation” of this analysis.

We fully agree with the criticism by the Reviewer. The limitation of the small number of patients is already mentioned in the results (page 6, line 25). We have now further highlighted this point in the Discussion (page 7, lines 47-50; page 8, lines 1-2): “It should be noted that the collapsing of the initial four risk groups (0,1,2 or 3 risk factors) into the final two was largely the result of the relatively small sample size, which represents a limitation of this analysis.
Given the heterogeneity of mRCC, separation into more risk groups may be more informative as indeed was suggested by our statistical analysis. For these reasons, we plan to further study and validate our model in larger cohorts of patients”.

Editorial points
1) Please clarify if any ethical approval or permission was needed for the use of the data in the study.

It is common practice in HECOG to obtain written permission by the patients for future analysis of their data prior to the initiation of any anti-cancer therapy. This is now stated in the text (page 4, lines 8-10).

2) Acknowledgements? We strongly encourage you to include an Acknowledgements section between the Authors’ contributions section and Reference list. Please acknowledge anyone who contributed towards the study by making substantial contributions to conception, design, acquisition of data, or analysis and interpretation of data, or who was involved in drafting the manuscript or revising it critically for important intellectual content, but who does not meet the criteria for authorship. Please also include their source(s) of funding. Please also acknowledge anyone who contributed materials essential for the study.

Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements.

Please list the source(s) of funding for the study, for each author, and for the manuscript preparation in the acknowledgements section. Authors must describe the role of the funding body, if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

There has been no specific funding for this work. Anyone who contributed in this work met the criteria for authorship has been included among the authors.