

COMMENTS BY REVIEWER#1

POINT#1: “[.....] just a few points for improvements. The authors discuss how to resolve discrepant trial findings but ignore influences of other factors. There are many environmental and lifestyle factors that influence immune cells, the microbiota, tumor development and response to therapy. Those differences may explain the observed discrepancies. The authors should discuss those points.”

AUTHOR’S RESPONSE: In the Discussion of our revised paper, we have specifically addressed this point, by introducing some sentences that mention a number of potential factors (environmental and lifestyle factors, tissue biomarkers, molecular pathological epidemiology, the microbiota, etc) that might influence tumor development and response to therapy. Differences in these factors could explain the discrepancies observed across the trials included in our analysis.

POINT#2: Many factors influence response to therapy in each patient differentially. Along with these points, research on environment factors, microbiome, immunity, and molecular tissue biomarkers should be pursued. The authors should discuss molecular pathological epidemiology, which can integrate those factors, molecular pathologies, and clinical outcomes in cancer [.....]. Molecular pathological epidemiology research can be a promising direction and improve prediction of response to therapy such as lutetium-based treatment.

AUTHOR’S RESPONSE: In the Discussion of our revised paper, we have also added a sentence emphasising that “molecular pathological epidemiology research can be a promising direction and improve prediction of response to therapy such as lutetium-based treatment.”

COMMENTS BY REVIEWER #2

POINT#1: Authors employed a new technique (Shiny method) to pool the survival data of these two trials and evaluate to what extent the lutetium cohorts differed from one another. I think this is a valuable job.

AUTHOR’S RESPONSE: We thank Reviewer #2 for this favourable comment.

COMMENTS BY SCIENCE EDITOR:

POINT#1: It is suggested to analyze the impact of more other factors in the discussion.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

AUTHOR’S RESPONSE: See our response to Points #1 and #2 raised by Reviewer #1.

COMMENTS BY COMPANY EDITOR-IN-CHIEF:

POINT#1. The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words).

AUTHOR’S RESPONSE: The title of the manuscript has been shortened (new title: “Lutetium in prostate cancer: reconstruction of patient-level data from published trials and generation of a multi-trial Kaplan-Meier curve”, word count 18).

POINT#2: Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

AUTHOR’S RESPONSE: Our Figure 1 has been converted onto the Powerpoint format.

EDITORIAL OFFICE'S COMMENTS

POINT#1: Requirements for Figures: Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file, and submit as "72756-Figures.pptx" on the system. The figures should be uploaded to the file destination of "Image File".

AUTHOR'S RESPONSE: Our figure has been uploaded as a separate file named 72756-Figures.pptx.

POINT#2: Requirements for Tables: Please provide decomposable Tables (in which all components are movable and editable), organize them into a single Word file, and submit as "72756-Tables.docx" on the system. The tables should be uploaded to the file destination of "Table File".

AUTHOR'S RESPONSE: Not applicable because there are no tables.

POINT#3: Reminder: Please click and download the [Guidelines for preparation of bitmaps, vector graphics, and tables in revised manuscripts](#) (PDF), and prepare the figures and tables of your manuscript accordingly.

AUTHOR'S RESPONSE: We have taken into account the recommendations reported in the above-mentioned file.

POINT#4: Please download all the uploaded documents [see list below] to ensure all of them are correct.

- 72756-Answering Reviewers
- 72756-Audio Core Tip
- 72756-Biostatistics Review Certificate
- 72756-Conflict-of-Interest Disclosure Form
- 72756-Copyright License Agreement)
- 72756-Signed Informed Consent Form(s) or Document(s)
- 72756-Non-Native Speakers of English Editing Certificate
- 72756-Image File
- 72756-Table File (not applicable because there are no tables).

The files that make up our revised paper have been named as indicated above, along with the additional files named "72756-BPG Letter proposing waiving the article processing fee", "72756-Manuscript (track changes version)", and "72756-Manuscript (clean version)",

OTHER POINTS:

POINT#1: "When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript."

AUTHOR'S RESPONSE: This criterion has been handled on the basis of the same document attached to our initial submission.

POINT#2: Copyright license agreement (CLA).

AUTHOR'S RESPONSE: The CLA has been uploaded.

POINT#3: CONFLICT-OF-INTEREST DISCLOSURE FORM: Please click and download the fillable [ICMJE Form for Disclosure of Potential Conflicts of Interest](#) (PDF), and fill it in. The Corresponding Author is responsible for filling out this form.

AUTHOR'S RESPONSE: The Conflict-of-Interest Disclosure Form has been uploaded.

FINAL POINTS:

#1: This paper was meant to be a Mini-Review. However, while the BPG website has classified it as an observational study, it seems that this classification cannot be edited on the journal's website.

#2: The abstract is not structured according to the classification of this paper as a "Mini-review" that has been proposed to the Editors' attention.