Author's response to reviews

Title: Sensitivity of initial biopsy or transurethral resection of bladder tumor(s) for detecting histological variants on radical cystectomy

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Author's response to reviews: see over
Reply to the comments

Dear Editors,

We feel great thanks for the nice comments on our article. All those comments have contributed a lot to improve the quality of our article. According to the associate editor and reviewers’ comments, we have made revisions to our previous draft and to make our results convincing.

The detailed point-by-point responses are listed below.

Deputy/Senior Editor Comments 1:

Acknowledgements:
By way of a section ‘Acknowledgements’, please acknowledge anyone who contributed towards the article 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 the source(s) of funding for each author, and for the manuscript preparation. Authors must describe the role of the funding body, if any, in 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. Please also acknowledge anyone who contributed materials essential for the study. If a language editor has made significant revision of the manuscript, we recommend that you acknowledge the editor by name, where possible.
The role of a scientific (medical) writer must be included in the acknowledgements section, including their source(s) of funding. We suggest wording such as 'We thank Jane Doe who provided medical writing services on behalf of XYZ Pharmaceuticals Ltd.' Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements section.

Response:
We have added the “Acknowledgements” section (Line313 – Line316 in revised manuscript).

313  *Acknowledgements*

314  The authors are thankful for the Wu Jieping Medical Foundation(No. WJP-LC-12036). The authors declare that the sponsor had no role in the study design, data collection, data analyses, data interpretation, or writing of the manuscript.
Deputy/Senior Editor Comments 2:

Please also highlight (with 'tracked changes/coloured/highlighted text) all changes made when revising the manuscript to make it easier for the Editors to give you a prompt final decision on your manuscript. We prefer if you can make text look like it was marked with a highlighter pen the modified part of the original manuscript.

Response:
In the revised edition, we highlighted all the changes we made with bright color. Yellow indicates the changes we made according to minor revisions in the comments from the reviewers and green means other corrections we made (for example language correction, format modification).

Comments from the two reviewers

Reviewer#1:

Minor Essential Revisions
1. Line 29 should say "147 patients with variant histology"(Line 26 in revised manuscript)
Response: We have rewritten the sentence as recommended.

26  Methods: Clinical and histopathological characteristics of 147 patients with variant histology

2. Line 48 should say "cystectomy specimens have inferior survival"(Line 46 in revised manuscript)
Response: We have rewritten the sentence as recommended.

45  differentiation on cystectomy is relatively low. Patients with variant differentiation on

46  cystectomy specimens have inferior survival.

3. Line 74 - Delete "pronounced"(Line 70 in revised manuscript)
Response: We have deleted the word “pronounced”.

4. Line 93 - Delete “a” (Line 90 in revised manuscript)
Response: We have deleted “a”.

5. Line 99 - Delete "Herein" and say "This study WAS aimed at..." (Line 96 in revised manuscript)
Response: We have rewritten the sentence as recommended.

Discretionary Revisions
More discussion on the implications of variant histologies on neoadjuvant chemotherapy prior to cystectomy
Response:
Firstly, we are thankful for this nice suggestion. We did not discuss this issue in the draft, because
1) More than 15 variant morphotypes have been reported in the literature. Each variant differentiation may response differently to neoadjuvant chemotherapy (PMID: 23384236). The implications on the implications of variant histologies on neoadjuvant chemotherapy prior to cystectomy are of great importance in clinical practice and actually remains in debate. In order to get convincing evidence, we think a systematic review and/or meta-analysis is needed.
2) This manuscript aimed to investigate the efficacy of initial biopsy or transurethral resection of bladder tumor for detecting histological variants on radical cystectomy and to assess the prognostic significance of variant histology on urothelial carcinoma outcomes after radical cystectomy. There were very few patients in this series who received neoadjuvant chemotherapy prior to cystectomy. It seemed impossible to draw a conclusion.
This is an interesting topic and we thanks for the reviewer’s reminding again.

Reviewer#2:

Minor essential revisions:
Use either the term multivariable OR multivariate but remain consistent throughout the manuscript. Currently both appear in the context of Cox regression analyses

Response: We now use only multivariable in the manuscript (Line 41,143,187 and 273 in revised manuscript).

Thanks for your nice suggestions again. And we hope the revised manuscript could be acceptable for you.