Peer Review File

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Reviewer A

1. line 77-79, please update the statistic results according to the newest reference.
Reply 1: We have modified our text as advised.
Changes in the text: see page 3, lines 78-79.

2. line 183-184, why divide stage II, III and IV into a group and compare FGFR3 mutations in this group with stage 0a and I patients?
Reply 2: Stage 0a and I belong to non-muscle-invasive bladder cancer, while Stage II, III, and IV belong to muscle-invasive bladder cancer. so they are divided into two groups.
Changes in the text: see page 6, lines 191-192.

3. line 192-193, the data were inconsistent.
Reply 3: We have modified it.
Changes in the text: see page 6, line 201.

4. the analysis with seq data was too simple to support the conclusion.
Reply 4: In this study, our primary purpose is to investigate the mutation of FGFR in the Chinese population with bladder cancer and to provide some ideas for the treatment of bladder cancer. In the future, we will use more abundant sequencing data analysis to explore further the relationship between genomic variation in patients with bladder cancer and its pathogenesis and prognosis.

5. I am confused about the setting of patient samples. There are significant differences between different stages. 'Among the 82 patients, 41 (50.00%), 4 (4.88%), 12 (14.63%), 20 (24.39%), and 5 (6.10%) patients had clinical stages 0a, I, II, III, and IV, respectively.'
Reply 5: Since we have continuously collected samples from bladder cancer patients treated in our hospital for a period of time, there may be differences between different stages.

6. Some recently publications might help to polishing the manuscript contents or address part of the above concerns. For examples:
https://doi.org/10.1016/j.phrs.2023.106654
https://doi.org/10.3390/cells9051213
https://www.ijbs.com/v13p1373.htm

https://doi.org/10.3892/or.2015.3933
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0175290
Reply 6: Thank you for your valuable advice.
We have enriched the introduction and discussion sections, and added references.
Change in the text: see page 3, lines 99-100; page 4, lines 110-114; page 9, lines 280-300.

Reviewer B

This study addresses a current topic.

The manuscript is quite well written and organized. English could be improved.
Figures and tables are comprehensive and clear.
The introduction explains in a clear and coherent manner the background of this study.

We suggest the following modifications:
* Introduction section: although the authors correctly included important papers in this setting, we believe the systemic treatment scenario for renal cell carcinoma should be discussed within the introduction and some recently published papers added (PMID: 35858936; PMID: 36368251 ; PMID: 33516645 ; PMID: 32498352), only for a matter of consistency. We think it might be useful to introduce the topic of this interesting study.
* Methods and Statistical Analysis: nothing to add.
* Discussion section: Very interesting and timely discussion. Of note, the authors should expand the Discussion section, including a more personal perspective to reflect on. For example, they could answer the following questions - in order to facilitate the understanding of this complex topic to readers: what potential does this study hold? What are the knowledge gaps and how do researchers tackle them? How do you see this area unfolding in the next 5 years? We think it would be extremely interesting for the readers.

However, we think the authors should be acknowledged for their work. In fact, they correctly addressed an important topic, the methods sound good and their discussion is well balanced.

One additional little flaw: the authors could better explain the limitations of their work, in the last part of the Discussion.

We believe this article is suitable for publication in the journal although major revisions are needed. The main strengths of this paper are that it addresses an interesting and very timely question and provides a clear answer, with some limitations.

We suggest a linguistic revision and the addition of some references for a matter of consistency. Moreover, the authors should better clarify some points.

Reply: Thank you very much for your professional advice. We have modified our text as advised.

In the introduction section, we have enriched the introduction and added references.

Change in the text: see page 3, lines 98-101; page 4, lines 110-114.

In the Discussion section, we add the value of FGFR studies addressing knowledge gaps and potential for future research. In addition, we discuss the potential limitations of this study.

Change in the text: see page 9, lines 281-300.

Reviewer C

1. Introduction- is too long- would abbreviate and explain rationale for this study

Reply 1: We have simplified the introduction part, and explain the purpose of this study in methods section.

Changes in the text: page 3; and pages 4, lines 121-125.

2. Methods-please clarify- were all stages included -including non-invasive?

Reply 2: The samples covered all clinical stages, included both non-muscle-invasive samples and muscle-invasive samples.

Changed in the text: page 4, lines128-130; and page 6, lines191-192.

3. Methods- why were only 82 patients included- did only 82 undergo genomic analysis?

Reply 3: We continuously collect 82 patients who have undergone commercial Multi-gene panel detection and are treated in our hospital simultaneously.

4. Methods- how many genes were tested and what was the gene panel used-please show in supplement. Was FGFR2/3 fusion not evaluated?

Reply 4: This commercial panel included 20 genes; the detail listed in Supplementary Table 2. In this study, we did not analyze FGFR2/3 fusion.

5. Results-correlations with outcomes- need a multivariable analysis adjusting for pathologic stage.

Reply 5: We added the results of multivariable analysis as Supplementary Table 3.

Changes in the text: page 7, lines 209-211.

6. Results-the top 10 mutations are not expected-can authors discuss? Can they explain why p53 and ARID1A are not in this list?

Reply 6: As we described in results section "Multi-gene panel targeted *NGS* was performed on samples from the 82 *BC* patients to detect somatic mutations (**Table S2**)". In the Table S2, we listed all genes of Multi-gene panel. However, this commercial Multi-gene panel does not contain the p53 and ARID1A.

7. Discussion- could enhance discussion by mentioning recent data for erdafitinib in non-muscle-invasive bladder cancer (GU asco symposium 2023)

Reply 7: We have added in the discussion section.

Changes in the text: page 9, lines 283-287.

8. Discussion-was tumor mutation burden not evaluated – what is the relation of TMB with FGFR3 mutations.

Reply 8: Although the data in this study are unsuitable for analyzing TMB, we have added the discussion of TMB and FGFR in the discussion section.

Changes in the text: page 9, lines 293-300.