Author’s response to reviews

Title: Neoadjuvant docetaxel, cisplatin and ifosfamide (ITP) combination chemotherapy for treating penile squamous cell carcinoma patients with terminal lymph node metastasis

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Author’s response to reviews:

Editor Comments:

1. Currently, there are not enough contributions for the authors which were added between the original submission and the first revision (ShiMiao Zhu, QiLiang Cai, Zhun Wang, Xiong Yang, HongTuan Zhang). We would ask that you either remove these authors or provide further contributions for these authors.

An 'author' is generally considered to be someone who has made substantive intellectual contributions to a published study. Authors are expected to fulfil the criteria below (adapted from McNutt et al., Proceedings of the National Academy of Sciences, Feb 2018, 201715374; DOI: 10.1073/pnas.1715374115; licensed under CC BY 4.0):

Each author is expected to have made substantial contributions to the conception OR design of the work; OR the acquisition, analysis, OR interpretation of data; OR the creation of new software used in the work; OR have drafted the work or substantively revised it

AND to have approved the submitted version (and any substantially modified version that involves the author's contribution to the study);
AND to have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

Acquisition of funding, collection of data or general supervision of the research group, alone, does not usually justify authorship.

Please provide a new authorship change form with the new contributions, or if you remove these authors, please also provide a new authorship change form with the signatures of all authors that they agree with the change in authorship.

Respond: Revision of author's contribution

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Authors' contributions

JX designed the conception, collected data, carried out statistical analysis, and drafted the manuscript. GL contributed to the conception, acquisition of data, drafted the manuscript, and provided critical revision of the manuscript. SMZ and QLC made substantial contributions to analysis and interpretation of data; ZW, XY and HTZ made substantial contributions to design and acquisition of data. YJN contributed to the conception, design, acquisition of data, data analysis, and drafted the manuscript, and provided critical revision of the manuscript. All authors read and approved the final manuscript.

2. We note that the current submission contains some textual overlap with other previously published works (27%). Please see the attached screen shots of the overlap which must be reduced. While we understand that you may wish to express some of the same ideas contained in these publications, please be aware that we cannot condone the use of text from previously published work. Please re-phrase these sections to minimise overlap.
The TPF protocol, including cisplatin (DDP), 5-fluorouracil and paclitaxel, is becoming widely accepted as the first-line treatment option because of good efficacy and low toxicity. However, a new study suggested that neoadjuvant TPF-chemotherapy obtained an imaging-based response in 60% of patients. However, pathologic complete response rate was only 4%. The 2-year PFS and DSS probability were only 12% and 28%, respectively. Toxicity was considerable in every study patient. TPF chemotherapy should be used with caution because of poor tolerance and disappointing survival rates[10]. Bermejo and his colleagues reported that four-fifths of patients receiving ITP neoadjuvant therapy (paclitaxel, cisplatin and ifosfamide) had a complete response, and three of them had a histologically confirmed complete response[11]. A larger sample study in the United States showed that 30 men received ITP treatment, of which 15 (50.0%) had an objective response, 22 (73.3%) underwent surgery and 9 had long-term survival[12].

All patients were clinical or pathological stage Tany and N1–3 penile cancer. Fifty-four patients (88.5%) received ITP chemotherapy and seven received other initial therapy. CRs or PRs were found in 64% of regionally advanced penile cancer patients receiving ITP chemotherapy. OS of patients with objective response to chemotherapy (CR or PR) was 50.1% in 5 years. Despite the optimistic results, there are still many difficulties to overcome in these studies. Despite the optimistic results, there were still many difficulties that need to be overcome in these studies. As the paper said, because of the clinical or pathological stage N1-3, chemotherapy may delay the definitive operation, rendering some unresponsive patients unable to operate. The lack of chemotherapeutic regimen standardization and dose optimization limited the broader application of the ITP regimen.

3. Please include the email addresses for all authors on the title page. The corresponding author should still be indicated.

Respond: Added email addresses

Email addresses: Jian Xu,xujianwf@126.com; Gang Li, 797980@sina.com； ShiMiao Zhu, shimiaozhu@qq.com； QiLiang Cai, caiqiliang@tmu.edu.cn； Zhun Wang, wangzhun2011@163.com； Xiong Yang, briskey-yangxiong@hotmail.com； HongTan Zhang, zhtlml@163.com.

4. Please change the Purpose heading to Background.

5. Please change the Introduction heading to Background.

6. Please change the Materials and Methods heading to Methods.
7. Please confirm whether informed consent, written or verbal, was obtained from all participants and clearly state this in your Methods and Ethics approval and consent to participate sections. If verbal, please state the reason and whether the ethics committee approved this procedure. If the need for consent was waived by an IRB or is deemed unnecessary according to national regulations, please clearly state this, including the name of the IRB or a reference to the relevant legislation.

8. Please include the ethics approval reference number in the Ethics approval and consent to participate section, if applicable.

Respond:

Ethics approval and consent to participate

This study was approved by an independent ethical committee/institutional review board of the Second Hospital of Tianjin Medical University, Tianjin, China. Written informed consent was obtained from all participants.

9. Please note, the role of the funding body in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript should be declared in the Funding section.

Respond: Added the following sentence in "Funding".

The funding bodies played no role in the design of the study, data collection, analysis, or interpretation of data.

Please amend the References, BMC Cancer uses Vancouver style referencing, with the references being numbered in the order they appear in the text, and then cited in the text using the appropriate number in square brackets.

Respond: The references have been revised

References


11. Please provide figure titles/legends under a separate heading of 'Figure Legends' after the References. If Figure titles/legends are within the main text of the manuscript, please move them.

Figure files should contain only the image/graphic, as well as any associated keys/annotations. If titles/legends are present within the figure files, please remove them.

12. Please put your responses to the reviewers' comments in the Response to Reviewers box in Editorial Manager, please do not upload a separate letter.

13. At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours.
All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files.

Respond: All modifications were made as required. Figure has added title and made corresponding modifications. See Figure for details.

Reviewer 2 (Reviewer 2): "REVISION ASSESSMENT FROM THE ACADEMIC PEER REVIEWER:

Has the author addressed your concerns sufficiently for you to now recommend the work as a technically sound contribution? No

Reviewer comments: Some of the changes have been done. However a consort diagram would help readers with the flow of the article. Some sentences have to be rephrased, for example Page 23 Line 17 to 20; ""This population is so small that it is impossible to perform any randomized study""; this might sound like speculation and can be rephrased as ""Due to limitations of small sample size further evaluation is necessary"".

Some parts of the article need to be re-structured; for example Page 14 line 48; the description of your cohort should only be limited to methods and materials section.

Some sentences do not make sense. For example page 16 line 37; ""This requires to strengthen education of penile cancer prevention and treatment"

Respond: "This population is so small that it is impossible to perform any randomized study" The original text has been amended to "Due to limitations of small sample size further evaluation is necessary."

the description of your cohort should only be limited to methods and materials section. In the original text, "Methods" was modified at the beginning.

The vast majority of penile cancer is squamous cell carcinoma and other uncommon malignant penile diseases include Paget disease, basal cell carcinoma and melanoma. Following institutional review board approval, 19 patients who were recruited in our study were squamous cell carcinoma of the penis, which were confirmed by fine needle aspiration biopsy and treated from June 2009 to June 2016 in a single medical institution comprised the initial study cohort.

"This requires to strengthen education of penile cancer prevention and treatment" has been deleted.