

High-grade neuroendocrine small-cell carcinoma of the anal

canal: Longterm remission with chemoradiotherapy

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Handling editor: Michal Heger Department of Pharmaceutics, Utrecht University, the Netherlands Department of Pharmaceutics, Jiaxing University Medical College, Zhejiang, China

Review timeline:

Received: 25 October, 2020 Editorial decision: 5 November, 2020 Revision received: 12 November, 2020 Editorial decision: 15 November, 2020 Published online: 2 February, 2021

1st Editorial decision 05-Nov-2020

Ref.: Ms. No. JCTRes-D-20-00127 High-Grade Neuroendocrine Small-Cell Carcinoma of the Anal Canal: Longterm Remission with Chemoradiotherapy Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a pointby-point response to every comment. An exemplary rebuttal letter can be found on at http://www.jctres.com/en/author-guidelines/ under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Dec 05, 2020.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.



Yours sincerely,

Michal Heger Editor-in-Chief Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: Unusual tumor type, novel findings, adequate description, spectacular outcome, field is covered nicely. A few remarks to consider:

1. The discussion should cover the underlying genetics in greater detail. For example, some mutations in anal small cell carcinomas could motivate targetet therapy (PIK3CA mutations etc.). Also, the HPV section could be expanded somewhat as well.

2. Figure 1 need to be more extensive in terms of the figure legend; what level of magnification was used for the different inserts? What is the IHC stain (I believe it is synaptophysin?). Why are the two inserts in the right column duplicates?

3. Figure 2 could be marked up so that the readers know what to look for, alternatively more detailed in terms of the figure legend.

4. What are the lessons learned from this case? The authors could speculate more as to why this patient with such an advanced tumor had such a great outcome. Any potential contributing factors worthy of exploration in follow-up studies?

Reviewer #2: The article is well wirtten and stressed the management of a neuroendocrine carcinoma

Table and figures are well appropriated

No queries

TO my point of view the article is suitable for publication in its current form

Authors' response

Prof. Michal Heger Department of Pharmaceutics, Jiaxing University Medical College, Zhejiang, China Journal of Clinical and Translational Research November 8th, 2020

Subject: Submission of a revised version of the manuscript entitled "*High-Grade Neuroendocrine Small-Cell Carcinoma of the Anal Canal: Longterm Remission with Chemoradiotherapy*".

Dear Prof. Heger,



We would like to thank you, the editorial board and the reviewers for taking the time to review the manuscript and outlining elements that will improve the quality of the work.

The comments of the reviewers were taken into consideration and improvements were made to the manuscript accordingly.

Please find below a detailed list of the changes that were performed in the revised version:

Reviewer #1: Unusual tumor type, novel findings, adequate description, spectacular outcome, field is covered nicely. A few remarks to consider:

- 1- The discussion should cover the underlying genetics in greater detail. For example, some mutations in anal small cell carcinomas could motivate targeted therapy (PIK3CA mutations etc.). Also, the HPV section could be expanded somewhat as well.
- This is a very relevant comment, and potential mutations of interest were further discussed, and data on their role, mainly is the more common squamous cell carcinoma, was briefly presented. The importance of future work on their involvement in the scarcer small cell carcinoma was highlighted as well.
- 2- Figure 1 need to be more extensive in terms of the figure legend; what level of magnification was used for the different inserts? What is the IHC stain (I believe it is synaptophysin?). Why are the two inserts in the right column duplicates?
- Figure 1 was improved as suggested and include the level of magnification, the IHC stain that was used. The legend was further detailed to reflect the content of the figure.
- 3- Figure 2 could be marked up so that the readers know what to look for, alternatively more detailed in terms of the figure legend.
- An arrow was added to the figure for more clarity as suggested.
- 4- What are the lessons learned from this case? The authors could speculate more as to why this patient with such an advanced tumor had such a great outcome. Any potential contributing factors worthy of exploration in follow-up studies?
- This point was further addressed in the conclusion, with respect to the importance of future data to properly assess potential prognostic factors and their role in the evolution of this disease.



Reviewer #2: The article is well written and stressed the management of a neuroendocrine carcinoma

Table and figures are well appropriated

No queries

To my point of view the article is suitable for publication in its current form

Please note that all changes were highlighted in the manuscript for clarity. We hope that the revised version is in order and remain at your disposal for any further enquiries.

Best regards,

Rel mostric A

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2nd Editorial decision 15-Nov-2021

Ref.: Ms. No. JCTRes-D-20-00127R1 High-Grade Neuroendocrine Small-Cell Carcinoma of the Anal Canal: Longterm Remission with Chemoradiotherapy Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,



Michal Heger Editor-in-Chief Journal of Clinical and Translational Research

Comments from the editors and reviewers: