

## Answer to Reviewer

### Dear the Editor and Reviewers,

Thank you for the comments, all changed are highlighted, new paragraphs and recent references have been included in the manuscript to answer the reviewers' comments.

We are hoping the manuscript will be considered for publication in the esteemed World Journal of Clinical Cases.

#### Reviewer 1#

Specific Comments to Authors: The topic of this editorial has a certain novelty. It studies the differences in etiology and treatment of two types of prostate cancer: NEPC and t-NEPC, as well as related research progress. But please check the formality of the manuscript carefully, there are some mistakes. And as an editorial, about half of the references cited are articles from 5 years ago. Please update the references.

#### Answer

Thank you for the valuable comments.

1- please check the formality of the manuscript

Response: Typesetting and editing were done.

2- Please update the references.

Response: Additional recent references were added.

#### Reviewer 2#

Specific Comments to Authors: The author systematically elucidates a distinct subtype of prostate cancer, neuroendocrine prostate cancer (NEPC), focusing on its occurrence, characteristics, and prognosis. The author highlights the unfavorable prognosis associated with t-NEPC, emphasizing the need for clinical attention. The article also delves into the relationship between t-NEPC development and genomic, epigenetic, and transcriptional changes, providing a comprehensive understanding of t-NEPC. 1. How is the efficacy of androgen deprivation therapy currently assessed in clinical practice? Are there standardized criteria or indicators to detect t-NEPC at an early stage? 2. The existing diagnostic markers for t-NEPC show no correlation with prognosis or treatment benefits. Are there other relevant indicators that can better assess prognosis and treatment outcomes? 3. Since epigenetic and transcriptional changes are associated with the development of t-NEPC, are there corresponding epigenetic markers or transcriptional sites that can serve as intervention targets? Can certain gene sequencing techniques be employed for early assessment of disease progression?

#### Answer

Thank you for the valuable comments, and the high scientific question that encouraged us to add updated studies, we tried to make the answers as short as possible due to the form of the manuscript "Editorial".

**Comment 1:** How is the efficacy of androgen deprivation therapy currently assessed in clinical practice? Are there standardized criteria or indicators to detect t-NEPC at an early stage?

**Answer:** Androgen deprivation therapy (ADT) is the approved treatment for PCA. We added a paragraph on the limitations of repeat prostate biopsy and liquid biopsy to early detection of t-NRPC. We added, too, paragraphs on recent data on the molecular and genetic aberration of NEPC which will be used for early detections of t-NEPC.

**Comment 2:** The existing diagnostic markers for t-NEPC show no correlation with prognosis or treatment benefits. Are there other relevant indicators that can better assess prognosis and treatment outcomes?

**Answer:** Repeat tissue or/ and liquid biopsy for genomic diagnosis is currently going on in limited sample size research, this approach needs consensus and approval on timing of follow-up and which marker to be used (A paragraph is added).

**Comment 3:** Since epigenetic and transcriptional changes are associated with the development of t-NEPC, are there corresponding epigenetic markers or transcriptional sites that can serve as intervention targets? Can certain gene sequencing techniques be employed for early assessment of disease progression?

**Answer:** New 2 paragraphs were added addressing this point, the future will be the immunotherapy, gene therapy and the recent modalities.

**Comment 4:** Minor language polishing

**Answer:** Language editing was done.