

List of Responses

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "A Case Report : Advanced cervical cancer patients with chemotherapy induced grade IV myelosuppression achieved complete remission with cadonilimab monotherapy"(Manuscript NO.: 90743, Case Report). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in yellow in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Reviewer #1:

1. Response to comment: The title must be changed and replaced by: "A Case Report : Advanced cervix cancer patients with chemotherapy induced grade IV myelosuppression achieved complete remission with cadonilimab monotherapy" not to be confused with the neck (cervical region). the same should be done in the abstract.

Based on the reviewer's opinion, we adjusted the title to "An advanced cervix cancer patient with chemotherapy-induced grade IV myelosuppression achieved complete remission with cadonilimab: A case report". The abstract also underwent a change, with cervical cancer being replaced by cervix cancer.

Reviewer #2:

1. Response to comment: Title: The title needs to be restructured.

We have changed the title to “ An advanced cervix cancer patient with chemotherapy-induced grade IV myelosuppression achieved complete remission with cadonilimab: A case report” according to the comments of the reviewer.

2. Response to comment: Abstract: Few sentences in the abstract need to be restructured. Please make the abstract completely structured or non-structured as per the guidelines of the journal.

As Reviewer suggest that we make the abstract completely structured as follows.

Abstract

BACKGROUND: The prognosis for advanced metastatic cervix cancer (MCC) patients is poor, and the disease continues to pose a considerable therapeutic challenge. Despite the administration of first-line regimens consisting of cisplatin, paclitaxel, and bevacizumab, survival rates for patients with metastasis remain poor. The emergence of bispecific antibodies (BsAbs) offers a novel treatment option for patients diagnosed with MCC.

CASE SUMMARY: In this report, we present a patient with MCC who was treated with cadonilimab monotherapy at a dose of 6 mg/kg every two weeks after chemotherapy proved to be intolerable. The patient exhibited a sustained complete response (CR) for a duration of 6 months, demonstrating an optimistic outlook.

CONCLUSION: This case illustrates the considerable efficacy of cadonilimab in treating advanced MCC. It shows that BsAb therapy is a promising strategy for effectively treating patients with advanced MCC and should be considered an option when there is intolerance to standard chemotherapy.

3. Response to comment: Key Words: Please omit 'case report' keyword from the keywords list and add more relevant keywords if any.

We carefully considered the reviewer's suggestions. However, CARE Checklist-2016 requires case report as one of the key words. In addition, we added programmed death protein 1 and cytotoxic T-lymphocyte-associated antigen-4 as key words.

4. Response to comment: Add "Core tip".

As suggested by the reviewer, we should add the 'Core tip' as follows.

Core Tip: Advanced metastatic cervical cancer (MCC) has a poor prognosis and a low survival rate. The emergence of bispecific antibodies offers a novel treatment option for patients with MCC. Cadonilimab is a tetravalent bispecific antibody designed to simultaneously block the programmed death protein 1 (PD-1) and cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) pathways while substantially reducing toxicities compared to combination therapy with PD-1 and CTLA-4 antibodies. We report the case of a patient with advanced MCC who achieved a complete response with cadonilimab monotherapy despite chemotherapy-induced grade IV myelosuppression.

5. Response to comment: Introduction: Don't use complete terminology multiple times, instead use appropriate abbreviations subsequently.

Thanks to the Reviewer's reminder, we have replaced the complete terminology with appropriate abbreviations.

6. Response to comment: Case Description: 1. Please clarify whether the initial treatments (June 2021 and Nov 2021) were performed in the same hospital where the authors are affiliated to or in some other hospital, as the initial sentence creates confusion regarding the same.

I apologize for the confusion caused by my unclear expression to the reviewers. The treatments in June 2021 and November 2021 were performed at the same hospital, but not our hospital. I have changed the sentence to "The patient presented to the Second Affiliated Hospital

of Soochow University in June 2021 with a 2-month history of abnormal vaginal bleeding.”. At the same time, the full name of our hospital was included in the chief complaint.

7. Response to comment: Case Description: 2. This paragraph ‘Considering the patient’s young age and strong will to survive, she expressed a strong desire to be transferred to our hospital for further treatment. Therefore, both the patient and her family members were successfully transferred to our hospital in July 2022’ is purposeless and needs to be omitted.

We have omitted the sentence referred to by the Reviewer.

8. Response to comment: Case Description: 3. This paragraph ‘The patient suffered an accidental fall in August 2022, resulting in a fracture of the right intertrochanteric femur and a suspected fracture of the right subpubic branch. The orthopedic department performed surgical intervention to address the right intertrochanteric femoral fracture, and the postoperative recovery was satisfactory’ may be omitted if not relevant to the context of this case report.

We have omitted the sentence referred to by the Reviewer.

9. Response to comment: Case Description: 4. Please confirm whether the date ‘On August 27, 2020’ as mentioned is correct or not.

Thank you very much for the reviewer's reminder. It is likely a clerical error that caused the mistake in this date. It has now changed from On August 27, 2020 to On August 27, 2023.

10. Response to comment: Discussion: Please mention whether the patient had experienced any adverse effect during cadonilimab monotherapy.

Considering the reviewer's suggestion, we did not mention whether the patient experienced adverse reactions during the medication in the article. Therefore, we have added the following statement: "The patient we reported did not experience any adverse effects during treatment with cadonilimab. However, due to considerations related to immune medications, the Euthyrox

dosage was increased from 25 µg qd to 75 µg qd."

11. Response to comment: Conclusion: Please make conclusion a paragraph under separate sub-heading.

We have made conclusion a paragraph under separate sub-heading, as follows:

Conclusion

This case demonstrated the marked effectiveness of single-agent cadonilimab treatment in cases of advanced MCC where chemotherapy is not well tolerated. The therapy was well tolerated; however, vigilant monitoring for immune-related adverse events is recommended for patients with a prior medical history. BsAbs offer a promising therapeutic approach for patients with advanced MCC and should be considered as an option after standard chemotherapy fails.

12. Response to comment: Figures: 1. Please reduce the font size of Texts in Figure A as appropriate.

The format and size of the font have been adjusted according to the requirements of the journal, thanks to the reviewer's reminder.

13. Response to comment: Figures: 2. lease provide elaborated figure legend for Figure 3.

After thinking for a long time, we decided to change the figure into a table in order to gain a clearer understanding of the patient's tumor indicators and changes in thyroid function.

14. Response to comment: Other Comments: 1. The authors need to use more scientific terminologies as appropriate throughout the article.

Thanks for your suggestion. We have tried our best to polish the language in the revised manuscript. Meanwhile, we have asked a professional agency to proofread our article.

15. Response to comment: Other Comments: 2. The authors need to avoid use of different text fonts and size randomly throughout the article. The article needs to be revised accordingly with appropriate text font and size as per the journal guidelines.

We have revised the text font and size accordingly, following the journal guidelines.

16. Response to comment: Other Comments: 3. Grammatical and sentence construction errors need to be rectified appropriately throughout the article.

We apologize for our poor writing, but we have sent the manuscript to a professional English language editing company for further polishing. Additionally, we have included a new language certificate with the revised manuscript.

Special thanks to you for your good comments.

Other changes in the manuscript, such as abbreviations and punctuation, are highlighted in yellow.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked in yellow in revised paper.

We appreciate for Reviewer's warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions