

ANSWERING REVIEWERS

August 3, 2021

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 66730_Auto_Edited.docx).

Title: The tsunami of immunotherapy reaches mesothelioma

Authors: Mielgo-Rubio X, Cardena A, Sotelo Peña V, Sánchez Becerra MV, González López AM, Rosero AC, Trujillo-Reyes JC and Couñago F.

Name of Journal: *World Journal of Clinical Oncology*

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The manuscript has been modified according to the recently published evidence and the reviewer suggestions:

- 1) The manuscript has been updated
- 2) The language has been polished
- 3) Modifications were done according to the reviewer suggestions as follows:

Comment 1: Please consider replacing all tables with a three-line tables, and improve Table 2 to make its content more clear. References should be included in the tables.

Response: We have replaced Table 1 and Table 2 as suggested by reviewer to make them more simple and clear. We also improved Table 2 content to be easier to understand. References are included in the tables.

Comment 2: Please try to summarize the advantages of nivolumab and ipilimumab as a new first-line treatment strategy compared to previous regimens. Please try to merge it into a table.

Response: We added Table 3 comparing efficacy and toxicity of frontline nivolumab and ipilimumab vs previous chemotherapy (EMPHACIS) or chemotherapy + bevacizumab (MAPS) regimens.

Comment 3: This article introduces the therapeutic effect and adverse effects of doublet chemotherapy with cisplatin and pemetrexed on mesothelioma, as well as the effect of novel nivolumab and ipilimumab immunotherapy. However, the adverse effect of nivolumab and ipilimumab immunotherapy was not introduced.

Response: We added a new section presenting CONFIRM study evaluating nivolumab monotherapy in pretreated malignant mesothelioma. In this paragraph we exposed efficacy data and we also introduced toxicity profile. In the section of frontline nivolumab and ipilimumab we added toxicity data of the combo of nivolumab and ipilimumab vs chemotherapy and immune-related adverse events.

Comment 4: In the treatment of malignant mesothelioma targeting PD-L1, nivolumab and ipilimumab had shown different results. In addition, how does the nivolumab and ipilimumab act as an inhibitor on the PD-1/PDL-1 pathway? Please try to explain these reasons.

Response: In “Immunotherapy-based treatment strategies for mesothelioma” section, before talking about the results of studies with immune checkpoint inhibitors, we added a paragraph explaining the mechanism of action of CTLA-4 inhibitors and PD-1/PD-L1 inhibitors.

Overall, we would like to thank the reviewer remarks which have help us to improve substantially our manuscript.

Thank you again for publishing our manuscript in *World Journal of Clinical Oncology*.

Sincerely yours,

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