Peer Review File

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Review Comments:

Comment 1: First of all, my major concern for this study is the problematic feasibility of meta-analysis, which was used to pool the short-term efficacy and safety outcomes of neoadjuvant immunotherapy alone or in combination with chemotherapy. The authors should aware that meta-analysis is often used to address the controversy regarding the efficacy and safety of an intervention, however, the authors did not present the conflicting findings on the efficacy and safety of neoadjuvant immunotherapy, and did not analyze the reasons for the contrivers to indicate meta-analysis is appropriate. The further methodology problem is the intervention of interest of this study is clinically heterogeneous, so the pooled results are problematic and not convincing.

Reply 1: We are grateful to the Reviewer for bringing this issue to our attention. We did not present the conflicting findings on the efficacy and safety of neoadjuvant immunotherapy. Short-term outcomes and safety in clinical trials were proved satisfactory. However, comparison between combination therapy and single drug therapy was deficient. We have added the present suspicion on the background in the abstract section and introduction section.

Changes in the text: “Abstract” section (see Page 2 line 25); “Introduction” section (see Page 4 line 67).

Comment 2: Second, in the title the term “Exploratory meta-analysis” is incorrect, and the authors did not explain why this study is an exploratory meta-analysis.

Reply 2: We are grateful to the Reviewer for bringing this issue to our attention. In our article, we tended to explore the relationship between PD-L1 expression and pathological response. We also demonstrated relationship between radiologic response and pathological response. However, another meta-analysis focusing on PD-L1 expression and pathological response and pathological response has been published in

the last year. We agree your suggestion and revised our title.

Changes in the text: title: Meta-analysis on efficacy and safety of neoadjuvant immunotherapy in non-small cell lung cancer.

Comment 3: Third, in the introduction of the main text and the background of the abstract, the authors did not present the clinical controversy regarding the efficacy and safety of neoadjuvant immunotherapy alone or in combination with chemotherapy and did not explain whether meta-analysis is suitable to address the controversy. Given the clinical heterogeneity in included studies, I suggest the authors to do a qualitative systematic review. The clinical question was described "Few long-term survival data have been published", however, "we utilized pathologic response and radiologic response as surrogate end points" cannot address the problem of the lack of long-term survival outcomes. The clinical significance and needs need to be described again.

Reply 3: We are grateful to the Reviewer for bringing this issue to our attention. We have explained the clinical controversy in the first question. About the surrogate end points, we added that "previous study shown that histopathologic response related strongly to long-term OS" and mentioned it again in the discussion section. Also, we mentioned sincerely the limitation.

Changes in the text: "Abstract" section (see Page 3 line 48); "Introduction" section (see Page 4 line 72); "Discussion" section (see Page 12 line 260); "Conclusion" section (see Page 15 line 309);

Comment 4: Fourth, in the methodology of the main text, the literature search has language bias since no non-English language databases were searched. The inclusion of studies was not described according to the PICOS principles, and the risk of bias of included studies were not assessed. In statistics, the authors only can pool the efficacy and safety data from studies by using the same treatment strategy, the same medication and the same clinical research design. I suggest the authors not to directly compare the outcome data of different ICIs unless the data are from multiple head-to-head comparison studies. MINORS cannot be used to assess the risk of bias of single-arm

clinical trials because it is suitable for non-randomized controlled trials. The authors need to consider the sources of bias in single-arm clinical trials to construct the risk of bias assessment tool.

Reply 4: We are grateful to the Reviewer for bringing this issue to our attention. As to the lack of non-English language databases, we have mentioned the language bias in our limitation. We have changed the inclusion criteria according to the PICOS principles. Description and figures of different ICIs have been deleted. In regard to the MINORS, it is suitable for non-randomized trials. This tool has been applied in "Short-term outcome of neoadjuvant immunotherapy and chemotherapy in non-small cell lung cancer: A systematic review and meta-analysis" for single-arm clinical trials and we thought that it can be taken into consideration.

Changes in the text: "Methods" section (see Page 5 line 89); "Methods" section (see Page 6 line 123); "Discussion" section (see Page 14 line 301); "Figure 6", "Figure S4-S5" and section related to different types and cycles of ICIs in the past was deleted.