Peer Review File

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Reviewer A

This manuscript is interesting research regarding prognosis of immunotherapy for non-small cell lung cancer with CDKN2A loss of function. Although it is a retrospective study at a single institution, the authors had considered this topic in detail. However, there are crucial issues in this manuscript.

Comment 1: # Author described the effect of immunotherapy in LOF group in Figure 2C and D. I think that those data should be described in wild type group.

Reply1: thank you for your reply. In the second part of RESULT (figure 2), we only discuss the effect of immunotherapy in LOF group. So we draw the specific effect of immunotherapy of every patient (Figure 2D), and the overall effect of immunotherapy (Figure 2C) in LOF group. We have also described the effect of immunotherapy of wild type in the third part of RESULT (Figure 3). However, it is hard to draw a picture of the specific effect of immunotherapy of every patient in wild type group (just like Figure 2D).

Comment 2: # It is unclear that represented image of p16 IF staining in CDKN2A LOF and wild type patients in Figure 2A.

Reply2: for the LOF group, the representative image of p16 IF should be negative, so it is right that we hardly find any staining in this group. For the wild type group, we have added arrow in wild type group to indicate the p16 IF staining. And we also upload high resolution image of Figure 2 in the system.

Change in the text: we have added arrow in figure2A and uploaded high resolution image of Figure 2（see page 7, line 152）.

Reviewer B

The outcomes of the study are undeniably intriguing; however

Comment1. The article is composed in a rather deficient form of English, with instances where it is not understandable.

Reply1: We feel sorry about our poor English writing, and we have made a lot of writing amendments and request the language re-editing of the journal to help us.

Change in the text: we have changed many places in the whole manuscript.

Comment2. There are inaccuracies in the introduction.

Reply2: we feel sorry about the inaccuracies in the introduction, and have made amendment in the introduction part.

Change in the text: we have made amendments in the introduction part.(see page 2, line 48, line 53-55; page 3, line 70-72)

Comment3. The Method section lacks clarification of the precise procedures undertaken.

Reply3: we have added the precise procedure in some part of method section and deleted some unnecessary part of method section.

Change in the text: see page 3, line 83-85; page 4, line 94-99, line 104-111.

Comment4. An absence of elucidation is evident regarding the exceedingly low PD-L1 values exceeding 50% and the concomitant high PD-L1 negatives.

Reply4: we have modified table 1 and list the precise cases of PDL1 $\geqslant$ 50%, PDL1 $\geqslant$ 1% & < 50% and PDL1 < 1% subgroups in both CDKN2A wild type and LOF group.

Change in the text: see page 6, table 1.

Comment5. The baseline lacks a comprehensive depiction of the treatments administered to patients and offers insufficient elucidation regarding the presence of patients with driver mutations in the various groups.

Reply5: the basic information of initial treatment could be found in the first part of Result section (page 5, line 131-134). We have also demonstrated the treatment

information in the Method section (page 3, line 85-86). In our study, we exclude the commonly driving gene mutation such as EGFR and ALK.

Change in the text: we have added information to demonstrate that we exclude the commonly driving gene mutation such as EGFR and ALK in our study (page 3, line 70-72; line 83-84)

Reviewer C

In this manuscript, the authors tried to analyze the different prognosis of NSCLC with CDKN2A loss of function (LOS), treated with immunotherapy as monotherapy or in combination. The article is well written and structured and speaks about a very interesting topic in thoracic oncology. The number of patients is satisfactory. The conclusions are moderately in line with the results. I would consider this manuscript for publication after addressing these comments.

Comment1: The authors didn't mention NSCLC stage of patients included. Were all NSCLC deemed unresectable or not suitable for surgery or they also included patients after surgery? Please specify the clinical or pathological stage.

Reply1: Thank you for your nice and careful review. In fact, all patients we collect are stage IV from initial treatment. We have added this important information to manuscript.

Change in the text: we have added the stage information in the manuscript (see page 3, line 83-84; page5, line129-130).

Comment2: secondly, is there a reason why authors included for the treatment only PD-1 inhibitors and not also PD-L1 inhibitors?

Reply2: there are 2 reasons why our study excludes PDL-1 inhibitors. Firstly, the price of PDL-1 inhibitors is far more expensive than PD1 in China, meaning we could hardly collect PDL-1 inhibitors in stage IV NSCLC patients. Secondly and more importantly, until Feb. 2022, PDL-1(Durvalumab) is only approved in unresectable stage III NSCLC after concurrent chemoradiotherapy by China National Drug Administration (CNDA) in NSCLC. Another PDL-1(Atezolizumab) is approved in NSCLC by CNDA in late

2021.