Peer Review File

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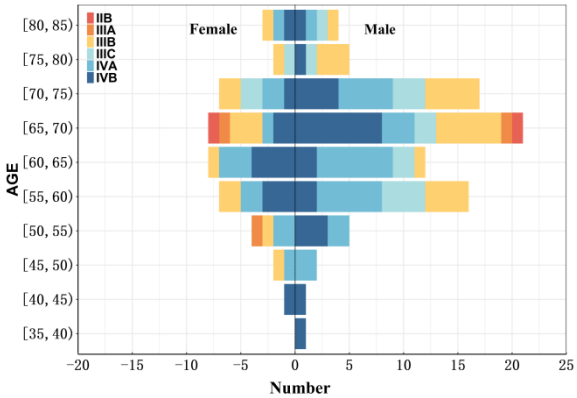
Reviewer A

This paper discusses biomarker of irTDs. The main contribution of the paper is prediction common irAE, irTDs. I recommend that this paper be accepted after minor revision.

Comment 1. PFS and OS were affected by PD-L1 expression, did you consider data each PD-L1 expression?
Reply 1: The clinical outcomes of the patients who had received or were receiving ICIs were affected by the PD-L1 expression. However, in our research, the PD-L1 expression was known in just 29 (23.0%) patients. There was no statistical difference (p=0.9) in the PD-L1 expression level between the patients with or without irTDs. So we consider the PD-L1 expression level was balanced between the patients with or without irTDs.
Changes in the text: No modification was made according to this comment.

Comment 2. It is difficult to understand Figure.1, because the unit of measure for the horizontal axis is not written, so please show that.
Reply 2: The figure 1 has been revised and attached below.



Changes in the text: we have modified figure 1 as advised and re-submitted.

Comment 3. Please write detail of gene mutation in Table 1. If EGFR mutations were major mutation such as ex19del or L858R, were ICI conducted for 1st line chemotherapy?
Reply 3: Unfortunately, the details of EGFR mutation in all two patients were missed although the EGFR mutations were recorded in the clinical data. The details of gene mutations were revised in Table 1. All the ICIs involved were conducted for the 1st line treatment (line 86-89).
Changes in the text: we have modified Table 1 as advised (blue-colored text and

underlined).

Comment 4. Does this study include combination therapy with cytotoxic anticancer agents?
Reply 4: Yes, some patients received cytotoxic anticancer agents as adjunctive chemotherapy and some also received adjunctive radiology as well (line 129-132 and as showed in Table 1).
Changes in the text: No modification was made according to this comment.

Reviewer B

This is a comprehensive and well-written analysis of thyroid irAE in NSCLC patients treated with ICI. The subject is clinically relevant and very interesting because of the broad use of these drugs. I have one main comment:

Comment 1. Several other analysis using larger patient cohorts have shown that the outcome of patients with irAE, including thyroid irAE, is better than that of patients without irAE. This becomes evident if patients with irAE are compared to patients without any irAE. One limitation in the survival analysis of the the authors are the small patient numbers, but another even more important one is that they compared patients with thyroid irAE vs. all other patients (which includes also patients with skin, pulmonary, liver and may other irAE), instead of having a control group of patients without any irAE. Large retrospective analyses have shown that endocrine irAE comprise about 20% of all irAE in NSCLC (e.g. https://pubmed.ncbi.nlm.nih.gov/34268127/), so that the control group of the authors contains actually more patients with irAE than the thyroid irAE patient group. This could explain why the authors did not find any impact of thyroid irAE on patient outcomes and should be included in the Discussion of the manuscript.
Reply 4: Actually the 84 euthyroid patients enrolled as the control group in our research were free from any irAEs. Thanks for your question, we highlighted the information of the euthyroid patients in line 126-127.
Changes in the text: We have made revision as advised (blue-colored text and underlined, line 126-127).