

Peer Review File

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Reviewer Comments-reviewer A

The authors retrospectively collected adverse events (AEs) of advanced NSCLC patients treated with the combination of ICIs and antiangiogenic agents at their Institution from 2019 to 2021.

As already reported in literature there is a relationship between higher BMI (overweight-obesity) and increased risk of irAEs in patients on ICI therapies as well as hypothyroidism is a well-established toxicity of ICIs and antiangiogenic agents. The study is interesting because few data exist in literature about the incidence of hypothyroidism caused by the concomitant use of ICIs plus antiangiogenic agents and the relationship with other risk factors including BMI.

Unfortunately, the authors did not report the OS in this cohort of patients to evaluate the relationship between hypothyroidism and survival.

I suggest to add the results of the meta-analysis published by Guzman-Prado et al. (Cancer Immunol Immunother. 2021 Jan;70(1):89-100) and of the large real-life observational study published by Cortellini et al. (EJC 2020, 128: 17-26).

Reply: Thank you for bringing this to our attention. We agree that the relationship between hypothyroidism and survival is an important factor to consider, and we appreciate your suggestion to include the results of the previous studies. We have thoroughly reviewed these studies and integrated their findings into our work, along with appropriate citations. We appreciate your constructive feedback.

Changes in the text: we have modified our text as advised (see Page 10, the last paragraph of the Discussion section).

Reviewer Comments-reviewer B

1. Figure 1

- a) Please provide an editable version of the flow chart (figure 1) in DOC/PPT.
- b) Please explain TFTs in the legend.

Response : Thank you for your suggestion.

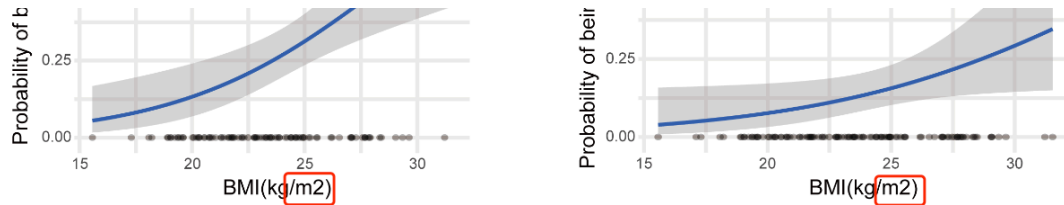
- a) Since the original Figure 1 was created using CorelDraw software, it could not be converted

into an editable version in DOC/PPT. Therefore, I have created a new version of Figure 1 using PPT.

b) We have added an explanation for TFTs in the figure legend.

2. Figure 2

Please revise “m2” to “m²”.



Response : The requested revision has been made to Figure 2.

3. References/Citations

Please double-check if more studies should be cited as you mentioned “studies”. OR use “study” rather than “studies”.

41). Large real-world observational studies have also confirmed that baseline obesity is significantly associated with improved objective response rate, progression-free survival, and overall survival in metastatic non-small cell lung cancer patients with a PD-L1 expression of $\geq 50\%$, receiving first-line single-agent pembrolizumab, and that there is a significant improvement in ORR, PFS, and OS in patients with slight weight gain during immunotherapy (42). Finally, since the interval between TFTs was not

Response : Thank you for bringing that to our attention. The word "study" has been used instead of "studies". We appreciate your thorough review and attention to detail.