Peer Review File

Article information: https://dx.doi.org/10.21037/jtd-23-387

Reviewer A

The present study, which focused the efficacy of nab-PAC plus camrelizumab in the second or later line treatment of advanced non-small cell lung cancer patients is interesting but I have the following suggestions.

1. How did you define cachexia included in the exclusion criteria?
Reply: Tumor cachexia has a clear definition. It has been clearly described in many literatures, and due to space limitations, we did not describe it in detail in the research methods.

2. Why are 19 patients with PS 2 or higher included in Table 1, even though the inclusion criteria list patients with PS 0-1?
Reply: Thank for your very careful observation. In order to be more in line with the treatment conditions in the real world, a small number (about 36%) of patients with poor physical fitness scores (PS=2 points) were indeed included in this study. We have modified our text as advised (see Page 5. Line 144-145& Page 23. Line 224-226) .

3. Did you use a statistical method such as the log-rank test to compare survival times between the two groups? 95% confidence intervals for ORR, DCR, PFS, and OS should be mentioned. Kaplan-Meier curves should include number at risk.
Reply: In order to further discover the advantageous population receiving the treatment of this regimen, we also used the log-rank test to compare and analyze the survival time of different populations. The confidence interval and HR value will also be added to the subsequent result analysis part. We have modified our text as advised (see Page 6-7. Line 202-211& Page 22. Line 214-215; see Page 8. Line 246-211& Page 8. Line 258-259).

4. Were there any characteristics of the patients with Treg ratio changes before and after? You should mention it in the discussion part.
Reply: We did not find significant differences in the clinical characteristics of patients whose proportion of lymphocyte subsets changed before and after treatment, such as the severity of tumor burden, the proportion of liver and brain metastases, and the expression level of LDH. Subset changes are expected to serve as a potential predictor

of efficacy of this regimen, which we also describe in the Discussion section. We have modified our text as advised (see Page 10. Line 332-339).

5. The first-line treatment for advanced non-small cell lung cancer is mainly chemoimmunotherapy and immunotherapy, and immune checkpoint inhibitors are mostly used as the first*-line treatment. What kind of patients do you think combined regimen of nab-PAC and camrelizumab used in the second or later lines would be effective for? You should mention it in the discussion part.

Reply: Although immunotherapy combined with chemotherapy has become the standard treatment for driver gene-negative advanced nsclc, exploring the potential biomarkers for efficiency prediction has always been the focus and difficulty of clinical research. According to the preliminary conclusions of our study and the published research data, the patients who receive this program are more effective or the priority population are likely to be those with better physical fitness score (PS score 0-1 points), no liver and brain metastases, Patients with a significantly lower proportion of Treg after treatment , but there is clearly still a lot of work to be done in this field. We have modified our text as advised (see Page 9. Line 296-299).

Reviewer B

1). First, the title needs to correctly describe the clinical research design of this study, i.e., a retrospective cohort study.

Reply: We have modified our title as advised (Efficiency and toxicity of nab-paclitaxel and camrelizumab in the second or above line treatment of advanced non-small cell lung cancer: a retrospective cohort study) (see Page 1. Line 2-3).

2). Second, the abstract is not informative and needs further revisions. The background did not indicate the clinical importance of this research focus and why nab-paclitaxel and camrelizumab is potentially effective and safe. The methods did not describe the inclusion of subjects, the assessment of baseline clinical factors, follow up procedures, and measurements of efficacy and safety outcomes. In the results, please first summarize the clinical characteristic of the study sample and quantify the findings on the safety outcomes. The conclusion needs more detailed comments for the clinical implications of the findings.

Reply: Paclitaxel-based chemotherapy represented by nab-paclitaxel combined with PD-1 has become the standard model for the 1st treatment of advanced NSCLC with negative driver genes (such as EGFR, ALK et al), indicating that nab-paclitaxel and PD-1 are likely to have a good synergistic effect. PD-1 alone or chemotherapy single

has limited curative effect in the second-line and above treatment of nsclc, so it is of great significance to explore the combination of PD-1 and nab-paclitaxel to further improve the therapeutic efficiency in such field. We have modified our abstract as advised (see Page 1-3. Line 31-52).

3). Third, the authors need to have comments on the limitations of available second-line treatments and explain why the combination of nab-paclitaxel and camrelizumab is superior to these treatments in terms of efficacy and safety outcomes.
Reply: The potential of nab-paclitaxel combined with PD-1 has been shown in many solid tumors including lung cancer, but there is still a lack of similar research and reports in the second-line and above treatment of advanced non-small cell lung cancer. From the perspective of enhancing efficiency through combination therapy, nab-paclitaxel combined with PD-1 may have great potential in the second-line treatment of advanced non-small cell lung cancer. In addition to the promising efficacy, either the safety of PD-1 monotherapy or nab-paclitaxel has also been widely confirmed in lung cancer. Furthermore, even under the premise that some advanced nsclc patients are in poor physical condition in the real world, the low-dose nab-paclitaxel used in this study will be a new innovation compared with previous studies. We have modified our text as advised (see Page 9. Line 296-299).

4). Fourth, the methodology of the main text needs to describe the clinical research design, sample size estimation, assessment of baseline clinical factors, and follow up details. In statistics, the authors need to describe how the descriptive statistics were performed and ensure $P<0.05$ is two-sided.
Reply: We refer to the design of similar real-world studies and estimate the effective sample size to satisfy the statistical requirements, together with the clinical characteristics of patients and follow-up, which are also corrected and explained in the Methods and Materials section. We have modified our text as advised (see Page 6-7. Line 186-216).

5). Finally, please consider to cite the below related papers: 1. Chen B, Wang J, Pu X, Li J, Wang Q, Liu L, Xu Y, Xu L, Kong Y, Li K, Xu F, Liang S, Cardona AF, Wu L. The efficacy and safety of immune checkpoint inhibitors combined with chemotherapy or anti-angiogenic therapy as a second-line or later treatment option for advanced non-small cell lung cancer: a retrospective comparative cohort study. Transl Lung Cancer Res 2022;11(10):2111-2124. doi: 10.21037/tlcr-22-697. 2. Choi MG, Choi CM, Lee DH, Kim SW, Yoon S, Ji W, Lee JC. Impact of gender on response to immune checkpoint inhibitors in patients with non-small cell lung cancer undergoing second- or later-line treatment. Transl Lung Cancer Res 2022;11(9):1866-1876. doi:

10.21037/tlcr-22-146. 3. Gao G, Zhao J, Ren S, Wang Y, Chen G, Chen J, Gu K, Guo R, Pan Y, Wang Q, Li W, Yang X, Zhou C. Efficacy and safety of camrelizumab plus apatinib as second-line treatment for advanced squamous non-small cell lung cancer. Ann Transl Med 2022;10(8):441. doi: 10.21037/atm-21-4792.

Reply: We cite the recommended articles as requested by the reviewers. (see references 27, 28 & 38)