TRANSLATIONAL LUNG CANCER RESEARCH

Peer Review File

Article Information: Available at http://dx.doi.org/10.21037/tlcr-20-541

Review Comments

Reviewer A

I advise the authors to revise or clarify some minor comments described below.

Minor Comment

Comment 1. In the Running Title, 'Ansclc' is an unfamiliar abbreviation.
Reply: The abbreviation has been changed.
Changes in the text: Line 5
Comment 2. P9, L182, and P11, Line 232; What do you mean by 'baseline N, L, or P values' ? N=neutrophil, L=lymphocyte, or P=platelet?
Reply: All the such abbreviations noted have been changed.

Comment 3. Page 10, Line 220-222 and supplemental Figure 1; I know that the additional cut-off points (3 and 5 for NLR, 180 for PLR) had been adopted in many past studies, and the authors also mention varieties of thresholds in Discussions. For what did this study use these traditional cut-off points, though the optimal cut-off points had already been identified for this study?
Reply: References for the cut-offs mentioned have been added to the discussion section.
Line: 296 and 297

Comment 4. The lines of Q1-4, especially Q1-2, in Fig.2 appear similar. Can the authors make these lines more different?
Reply: The requested changes have been made to Figure 2.

Comment 5. What do you mean by 'aNSCLC at presentation' in Table 1 and 2? Please explain it more concretely.
Reply: The term 'advanced nonsmall cell lung cancer' (aNSCLC) is defined in the first line of the Methods section, "Stage IV, 7th edition UICC TNM classification or recurrent nonresectable disease not amenable to curative intent radiotherapy"
Line: 121 and 122

Comment 6. Statistical methods for comparison between low and high NLR and PLR are ambiguous in Table 2. There is no footnote symbol (*, †, ‡) in p-values of Gender, ECOG-PS,

Smoking status, Histology, aNSCLC at presentation, Liver metastasis, Brain metastasis, RT during pembrolizumab, Baseline NLR and Baseline PLR. Do you mean that p-values without symbol were all compared only by chi-square test?
Only characteristics 'Body mass index (%)' contains (%), though n(%) is already indicated.
Reply: Table 2 has been modified to reflect these comments.

Comment 7. In Supplemental Figure1, K-M curves according to NLR ⩾3 or <3, what do you mean by 'NR month' ? NR=not reached?
Reply: The figure caption describes the abbreviation NR as "Not reached"

Comment 8. Supplemental Table 1 and 2;
1) Why did this study analyze irAE development within 6 and 8 months? Was there any significant differences in irAE during only 2 months-interval?
Reply: 6 and 8 month landmarks were chosen as most patients would have experienced an irAE by that point. We had also conducted a 4 month landmark, but results were similar to the 6 month analysis.
Line:178 and 179
2) I am afraid that the multivariate Logistic regression included too many explanatory variables (N=11) for too small number of events (only 89 irAE).
Reply: We have redone the MVA logistic regression of irAE development at 6 and 8 month landmarks with three less variables (Charlson Comorbiditiy Index, Smoking status, an Body Mass Index were eliminated). The results of the MVA are essentially the same.
3) Did these analyses target all grade irAE? However, were irAE of grade 1 or irAE of thyroid change clinically important? I do not think it important that all grades and all types of irAE were lumped all together as irAE.
Reply: We respectfully disagree with this comment. Patients treated in our cohort were older (median age 70years of age) and more symptomatic (40.5% were ECOG PS 2/3) than those in registration trials. It is well established that even low grade irAE such as grade 2 colitis or pneumonitis can be poorly tolerated by many patients and result in hospitalization or need for corticosteroids.

Reviewer B

This article addresses a very relevant and timely topic: the prognostic value of NLR (</⩾6.4) and PLR (</⩾ 441.8) ratios in PD-L1 ⩾50%, pembrolizumab-receiving, advanced NSCLC patients. The title is clear and concise, the study objective is clearly defined and the abstract is accurate and complete. The study design is appropriate, the methods are precisely described and the tables and figures are clarifying. The outcomes and results are clearly addressed and the statistics are used and described appropriately; the references are

up-to-date. The language is of excellent quality. The discussion and conclusions are justified by the results presented.

Globally, this paper is articulate yet easy to follow and represents a valid addition to the current state of the art. I would only suggest adding a brief and broader overview on the other currently explored prognostic biomarkers in advanced NSCLC, in order to better contextualize this topic.

Reply: We have made mention of other blood based prognostic markers including the derived neutrophil lymphocyte ratio, lung immune prognostic index, and monocyte lymphocyte ratio in the Introduction as requested.

Lines: 104-105