

Point-by-point response to reviewer 2

Manuscript title: “Baseline absolute lymphocyte count and ECOG performance score as predictors of survival in advanced non-small cell lung cancer undergoing PD-1/PD-L1 blockade”

jcm-526121

We thank the reviewer for the valuable input which has helped to improve our manuscript. The raised questions are answered in a point-by-point fashion and changes in the manuscript are highlighted in yellow.

„In this manuscript, Huemer investigated the correlation between baseline characteristics and the therapeutic efficacy of PD-1/PD-L1 inhibitors in 142 NSCLC patients. Predicting the effect of immune checkpoint therapies is a challenging topic in oncology, this work has great significance.“

R2#1:

„1. In table 1, for "Age", it is better to give mean and standard deviation.“

Authors' response:

Age is now represented as mean and standard deviation in Table 1.

R2#2:

„2. In Figure S1, please label A and B. Also put numbers at risk in this figure.“

Authors' response:

We have added the labels and numbers at risk in this figure. Please note that after recalculation of median PFS (from 4.1 to 3.9 months) and 95% confidence interval (from 3.1-6.3 to 3.1-5.7 months) and of median OS (from 13.6 months to 12.2 months) and 95% confidence interval (from 11.1-15.5 to 10.7-15.1), numbers have slightly changed as highlighted in yellow.

R2#3:

„3. Model selection, such as stepwise selection, is a better way to select significant variable of interest into the model rather than selecting variables one by one through univariate cox regression analysis.“

Authors' response:

We appreciate the comment of the reviewer, but since our aim is not to find the subset of variables in the data set resulting in the best performing model, rather we want to test if the variable of interest with a significant impact on survival is still significant even when other variables were included in the model we are thinking the procedure is appropriate.

However, as suggested by the first reviewer we have now repeated the analyses and included also the non-significant but clinically relevant parameters (age, sex, histology) in the multivariate model and additionally a model including all variables besides NLR, and ANC. In all tested models ALC showed a significant impact on PFS and OS.

R2#4:

„4. Since the sample size is limited and it has so many variables of interest to be included, propensity score method would be a better method when constructing cox regression model.“

Authors' response:

We are not aware of an advantage using propensity score matching in the case of limited sample size.

R2#5:

„5. In order to find the cut-off value, ROC curves are generally used. However, the author used the C-index to analyze the cut-off value (line 154). Could the author explain the difference between the two? Or, compared with the ROC curve, what is the advantage of calculating C-index?“

Authors' response:

ROC curve analysis for right censored data is time-dependent: the censored outcome can be dichotomized given time point t , e.g., being 1 if a subject has died prior to time t and 0 otherwise. To overcome the selection of a specific time we used the concordance index (C-index), which is an extension of area under a ROC curve (AUC) to survival analysis as has been proposed by Harrell et al. It is a conditional concordance probability measure between a survival outcome that is possibly right censored and a predictive score variable.

Harrell et al. Regression modelling strategies for improved prognostic prediction. Stat Med. 1984. 3:143-152.

Sima C, Gonen M. Optimal cutpoint estimation with censored data. J Stat Theor Pract. 2013. 7:345-359