Author’s response to reviews

Title: Pretreatment albumin/fibrinogen ratio as a promising predictor for the survival of advanced non small-cell lung cancer patients undergoing first-line platinum-based chemotherapy

Authors:

Jun Ying (yingjun666@139.com)
Danfei Zhou (bbfei2005@163.com)
Tongjie Gu (gutj1@163.com)
Jianda Huang (nbhuangjianda@sina.com)
Haijian Liu (liuhaijiantg@sina.com)

Version: 1 Date: 19 Jan 2019

Author’s response to reviews:

Reviewer reports:

Laura Bonanno, M.D. (Reviewer 1): The manuscript is overall well-written, although needing some language review.

Some points could be improved:

- The study lacks a control group analysis of patients not treated with platinum-based chemotherapy, to understand if the suggested marker is a predictive or a prognostic one.

Response: Thank you so much for your excellent suggestion! We have invited an English native speaker to review the language and we have corrected some grammar errors.

When designing this study, we choose the patients with same treatment (first-line platinum-based chemotherapy) in order to exclude the impact of treatment strategies on the prognosis. Our results showed AFR was a predictor for survival in advanced non-small cell lung cancers with first-line platinum-based chemotherapy. However, we have ignored that this study lacks a control group analysis of patients with radiotherapy or not treated with platinum-based chemotherapy. We have to admit that this is a great limitation for this study and we have added this into the end of “Discussion”. We have realized that we should use “predictive” instead of “prognostic”. We have also made the corrections. Furthermore, we will perform a study (advanced NSCLC patients with different treatment strategies including the control group of patients not treated
with platinum-based chemotherapy as you suggested) to investigating when AFR can serve as a prognostic factor for advanced NSCLC patients.

- The treatment of stage III patients is not clear. Since they were excluded from surgery (according to inclusion criteria), the authors should state if they have been excluded also from radical-intent radiotherapy and for which reasons. If they received radical-intent radiotherapy, they should be analyzed as a separate cohort of patients for the analyses.

Response: Thank you so much for your professional question! We are sorry that we haven’t made the treatment and exclusion clear. The patients receiving radical-intent radiotherapy were also excluded considering the impact of treatment strategies on the prognosis. We have added the context in the area of “Patients” as you required.

- In the introduction, the authors should discuss about the importance of predictive biomarkers in the context of the new therapeutic options available, thus referring to immunotherapy, combination treatment with ICI and chemotherapy and targeted agents.

Response: Thank you so much for your excellent suggestions! We have added the discussion about the new therapeutic options and the importance of predictive biomarkers as you required.

- Information about molecular characterization is missing.

Response: Thank you so much for your professional suggestion! We have added the molecular characterization (EGFR, EML4-ALK and K-ras) in Table 1 as you suggested.

- In the discussion the authors should put the new information depicted in the manuscript in the context of pre-existing studies about potential predictive/prognostic markers. Please discuss the potential role of molecular predictive markers of platinum-based chemotherapy and the lack of clinical application for these study and the potential (controversial) role of other circulating biomarkers such as NLR.

Response: Thank you so much for your professional suggestion! We have added the discussion about pre-existing studies about potential predictive/prognostic markers. We have also added the discussion about molecular predictive markers and other circulating biomarkers such as NLR as you required (in the area of “Discussion”).

At last, thank you again for all your constructive and professional suggestions! We really appreciate it!

Jonathan Dowell (Reviewer 2): Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.
Please overwrite this text when adding your comments to the authors.

Please clarify whether the mutation status of these patients was known, and if so, include in demographics.

Response: Thank you so much for your professional suggestion! We have added the mutation status of these patients (in table 1) as you required. Because some patients lack of the mutation information, so we didn’t clarify the information in the area of “Results”.

Were the radiologists blinded to the AFR? Did the radiologists go back and review all scans on these patients or were you relying on the original reports? On line 46 in the AFR and clinical characteristics section there is a type - it should read "high" AFR group.

Response: Thank you so much for your professional questions! Yes, the radiologists were blinded to the AFR and this study. Yes, the radiologists went back and reviewed all scans on the enrolled patients. We are so sorry that we haven’t made this clear. We have added the descriptions as you suggested. Thank you so much for pointing out our mistakes! We have made the corrections.

Please clarify the difference between the M0 and M1 group and the stage III and IV groups - shouldn't those be the same groups? How are there approximately 28% M0 patients but 45% stage III patients?

Response: Thank you so much for your professional questions! We are so sorry for our mistakes. While staging, we have confused the seven edition with sixth edition and we made some mistakes while counting numbers. Thank you so much for pointing out our mistakes. We have made the corrections. Furthermore, we excluded the factor “TNM stage” from the multivariate Cox analysis (the exclusion has no impact on the univariate Cox analysis results) and we did the data analyses again. We have made the corrections in Table 2 and 3.

Overall it is a reasonable retrospective look at a potentially novel prognostic/predictive marker. It would require further validation in larger prospective data sets. It might also be interesting to look at it with regards to immunotherapy.

Response: Thank you so much for your excellent suggestions! We have added these two limitations in the end of “Discussion”.

Finally, thanks again for all your excellent questions and suggestions! It means a lot for us!