TRANSLATIONAL
CANCER RESEARCH

Peer Review File

Article information: http://dx.doi.org/10.21037/tcr-20-1675

Reviewer A

1- Congratulations for the authors on this important work

Reply 1: Thanks for your comments. Hopefully, our data may provide guidance in personalized cancer treatment in the future.

2-Revise grammar and wording

Reply 2: We really appreciate your careful reading of our manuscript. English language copy editing has been done by one of professional editing companies (AME Editing Service).

Changes in the text: The editing version of manuscript, editing certificate and final revised manuscript are uploaded.

3- I would include the evidence of this histology subtype in other parts of the World that we have seen differences (Caucasians and Latin populations)

Reply 3: Thank you very much for your suggestion. However, we search in PubMed by using the terms “large cell carcinoma”, “histology”, “Caucasians” and “Latin” alone and in combination, and we unfortunately found no articles describe the histology subtype differences between different population. Would you please show us the relevant literature?

Reviewer B

This is a study of 322 LCC patients at the Shanghai Pulmonary Hospital who were diagnosed as per 2015 WHO criteria. They have summarized the clinicopathologic features and patient characteristics, presence of certain mutations and determined the disease-free survival for patients harboring mutations in tested genes versus those that did not. This study would be useful to the researchers in the lung cancer field, but comments below should be addressed.

In Figure1, IHC staining of LUAD and squamous cell carcinoma tissue sections should be included to serve as positive and negative controls for staining of the markers. They should also show the H&E and IHC staining for some of the mutation positive samples to definitively show the readers that these were not LUAD or squamous cell carcinomas specimens.

Reply 1: Thank you for your comments. IHC staining of LUAD and squamous cell carcinoma tissue sections have been included to serve as positive controls. H&E and

IHC staining for one case of KRAS-mutated LCC has been added as supplementary data.
Changes in the Text and Figure1: we have modified our text and figures as advised. (Please see Page 7, line 22, and Page 8, line 1-4, also see Figure 1 and supplementary data).

The authors could improve the information conveyed through table 1 by indicating the number of men, women, smokers and non-smokers in the different clinical stages. They should also show the median ages.
Reply 2: We have reorganized the Table 1. accordingly.
Changes in the Table 1: All the changes in the Table are shown in red.

The authors should determine if the presence of KRAS mutation alone can lead to worse DFS.
Reply 3: We have reanalyzed our data, and no significant difference in DFS was identified between the KRAS-positive patients and non KRAS-positive patients (p=0.232).
Changes in the Text: we have modified our text as advised. (Please see Page 9, line 18-22).