Reviewer's report

Title: Co-mutations of TP53 and KRAS Serve as Potential Biomarkers for Immune Checkpoint Blockade in Squamous-Cell Non-small Cell Lung Cancer: A Case Report

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Reviewer: Qian Li

Reviewer's report:

This manuscript reports the co-mutations of TP53/KRAS in a 64-year-old non-smoking patient with squamous-cell NSCLC. A therapy of pembrolizumab and combined with gemcitabine was given and attained a partial response that persisted for over seven months. The authors concluded that TP53/KRAS co-mutations in squamous-cell NSCLC served as a predictor for PD-1 inhibitor response. However, this paper needs serious improvement on the rationale for treatment, conclusion and English writing/editing, as described in the following issues.

Major issues:

1. Why it was stated that "immunohistochemistry was used to analyze PD-L1 related genes"? Immunohistochemistry detects PD-L1 expression at protein level, not at gene level. The abstract mentioned that this study used NGS to evaluate PD-L1 expression, which should be the gene level PD-L1 expression. I suggest authors do more literature review about bioinformatics profiling platforms, improve accuracy of terms and add references.

2. "a gene panel involving 416 genes associated with cancer, was utilized to analyze the postoperative tumor samples from patients in January 2018". Why was this mentioned? How was it linked to the reported case?

3. It was mentioned in Discussion and conclusion that 'the rationale for combined immunotherapy with chemotherapy depends on the hypothesis that cytotoxic chemotherapy will indiscriminately kill normal and cancer cells, while immunotherapy can "rev up" the immune system against cancer cells". This statement does not explain why the reported case may benefit more from this combined treatment compared to chemotherapy only. What are the potential results for not combining immunotherapy after chemotherapy?

4. This manuscript did not explain why co-mutations of TP53/KRAS was more important than other markers (i.e. low PD-L1 expression, MSI and TMB-low) in validating PD-1
blockade immunotherapy for the reported case. I suggest to review and reference more details in literature to support the rationale.

For example, Dong et al (2016) reported that co-mutations of TP53/KRAS was associated with strong/high PD-L1 and prolonged PFS. Summarizing the cases having co-mutations of TP53/KRAS but weak PD-L1 expression(from discovery and validation sets in Dong et al can validate PD-1 blockade immunotherapy for the reported case in this manuscript. There are other papers reporting the impact of TP53/KRAS on immune response in squamous-cell NSCLC too.

5. The conclusion that "TP53/KRAS co-mutations in squamous NSCLC can serve as a predicting factor" is too strong. TP53/KRAS co-mutations can be a potential factor to assess possible response to PD-1 blockade immunotherapy, but further studies with more cases are needed to confirm the prediction power.

6. I suggest the authors use English writing and editing resources to improve the language. There are also copyedit errors in this manuscript, e.g. "P53" should be "TP53" in abstract conclusion, terms are not consistent "squamous NSCLC, squamous-cell NSCLC", "co-mutations of TP53/KRAS, TP53 and KRAS".

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript
Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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