Author’s response to reviews

Title: Efficacy of anti-PD-1/PD-L1 antibodies after discontinuation due to adverse events in nonsmall cell lung cancer patients (HANSHIN 0316)

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Version: 1 Date: 11 Aug 2018

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12/Augst /2018

BMC cancer

Editor in chief

Alexandros Houssein

We appreciate you to give us a chance to revise our manuscript entitled “Efficacy of anti-PD-1/PD-L1 antibodies after discontinuation due to adverse events in non-small cell lung cancer patients (HANSHIN 0316)” for publication in BMC cancer as Research Article.
We made point-by-point response and ensured all changes to the manuscript indicated in the text by highlighting. We believe that the manuscript has been much improved, largely as a result of you and reviewer’s many thoughtful comments. We hope our answers are satisfactory for you. We believe that the findings described in this case report will be of special interest to the readers of BMC cancer. We are looking forward to your favorable consideration.

Yours Sincerely,

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Raheleh Roudi (Reviewer 1): In the current survey, the Tachihara et al analyzed the Efficacy of anti-PD-1/PD-L1 antibodies after discontinuation due to adverse events in non-small cell lung cancer patients.

→We appreciate to take time to review and give us the chance of revision. We believe that the manuscript has been improved, largely as a result of your comments. We hope our answers are satisfactory for you.

The authors need to consider some points;

1) The abbreviations for PR and SD should be added to abstract.

→We’re sorry. We added it.
2) The complete list of irAEs in lung cancer patients treated with anti-PD-1/PD-L1 antibodies has been evaluated in a study by Xiaoying Sun et al, 2017. This reference need to include in this section.

→ Thank you very much. The paper you pointed above was study protocol and it seems to be undergoing now. We added it in the reference 17) (p6, line 14).

3) Other treatment regimens in the patients need to include in the manuscript.

→ Thank you very much for your comment. We evaluated patients received either single-agent anti-PD-1 or PD-L1 antibody until August 31, 2016, and stopped due to AEs at institutions participating in our research group. The antibodies used in the patients such as described above were only nivolumab and atezolizumab in our institutions.

4) The results section has been categorized in three parts;

a) Patients characteristics

b) Data related to adverse effects

c) Data related to survival

→ Thank you very much. We categorized result section into three parts as your advice.

5) Resolution of the images needs to improve.

→ We’re sorry for poor resolution. Resolution has become worse because of stretching the image. It has been changed to be the same way as published in the format. I hope it will be enough for your wish.
6) The immunotherapy for lung cancer needs to expand in the discussion with more recent studies; including Jianwei Zhu et al, 2017 and Nicholas L. Syn et al, 2018.

→Thank you very much for your comments. The current literature (Jianwei Zhu et al, 2017) you listed first were evaluated the localized NSCLC patients (I to III, curative surgery or radiotherapy) who were treated with immunotherapy excluding immune checkpoint inhibitors. We learned a lot from that paper, but we think the targeted drug and objectives were different from our study, so we’re sorry for that we don’t add it. Next time, we will add it when it will be discussed in the same objective.

And is the reference you listed second (Nicholas L. Syn et al, 2018) correct below? We couldn’t find the paper except it. We added it in reference 18).


7) The conclusion needs to be elaborated.

→Thank you very much for your comment. We added it.

Reviewer 2 (Reviewer 2):

RE V IE WE R COMME NTS

This manuscript presents an interesting study on the response to one of the treatments for NSCLC. Although in a reduced and very specific cohort, it would be undoubtedly of interest for a number of readers. I would just suggest the authors to expand Table 1, since a very thorough description of the patient population will give other clinicians information on which are the patients susceptible to this type of treatments, and for how long. It would be desirable to have this table, containing the characteristics of the patients, already introduced in the Methods section (first paragraph).

Besides, it would be advisable to allow a native speaker to proof-read the manuscript, to focus some of the sentences which are written in an ambiguous way (e.g. "for a period of time" does not really give any information, especially in the Conclusions).
We appreciate to take time to review and have interest in our study. We added another table (supplementary TableS1) contains characteristics and clinical course of each patient as you and reviewer 3’s request.

And I’m sorry for our poor English although I ordered native speaker’s review already in Japan (http://www.japan-mc.co.jp/). We reviewed our manuscript and corrected some words.

We believe that the manuscript has been improved, largely as a result of your comments. We hope our answers are satisfactory for you.

ADDITIONAL REQUESTS/SUGGESTIONS:
- The authors could elaborate on the type of antibodies used as therapy, and add this information to Table 1. Is it just one? Does it work against the receptor, the ligand or the complex? (mode of action).

→Thank you very much for your comment. 18 of 19 patients were treated with nivolumab, one was with atezolizumab. I added it in abstract (p4, line 11), result section (p8, line 6), Table 1 and supplementary TableS1.

- The sections Patients and treatment and Clinical analyses seem not to be correctly delimited. The information regarding the patients’ medical records should probably be in Patients and treatment (with a mention to Table 1).

→Thank you very much for your point. We change it as you pointed.

Hidehito Horinouchi (Reviewer 3): Authors reported summary of clinical course of patients who was not able to continue immune checkpoint inhibitors because of adverse events. This manuscript contains important information which might be shared as practical clinical question by readers of BMC Cancer. As I understand the clinical relevance of this manuscript and would like to ask some revisions.

→We appreciate to take time to review and give us the chance of revision. We believe that the manuscript has been improved, largely as a result of your comments. We hope our answers are satisfactory for you.
Comments

1) Because the number of patients included in this analysis was small, we should be cautious to generalize the observations. It would be better to provide detailed information of each patients participated this analysis. Please consider add table which contains characteristics and clinical course of each participants. For example, the table would be informative if it contains patients' age, histology, treatment line, number of cycles he or she received immune check point inhibitors, objective response, type of adverse events and duration of progression free survival.

→Thank you very much for appropriate suggestion. I added supplementary TableS1 contains characteristics and clinical course of each patients.

2) As survival analyses, I would like to ask authors to add spider's plot information about response to immune checkpoint inhibitors.

→Thank you very much for appropriate suggestion. I added response in spider’s plot.