Author's response to reviews

Title: Consolidation Chemotherapy may Improve Survival for Patients with Locally Advanced Non-small-cell Lung Cancer Receiving Concurrent Chemoradiotherapy - Retrospective Analysis of 203 Cases

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Author's response to reviews: see over
Dear Editor,

Thank you for your review of our manuscript entitled “Consolidation Chemotherapy may Improve Survival for Patients with Locally Advanced Non-small-cell Lung Cancer Receiving Concurrent Chemoradiotherapy - Retrospective Analysis of 203 Cases” (MS: 1220672505157853). We appreciate the concerns and suggestions provided by the reviewers, and have revised our manuscript accordingly and highlighted in blue. At this time, we have re-submitted the revised manuscript for your consideration for publication in BMC Cancer. Below, please find our point-by-point responses to the comments of reviewers.

We deeply appreciate your consideration of our manuscript. If you have any queries, please don't hesitate to contact me at the address below.

Thank you and best regards.

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Responds to the reviewers’ comments:

Reviewer 1:

Major Compulsory Revisions

1. How many patients were assessed by pet scan prior to therapy? Was there a disparity between the cct and the non-cct group?

Response: Only 26.1% of patients had PET scan staging. There was no disparity between the CCT and the non-CCT group (24.8% vs. 27.8%; p=0.629). We have mentioned this in the revised article (page 9 line 3-4 and table 1).
2. Table 3 shows the overall toxicity between the groups, but it does not show the differences in toxicity between the groups after concurrent chemoradiation. Was the toxicity after concurrent chemoradiation a selection factor for CCT?

Response: Toxicities of patients for each phase (CRT and CCT) of treatment are listed in the revised Table 3, and no difference was observed in terms of toxicities between the two groups during and after concurrent chemoradiation.

The toxicity after concurrent chemoradiation was not a selection factor for CCT, though some patients didn’t receive consolidation chemotherapy due to a poor performance status.

3. The authors must account for the overall survival benefit associated with CCT despite not having differences in LRPFS or DMPFS.

Response: We agree with you and have mentioned that the overall survival benefit associated with CCT despite not having differences in LRPFS or DMPFS in the revised manuscript (page 13 line 16-18). In fact, based on our data, the median cancer specific survival (CSS) and 5-year CSS for the CCT group (28 months and 34.4%) in our study were also superior to those for the non-CCT group (17 months and 27.9%) ($p=0.022$), which was consistent with the OS results (page 10, line 5-8). Since this is a retrospective study, we mentioned that “further prospective investigations are needed to validate our results” in Conclusion (page 17 line 6-8).

4. What were the intervals used for CT scan surveillance? Did CT scan surveillance interval affect the results in #4?

Response: CT scan was repeated 1 month after CRT, then 3 months for the first year, and every 6 months for the following 2 years, and annually thereafter. The CT scan surveillance intervals are same between the CCT group and the non-CCT group. We have mentioned this in the methods section (page 6 line 18-22 and page 7 line 1).

Minor Essential Revisions

1. Although more patients in the CCT arm had a positive selection factors (younger age, female and a lighter history of smoking), the multivariate analysis was able to account for those selection factors. The authors should mention this statistical adjustment in their conclusion.

Response: Thank you for your suggestion. We had mentioned the statistical adjustment in the conclusion section (page 13 line 8-11).

2. How was local failure defined?

Response: Local recurrence was defined as primary tumor recurrence, and was determined based on a radiologic examination, histologic examination, or both. We have mentioned this in the revised article (page 7 line 1-4).
3. The y-axis on each of the graphs in figure 1 should be labeled appropriately? Only one y-axis should be labeled survival.

Response: We have revised labels of y-axis as OS, PFS, LRPFS and DMFS in figure 1 as your suggestion.

Reviewer 2:

Major Compulsory Revisions:

Methods

1. Authors fail to provide assessment criteria for treatment response (ie RECIST, etc). Please provide.

Response: Assessment criteria of RECIST version 1.1 was provided in revised Methods section (page 6 line 13-15).

Results:

1. The subgroup analysis showed that KPS was predictive for OS. Was this assessed at the beginning of treatment or at the time consolidation? This may introduce bias if only good KPS patients received CCT.

Response: KPS was assessed at the beginning of treatment, which has been clarified in the revised manuscript (ie page 3 line 18, etc).

2. What was the median time point of completion of CRT to CCT? Did a delay have an impact of OS?

Response: The median time interval between completion of CRT to CCT was 6 weeks. The median OS and 5-year OS for patients with intervals ≤6 weeks (28 months and 34.4%) are not statistically different from those with intervals >6 weeks (25 months and 24%) (p=0.281). We have mentioned this in the revised article (page 11 line 4-7).

Minor Essential Revisions: none

Discretionary Revisions:

Abstract:

1. Please define SD in results section

Response: Done (page 3, line 19).

Results:

1. Authors fail to identify consolidation chemotherapy regimens. I think this is important as no consensus exists as to which agents should be administered. This is especially true when the authors state a benefit was achieved in nonsquamous histology with no increase toxicity.

Response: We agreed with the reviewer. Thank you for your comment.
2. The authors did not include RT dose in the forest plot for OS and CCT. Was there a difference in RT dose between those getting CCT and those that did not?

Response: There was no difference in RT dose between the CCT and the non-CCT group (listed in table 1). And RT dose was added in the forest plot for OS and CCT (figure 2).