

Notice: Please give your response to the comments point-by-point as shown in the following format.

【At the END of each reply/response from you, please DO describe how you responded to the reviewer comment in the text, e.g., "we added some data(see Page xx, line xx)" or "we have modified our text as advised (see Page xx, line xx)"] .

Comment 1: *****

Reply 1: *****

Changes in the text: *****

Comment 2: *****

Reply 2: *****

Changes in the text: *****

Peer Review File

Article information: <http://dx.doi.org/10.21037/atm-20-3226>

Reviewer comments

The manuscript of Cen et al entitled “Additional chemotherapy improves survival in stage II-III pulmonary sarcomatoid carcinoma patients undergoing surgery: a propensity scoring matching analysis” reports on a large SEER dataset of PSC patients in an attempt to define the benefit of adjuvant chemotherapy in the context of this quite rare and aggressive malignancy. All in all, given the relevant question and large numbers accumulated, this manuscript is of general interest, however there are a number of issues the authors should address better:

1. While the authors tried to match the chemo and non-chemotherapy groups, however the SEER database has significant shortcomings as to allowing true matching and many confounders as to general condition/performance status etc could have been missed. This should be appropriately acknowledged in the manuscript.

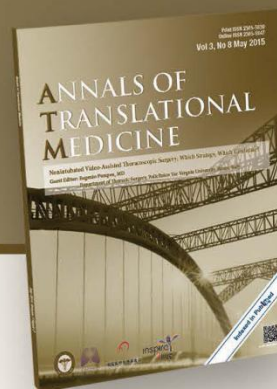
Reply 1: **Thank you very much for your suggestion. We addressed the potential weaknesses in the Discussion section.**

Changes in the text: **see Page 10, line 19-21.**

2. The abstract makes a statement as to “more beneficial to chemotherapy”- not clear what the authors meant and should be restated

Reply 2: **We modified the statement in our new manuscript.**

Changes in the text: **see Page 2, line 2-4.**



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3. Surprising that only 30% of patients received chemotherapy in a stage 2/3 context and one wonders whether patients who did not receive chemo might be overrepresented from an earlier era – if there are such differences, given better staging/supportive and general onc care etc, notable differences could be found just due to that. This should be clarified and if not done, temporal trends should be examined

Reply 3: According to our research, 38.2% and 42.7% of patients received chemotherapy at stage 2/3 respectively. Although the percentage of patients without chemotherapy in an earlier era was high, the actual number was low. The rate of patients received chemotherapy from different diagnosis era were varied, and Table 1 showed that patients without chemotherapy from a later era were even more than those from earlier one. We did not think that patients who did not receive chemo were overrepresented from an earlier era, and we clarified it and examined the temporal trends in the Discussion section.

Changes in the text: see Page 9, line 3-6.

4. Patients who received radiation were excluded- not clear why as postop radiation is given to a large number of stage 3 patients – excluding them on its own might confound study

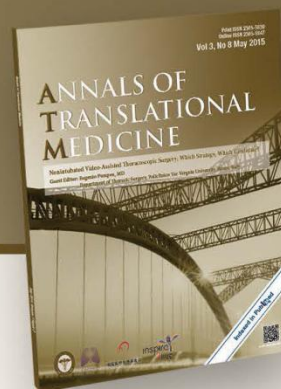
Reply 4: In non-small cell lung cancer, postoperative radiotherapy appears to improve survival significantly as an adjunct to postoperative chemotherapy in non-randomized analyses. We excluded patients receiving radiation to eliminate the confusion of neo-/adjuvant radiation.

Changes in the text: None.

5. It appears that the OS differences were not significant after the PSM analysis. If that is so, this should be more clearly stated in abstract/discussion- currently this statement is somewhat hidden in Results

Reply 5: We added a statement in abstract and modified the statement in discussion.

Changes in the text: see Page 1, line 21-23 and Page 9, line 11-13.



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6. Authors list a category of “pseudosarcomatous PSC” in Fig 6- this is not a current pathological subset- should be better defined and best omit from subset analyses as in its current form as it has no implications. Other tables

Reply 6: According to the 2004 World Health Organization Classification of Lung Tumors, 8033/3 is the morphology code of the international classification of disease for oncology for sarcomatoid carcinoma, which had five pathological subsets. To avoid confusion, we used the name, pseudosarcomatous carcinoma, in the Surveillance, Epidemiology, and End Results (SEER) database.

Changes in the text: None.

7. The discussion on the role of surgery needs to be strengthened and especially in this section, the English grammatical errors corrected.

Reply 7: We strengthened the discussion of the role of surgery and corrected the English grammatical errors.

Changes in the text: see Page 8, line3-9.

8. The figure labeling is confusing- there are 4 labels but only 2 curves- please provide clarification/improve

Reply 8: We modified our figures.

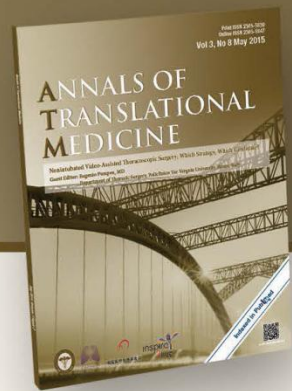
Changes in the text: see Figure 2, 3 and 4.

9. What factors were involved in the propensity score matching?

Reply 9: We modified the sentence in METHODS to express more clearly.

Changes in the text: see Page 5, line 1-2.

10. The survival curves have unusual shapes with long periods of plateaus- suggestive of no reporting for significant periods. Can authors explain this?



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Reply 10: The long periods of plateaus usually appeared in survival curves of subgroup analysis, resulting from the limited sample size. We addressed this weakness in the DISCUSSION section.

Changes in the text: see Page 10, line 21-23.

11. How come there are stage IV patients listed in the subset analysis?

Reply 11: The disease stages were manually adjusted based upon the American joint commission on cancer 8th edition tumor-node metastasis staging system by ourselves. To avoid missing cases, we included pulmonary sarcomatoid carcinoma patients at all stages in our study before disease stage adjustment. After data was consolidated and organized, we found that some patients at stage IV were surgically treated. Considering that a few patients at stage III were at stage IV after surgery in the real-world, we tried to explore the function of additional chemotherapy for these patients.

Changes in the text: None.

12. Subsets in Figure 4 subsets have very few cases- e.g. stage IIA + chemo- as low as 20- not very meaningful and these limitations should be stated

Reply 12: We stated the weakness of limited cases in some subgroup analysis.

Changes in the text: see Page 10, line 21-23.

13. In a way it seems that the overall data suggests that tumors >4cm + st II/III benefit from adjuvant chemotherapy- this indeed makes sense as it fits current adj ctx guidelines for other NSCLC- the authors should expand on it and comment how this should relate to shifting AJCC staging and treatment guidelines

Reply 13: We added the discussion that our findings were related to treatment guidelines.

Changes in the text: see Page 9, line 22-24 and Page 10, line 1-2.