Peer Review File
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Reviewer A

Question 1. Has there been an investigation into the type of platinum-based chemotherapy and the number of treatment cycle that may affect the results of survival analysis? Were vascular and/or lymphatic Invasion also considered in the propensity score (ps) as an independent prognostic factor?
Reply Q1: The types of platinum-based chemotherapy and the number of treatment cycle were based on 4 courses with vinorelbine, but left to the discretion of the attending physician. Data on completion rates were not available and were therefore included in the limitation. Vascular and/or lymphatic invasion was not used as a factor in the propensity score because it was considered to be reflected in the T and N factors.
Change in the text: We added comment in Limitation (see Page 13, line 1-3).

Question 2. The researchers did not investigate whether there are differences in OS and RFS between stage pII and stage pIII. Of course, there might be no significant difference in the effect of adjuvant platinum-based chemotherapy on the OS between the two groups, but the TNM classification in NSCLC has known to a strong prognostic factor affecting the OS. Hence, the comparative analysis of two groups separately is important.
Reply Q2: Thanks for your suggestion. We added supplement figure.
Change in the text: We added comment and figure (see Page 10, line 15-17, Supplement Figure 1).

Request 1. Because recurrence pattern and post-recurrence treatments are also the factors that may affect the OS, if data has been already collected and analyzed, please add the results of analysis to the supplement section!.
Reply R1: We added the results of analysis about recurrence pattern and post-recurrence treatments to the supplement section.
Change in the text: We added comment and figure (see Page 9, line 11-16, Page 11, line 3-8, Supplement Figure 2).

Question 3. The number of patients who have recurred since surgical resection, the number of patients who have taken EGFR TKI after recurrence, and their survival outcomes (PFS) after administration of EGFR TKI have a great influence on the OS time. Did the researchers consider these factors sufficiently to correctly interpret the results obtained from statistical analysis?
After the application of IPTW
In EGFR wild group, OS was significantly prolonged in adjuvant chemotherapy group compared to surgery alone group (HR 0.49, p=0.032)
In EGFR mutation group, there was no significant difference between adjuvant chemistry vs. surgery alone (HR 0.60, p=0.1003)
In EGFR mutation subtype, there was no significant difference of OS between Del19 and

L858R (HR 0.73), but HR>1 for uncommon EGFR mutation
In univariate analysis, HR in EGFR wild vs. EGFR mutation and Del19 vs. L858R ranged from 0.50 to 0.69, suggesting that there are some survival benefits by the adjuvant platinum-based chemotherapy.
In figure 3. The forest plot also shows that both EGFR wild and EGFR mutation groups except uncommon mutation obtained favorable survival outcome by platinum-based adjuvant chemotherapy, both before and after IPTW application.
Taken together, these results could be interpreted that the effect of adjutant platinum-based chemotherapy on the OS is relatively lower in the EGFR mutation group compared to the EGFR wild group. However, it seems to be excessive interpretation to conclude that there was no effect on the reduction of mortality rate.
Reply Q3: The reviewer was correct that it was excessive interpretation to conclude that there was no effect on the reduction of mortality rate. We have revised the text on this point.
Change in the text: We have modified our text as advised (see Page 12, line 6-10, Page 15, line 7-8).

Question 4. In order to accurately analyze the OS in patients who received adjuvant platinum-based chemotherapy after surgery, it is essential to evaluate compounding factors such as the number of patients who have recurred, the type of recurrence, the drugs administered after recurrence, the clinical outcomes of the drugs, the underlying co-morbidity, and death due to reasons not related to cancer etc. Did the researchers collect and analyze data on these clinical variables?
When the subjects in the EGFR wild group had recurred (66/99), it is estimated that cytotoxic chemotherapy have been given in most of patients, whereas in the EGFR mutation group, almost all patients (54/74) received EGFR TKI (44/54). Given that EGFR mutation-positive NSCLCs exhibit a high response rate to EGFR TKI with significantly prolonged progression-free survival, it would be reasonable to assume that EGFR TKI after recurrence has a significant impact on the OS time in the EGFR mutation group receiving postoperative platinum-based chemotherapy.
In addition, in the KM survival curve of RFS in figure 2, there was no significant difference between EGFR wild and EGFR mutation group. While, in the OS of KM survival curve, the EGFR mutation group maintains a clear survival advantage until about 4 years after surgery, but suddenly drops and crosses the survival curve of the EGFR wild group. It is believed that many patients with EGFR mutation eventually died of treatment failure while undergoing EGFR TKI and/or other chemotherapy after relapse, which supports the aforementioned assumption.
In addition, the interpretation of HR> 1 for the OS in the uncommon mutation group is too small to conclude. The researchers described that 'adjuvant platinum-based chemotherapy after surgery rather worsened the OS in the target population'. Since the response to EGFR TKIs in the patients with EGFR uncommon mutation is known to be relatively lower with shorter PFS than those of common EGFR mutation, it would be more appropriate to explain that it may be main cause that they had poor sensitivity to both postoperative platinum-based chemotherapy and EGFR TKIs used after recurrence.
Reply Q4: The reviewer is correct that the impact of platinum-based adjuvant chemotherapy

on OS is relatively lower in the EGFR mutation group than in the EGFR wild group. I have modified our text as advise. We have modified description of uncommon mutations.

Change in the text:

We have modified our text as advised (see Page 12, line 6-10, Page 12, line 16-17, Page 15, line 7-8).

Discussion

Request 2.

Please, transfer the statistical variables and numerical value described in the discussion to the result section as much as possible and describe them in detail!

Reply R2: We have corrected it as you pointed out.

Change in the text: We have deleted the statistical variables and numerical value in the discussion. We already described the statistical variables and numerical value in the results.

Request 3.

-page 8- Comparison with similar research

The researchers list all similar results of past clinical studies. Please, summarize them more concisely! Please, explain why several clinical studies showed conflicting results in the author's point of view! And, add that any differences existed when compared to this study! (e.g. clinical characteristics of the subject including TNM stage, type of adjuvant chemotherapy, cycles of the administration, etc.)

Reply R3: We have corrected it as you pointed out.

Change in the text: We have modified our text as advised (see Page 13, line 11-Pge 14, line 3).

Reviewer B

Thank you for your submission. I am not entirely sure how you derived to the conclusion based on the results.

Reply: In this study, wild-type EGFR showed an improvement in overall survival with platinum-based adjuvant chemotherapy in inverse probability of treatment weighting analysis, whereas those with EGFR mutations showed no significant difference in overall survival between the surgery-only group and the adjuvant group. We believed these results suggest that platinum-based adjuvant chemotherapy may be less effective in EGFR-mutant lung adenocarcinoma, regardless of the type of mutation.