Peer Review File
Article information: https://dx.doi.org/10.21037/jtd-22-704

Reviewer A

Abstract:
Comment 1: • Results need to state that the majority of patients (please give exact proportion and number of preoperative treatment lines) received 1L chemo followed by 2L ICI.
Reply 1: We have modified the abstract according to the reviewer's suggestion.
Changes made 1: line 117 "Eighteen patients (86%) progressed after first line chemotherapy and received second line ICI."

Comment 2: • Results need to state the delay in surgery from primary diagnosis (median 22 months, CI?). Please add values given in L280 to the abstract.
Reply 2: We've added the values given in L280 to the abstract.
Changes made 2: line 118 "The median time between diagnosis and surgery was 22 months (IQR 18-35)."

Comment 3: • Conclusion: The speculation that the late timing of surgery may contribute to complications needs to be mentioned
Reply 3: We added the sentence as suggested by the reviewer.
Changes made 3: Line 132 and 431 "The late timing of surgery may also contribute to complications".

Main text:
Comment 4: • L 263: Please give percentage.
Reply 4: The percentage was given.
Changes made 4: line 266 "The study group included 21 patients (0.43%) among 4862 patients who had surgery for major lung resection. No patients who were judged able to have the surgical resection refused it."

Comment 5: • L 267f: IVA: all M1b (oligometastatic? Were patients with pleural effusions or contralateral pulmonary metastases included? IVB: which and how many metastatic sites? (Table 1)
Reply 5: There was no patients with pleural effusions nor contralateral pulmonary metastases included. Concerning patients with stage IVB during initial staging, one patient had two other lung nodules in the same lung but not in the same lobe (this patient had a pneumonectomy), one patient had two bone metastases, one patient had two liver metastases and one patient had two brain metastases.
Changes made 5: no changes were made accordingly.

Comment 6: • L280 answers the following question: Although nonsignificant, please discuss that there was a non-significant trend towards longer delay in surgery in patients with complications.
Reply 6: We've added a phrase in the discussion to discuss the impact of longer delay surgery.
Changes made 6: line 365 "There was a non-significant trend towards longer delay in surgery in patients with complications."

Comment 7: • L314: Were there any pathological complete responses? The answer seems to be in Table 2 (pCR 33.4%?) and should be given in the text.
Reply 7: The reviewer is correct about the pathological complete response. We have given the response in the text.
Changes made 7: line 318 "…and complete pathological response was found in 7 patients (33.4%)".

Comment 8: • LL327f: please mention Nivo an pembro first because they are much more commonly used in this situation in general and in your cohort in particular.
Reply 8: We have mentioned Nivo and pembro first as suggested by the reviewer.
Changes made 8: line 331 ". ICIs against anti-programmed death 1 (PD-1) like nivolumab and pembrolizumab, and against anti-programmed death-ligand 1 (PD-L1), like durvalumab or atezolizumab,..."

Comment 9: • Discussion: please compare surgical complication rates in your population with that in other trials including the prospective trials with early resection (NADIM II (ASCO 2022), Checkmat 816) and discuss with respect to timing of surgery.
Reply 9: we have compared surgical complication rates with that of NADIM II and checkmate 816.
Changes made 9: line 372 "Severe adverse events (grade 3 or higher) in our study was lower compared to recent comparative randomized trials with resectable non-small cell lung cancer. In stage IB to IIIA patients, 83.2% of patients in the nivolumab-plus-chemotherapy group compared to 75.4% in the chemotherapy group alone underwent definite surgery with grade 3-4 adverse events being respectively 33.5% and 36.9% (23). In the Nadim II study which include patients in stage IIIA, definite surgery occurred in 91% patients who received nivolumab and chemotherapy in adjuvant setting compared to 69% patients with neoadjuvant chemotherapy with a moderate increase in grade 3-4 adverse events (24% vs 10%) respectively (24)."

Comment 10: • In the discussion, the low rate of pneumonectomy should be mentioned since this supports the neoadjuvant ICI approach.
Reply 10: we mention as suggested by the reviewer the low rate of pneumonectomy in the neoadjuvant context.
Changes made 10: line 391 "the low rate of pneumonectomy supports the neoadjuvant

ICI approach".

Comment 11• Conclusions: It should be suggested that resection should be performed as early in the course of the disease as possible and that the timing of resection needs further evaluation.
Reply 11: We agree with the reviewer that resection should be performed as early in the course of the disease as possible and that the timing of resection needs further evaluation.
Changes made 11: line 432 "Resection should be performed as early in the course of the disease as possible and the timing of resection needs further evaluation".

Figures:
Comment 12: • L443: in the context of resection, commonly "Event-free survival" rather than "recurrence free survival" is reported. Please check and change accordingly.
Reply 12: we have changed "recurrence-free survival" to "event-free survival" in the figure and in the text.
Changes made 12: we have made the change in line 324, line 456 and in figure 2.

Comment 13: • L454: it needs to be stated at some point (possibly here) that the use of durvalumab in this setting occurred "off label". I gather that it will be difficult to find out retrospectively why durvalumab was chosen?
Reply 13: we have stated in the methods section.
Changes made 13: line 193 "Decision to initiate systemic treatment was based on advanced unresectable clinical stage IIIB to IVB disease, with treatment protocols varying according to the oncologic center as well as the use of Durvalumab "off label"."

Tables:
Comment 14: • Table 2: p-staging refers to "operative or "pathological" staging, not "post-operative staging" Please change.
Reply 14: We have changed to "pathological staging" instead of "post-operative staging".
Changes made 14: we made the modification on table 2.

Reviewer B

Comment 15: The authors mentioned adding a new table3. However, there is only an old table3. Please show a new table3.
Reply 15: We apologize for the mistake. The new table 3 is intitled "Odd ratio of clinicopathological characteristics on post-operative complication".
Changes made 15: We added the new table 3.