Peer Review File

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Reviewer A

Line 73: Do you diagnose #4 lympho node as discreate N2 or infiltrative N2? (Ramnath N et al. Chest e314s-e340S 2013)
Reply: We diagnosed #4 lympho node as discrete N2, not infiltrative N2. (see Page 5, line 85).

Line 86: If #4R is infiltrative N2, I think this treatment strategy is salvage surgery or conversion surgery, not neoadjuvant therapy.
Reply: We diagnosed #4 lympho node as discreate N2.

Line 88: What does one cycle mean? 28days? I don't think it's a general expression. Please describe your one cycle mean.
Reply: We added the meaning of one cycle as advised (see Page 5, line 102). Thank you for your comment.
Changes in the text: Page 5, line 102

Line 95: "after 45 days alectinib therapy" mean initial day? or end day?
Reply: "after 45 days alectinib therapy" mean the day after the initial day, which means the patient accepted 45 days alectinib therapy, then right upper lobectomy with mediastinal lymph node dissection were performed.
Changes in the text: Page 6, line 109

Line 96: Is adhesion means invasion? or affect of alectinib?
Reply: It is uncertain which one mainly affect the adhesion, but we preferred the side effect of alectinib therapy (discussed in Page 9, line 171-174). And moderate tissue adhesion also occurred in the similar study as we attached. But the relationship of adhesion and targeted therapy has not been determined yet. It is essential to study the potential relationship between adhesion and targeted therapy.

Line 102: What mean MDT?
Reply: MDT means multi-disciplinary team consultation. we have modified our text as advised (see Page 6, line 117). Thank you for your correction.
Changes in the text: Page 6, line 117

Line 106: I think the combination of radiation and TKI is dangerous. Did you need radiation? Please describe in discussion.
Reply: As we said in the text, the patient received sequential radiotherapy (RT) after

the operation because without systematic mediastinal lymph node dissection (station 4R excluded) and major pathologic response (MPR) status was not met. So after multi-disciplinary team consultation by the department of respiratory, thoracic surgery, radiotherapy, pathology and radiology, we think the combination of radiation and TKI may achieved better local control and reduced the risk of distant metastasis. Moreover, the radiation field only contain the areas of the removed tumor and 4R lymph nodes. The patient didn't have any treatment-related adverse reactions. So the combination of radiation and TKI is safe and necessary. (Page 6, line 116-122; Page 9, line 175-191)

There is a similar previous study as attached. If you can afford it, please describe it.
Reply: We described the similar study in our paper. Thank you for your comment.
Changes in the text: Page 9, line 184-191

Reviewer B

The article present a dilemma in routine clinical work how to relate to the rapidly incoming new data rapidly changing guidelines. The case contributes to our knowledge of using perioperative Alectinib.

Questions/comments

1. Line 52 – please rephrase the sentence as it is incomprehensible/unclear
Reply 1: Sorry, the sentence was partially deleted by mistake during our revision. We have modified it. Thank you for your correction.
Changes in the text: Page 3, line 54-56

2. Introduction: maybe you can take a little other focus in introduction and mention that you have been inspired by the recently published reports showing feasibility and efficacy of Alectinib in the neoadjuvant setting and present the clinical dilemma.
Reply 2: Thank you for your comment. We added some words to describe feasibility and efficacy of Alectinib in the neoadjuvant setting (see Page4, line 65-71). Moreover, the studies about neoadjuvant alectinb is rare.
Changes in the text: Page 4, line 65-71

3. Line 59 – delete "have been" to make the sentence: "Owing to these improvements demonstrated in…"
Reply 3: we have modified our text as advised (see Page 4, line 72). Thank you for your correction.
Changes in the text: Page 4, line 72

4. Line 81- please provide the percent of rearranged cells in FISH.
Reply 4: We added the percent of rearranged cells in FISH as advised (see Page 5,

line 94). Thank you for your comment.
Changes in the text: Page 5, line 94

5. Line 84 – you may underline that surgery is not a standard in stage III/N2, and that in these patients with genomic defined NSCLC, a currently investigated option is the use of TKI in neoadjuvant setting.
Reply 5: We added the sentences as advised (see Page 5, line 96-98). Thank you for your comment.
Changes in the text: Page 5, line 96-98

6. Line 88 – can you provide the percent of shrinkage of the tumor as it is appeals better to the readers, thank you.
Reply 6: We provide the percent of shrinkage of the tumor as advised (see Page 5, line 102). Thank you for your comment.
Changes in the text: Page 5, line 102

7. Line 98 – please specify pathologic evaluation: only tumor, any other lymph nodes (N1?)
Reply 7: The pathologic evaluation was about only tumor (see Page 6, line 112). Thank you for your comment.
Changes in the text: Page 6, line 112

8. Line 105 – please specify what did the radiation field contain: the area of the removed tumor or N2 only?
Reply 7: The radiation field contain the area of the removed tumor and 4R lymph nodes (see Page 6, line 121-122). Thank you for your comment.
Changes in the text: Page 6, line 121-122

9.Line 130 – rephrase and point the percent of viable tumor cells, e.g. However, in the case published by Zhang et al., the patient completed two cycles of Alectinib achieving MPR with only 7% of residual viable tumor cells.
Reply 9: we have modified our text as advised (see Page 7, line 147). Thank you again for your comment.
Changes in the text: Page 7, line 147

10.Line 136 and on: mostly good discussion but please rephrase the final part from line 171. Your case is not only about to await the data from adjuvant trail as your patient was treated in neoadjuvant setting, but also data addressed using TKIs in the locally advanced NSCLC patients with druggable targets.
Reply 10: We rephrased the final part as advised (see Page 9-10, line 192-199). Thank you again for your comment.
Changes in the text: Page 10, line 193-201

Minor remarks

Please read rigorously the entire manuscript since there are many sentences requiring corrections:
Some of them are e.g.;
line 23 – remove double space between “who” and “received”
line 25 – remove double space between “was” and “achieved”
line 28 – remove double space between “Alectinib” and “and”
line 29 – please rephrase the sentence: “.. given because of excluded station 4R dissection”. Do you mean because of verified spread to station 4R?
line 33 – remove double space between “in” and “advanced”
Line 34 -remove double space between “in” and “accordance”
line 42 – remove double space between “or” and “who”
line 43 – set the space between “adenocarcinomas” and “(1)”
line 44 – remove double space between “been” and “considered”
Line 44 - set the space between “issues” and “(2)”

Reply: we have modified our text as advised. Thank you very much for your correction.