

## Peer Review File

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### Responses to the Comments by Reviewer A:

Thank you very much for your excellent suggestion.

Comment 1: Certainly, the Clinical case it is interesting however be careful, what is the definition of curability? Long-term recurrences after 10 or more years can occur almost always in patients that have already relapsed.

Reply 1: Complete response to gefitinib has been ongoing for more than 10 years, and no recurrence has been observed for about 5 years since terminating gefitinib, so we think gefitinib treatment has apparently cured her recurrent NSCLC.

Comment 2: What means "Class V adenocarcinoma"?

Reply 2: Papanicolaou classification is used for the interpretation of cytologic findings in Japan, and the class V means cytology conclusive for malignancy. We're sorry for we didn't know that Papanicolaou classification is not internationally used. We deleted the words "class V" from the text.

Changes in the text: We deleted the words "class V" from the text (Page 4, Lines 54).

Comment 3: Please provide information on NGS. Was it possible to examine co-mutations? Is there paired tissue from the tumor resection and from the recurrence?

Reply 3: We're sorry that we didn't use NGS for this case. Since gefitinib had a sufficient effectiveness, it seemed that further investigation was unnecessary from a clinical standpoint.

Comment 4: Was the tumor TTF1 positive?

Reply 4: Since the tumor was clearly an adenocarcinoma, immunohistochemical staining for TTF-1 was not performed.

Comment 5: Please provide imaging information, CTs.

Reply 5: We add CT images.

Changes in the text: We changed the sentence to "The right supraclavicular nodes are observed 15mm in size, and no other sites of recurrence were observed in CT (Figure 1A)." (Page 4, Lines 55-56), and added the word "(Figure 1B)" (Page 4, Lines 59). We added Figure Legends. (Page 7, Lines 111-114)

Comment 6: There were liquid biopsies?

Reply 6: We're sorry that we didn't use liquid biopsy for the same reason as Reply 3.

### Responses to the Comments by Reviewer B:

Thank you for your recommendation.

This is an interesting manuscript and addressed a long-term disease free status after initiating gefitinib. This manuscript is well written. The novelty of this case, however, is limited. I have some comments and listed as below.

Comment 1. Is EGFR mutation done for right supraclavicular lymph node recurrence?

Reply 1: We didn't check EGFR mutation for right supraclavicular lymph node. Since it was considered to be metastasis, we thought it would be sufficient to confirm EGFR mutation of the primary tumor.

Comment 2. Was there any additional treatment for right supraclavicular nodes including radiotherapy or surgical therapy?

Reply 2: No treatment except for gefitinib has been administered.

Comment 3. Was PET performed in this case?

Reply 3: PET was performed in 2014. We will add the findings to the text.

Changes in the text: We added the sentence "Positron emission tomography-CT showed no recurrence in June 2014." (Page 4, Lines 62-63)

Comment 4. Five-year is usually used for defining "cure" in post-surgery patients.

Reply 4: Complete response to gefitinib has been ongoing for more than 10 years, and no recurrence has been observed for about 5 years since terminating gefitinib, so we think gefitinib treatment has apparently cured her recurrent NSCLC.

### **Responses to the Comments by Reviewer C:**

Thank you very much for your helpful comments.

An interesting case of pulmonary adenocarcinoma was presented, which was completely cured by gefitinib.

Comment 1. Are CT scans that document the response to treatment available?

Reply 1: We add CT images.

Changes in the text: We changed the sentence to "The right supraclavicular nodes are observed 15mm in size, and no other sites of recurrence were observed in CT (Figure 1A)." (Page 4, Lines 55-56), and added the word "(Figure 1B)" (Page 4, Lines 59). We added Figure Legends. (Page 7, Lines 111-114)

Comment 2. Was PET-CT performed in the patient to confirm CR?

Reply 2: PET was performed in 2014. We will add the findings to the text.

Changes in the text: We added the sentence "Positron emission tomography-CT showed no recurrence in June 2014." (Page 4, Lines 62-63)

Comment 3. What was the safety of the treatment?

Reply 3: Adverse event of gefitinib was only seborrheic dermatitis and this symptom improved with a reduction of gefitinib.

### **Responses to the Comments by Reviewer D:**

Thank you very much for your invaluable comments.

The peculiarity of this case is that the patient survived without recurrence until 4 years after the end of EGFR-TKI.

The author suggested that the reason why long-term survival is a small disease burden.  
Comment 1. At the time of relapse, please describe whether you examined to check the metastasis status of extrathoracic organs.

Reply 1: We performed CT, and no other sites of recurrence were observed (Page 4, Lines 55).

Comment 2. If there is no metastasis to other organs and LN local recurrence, local treatment rather than systemic chemotherapy may be considered. What are your opinions?

Reply 2: Local treatment was also considered. However, this is the second recurrence for this patient and we thought that systemic chemotherapy should be used to treat the invisible metastasis.

Comment 3. Treatment duration after CR was very long in this case. Would you please describe any research on whether that treatment period has any meaning or if it is better to maintain the drug for how long after CR?

Reply 3: We're sorry that we can't find any research indicating how long treatment should be continued after CR. Instead, there is a case report showing relapse after almost 7 years of complete response to erlotinib (10.2147/OTT.S131756). Even after CR, it may be preferable to continue treatment as long as possible.