

Response:

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Review report on manuscript World Journal of Clinical Cases 61429 entitled "Triple osimertinib administrations followed by chemotherapy of advanced lung adenocarcinoma patient with acquired resistance improved patient survival: A case report" This study is to report the efficacy of multi-use of osimertinib after resistance acquired for patients with metastatic lung adenocarcinoma. My comments and suggestions are as below.

Please note the detail sample in which the 2nd and the 3rd ctDNA analysis was performed. 'The patient refused the third gene detection' sentence of the last line of page 4, 'the third gene detection' is considered to be a count of errors.

Answer: Thank you for your comments and suggestions. The problems you pointed out have been changed on page 6,7 "Treatment".

Please reveal the changes of CA19-9 level in the figure 3.

Answer: Thank you for your suggestions. CA199 had fewer detections in this patient, and its value fluctuates greatly. It is not appropriate to make a flow figure together with CEA. So it is not added in the figure 3 finally.

Please mark the references correctly in each sentence of the discussion which mentioned on the previous studies.

Answer: References have been revised according to your requirements.

Please correct misspellings throughout the manuscript and the wrong unit. Ex) u/mL, effectsis, and CEA(ug/ml).

Answer: Thank you for your comments and suggestions. The problems you pointed out have been changed on page 5 "Laboratory examinations".

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The original findings of this manuscript is the first report of re-challenge and tri-challenge of osimertinib successfully applied through multiple re-sensitization chemotherapy on an NSCLC patient. It is a new phenomena that were found through experiments in this study. All the ctDNA results confirmed the treatment in this study. The quality and importance of this manuscript is quite good. The conclusions do appropriately summarize the data that this study provided and they offer a useful reference for retreatment with osimertinib. Although the manuscript had offered the certification of Language Editing, there are still typos there, such as "disappered" and "slightly".

I suggested the authors could pay more attention to the English writing.

Answer: Thank you for your comments. The wrong writing mistakes have been

corrected. The revised version has been edited carefully by **MedE Editing Service** to minimize grammar and spelling mistakes.

Another minor revision is there are several times in the process using ctDNA sequencing without any details about the detection. The author should describe they had used the right detection method to monitor the genomics status of the patient. In brief, this study could impact clinical practice based on precise genetic testing.

Answer: Thank you for your comments and suggestions. The problems you pointed out have been revised on page 6,7 “Treatment”..

1. Science editor:

(1) The “Author Contributions” section is missing. Please provide the author contributions;

Answer: The “Author Contributions” section has been accomplished and can be found on page 1.

(2) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

Answer: The approved grant application certificate are provided in attachment.

(3) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Answer: Thank you for your suggestions. All figures using PowerPoint are provided in attachment.

(4) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

Answer: Thank you for your suggestions. PMID and DOI numbers has been supplemented in the reference list.

(5) The reference’s number should be put in the square bracket.

Answer: Thank you for your suggestions. The reference’s number has been put in the square bracket.

2. Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office’s comments and the Criteria for Manuscript Revision by Authors. The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words). Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company.

Answer: Thank you for your comments. The title of the manuscript has been shortened. And the wrong spelling mistakes have been corrected. The revised version has been edited carefully by **MedE Editing Service** to minimize grammar and spelling mistakes. The English Language Certificate is provided in attachment.