

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 70701

Title: Effective response to crizotinib of concurrent KIF5B-MET and MET-CD - rearranged non-small cell lung cancer: A case report

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03072151

Position: Editorial Board

Academic degree: MD, MSc

Professional title: Associate Professor, Attending Doctor, Surgeon

Reviewer's Country/Territory: Taiwan

Author's Country/Territory: China

Manuscript submission date: 2021-08-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-01 09:02

Reviewer performed review: 2021-09-05 15:58

Review time: 4 Days and 6 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

**Peer-reviewer
statements**

Peer-Review: [☒] Anonymous [☐] Onymous

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

I am honored to review the manuscript entitled “Effective response to crizotinib of concurrent KIF5B-MET and MET-CDR2-rearranged non-small cell lung cancer: a case report”. The study presents with good quality and deals with an important clinical issue.

I have the following remarks for the authors to address in their subsequent revision. □

As stated by the authors in the introduction section, several cases and clinical studies have already been reported regarding the efficacy of crizotinib in targeting MET amplification, exon 14 skipping and certain rearrangements in NSCLC patients. I would like to see a review of all reported cases that discuss on the same problem. An additional table with citing references would be appreciated to support that this is an unique rare case worth to be presented and published to raise the awareness of the clinician. □

Please expand all abbreviations in the abstract section. □ Wordings need to be corrected:

Introduction: “The mesenchymal-epithelial transition factor gene (MET),” should be changed to “The mesenchymal-epithelial transition (MET) gene,” □ The expansion of

RECIST is not properly demonstrated in the outcome and follow-up section. Besides, the authors stated that “However, the disease progressed afterwards in May, 2019 as per RECIST 1.1.” A more detailed description of how the disease progressed afterwards is

recommended, as this finally leads to mortality of the case. □ Please add a section in

discussion section describing the potential side effects of crizotinib. □ Please modify

figure 2 by inserting arrows to point the tumor mass in both panels. An additional panel

indicating the disease progression after May, 2019 is suggested if available for

comparison.

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Peer-review model: Single blind

Reviewer's code: 03252941

Position: Editorial Board

Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-06 23:21

Reviewer performed review: 2021-09-07 09:25

Review time: 10 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

**Peer-reviewer
statements**

Peer-Review: [☒] Anonymous [☐] Onymous

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

Liu et al. reported a young female patient, who was a non-smoker, with NSCLC that harbored concurrent KIF5B-MET and MET-CDR2 fusions. She once responded well to crizotinib.

The authors first reported MET-CDR2 fusion and effect of crizotinib to concurrent MET fusions. They also suggested the importance of comprehensive genetic profiling in lung cancers in which no known driver genes were mutated. Accordingly, this report will be very beneficial to audiences who are engaged in the clinical practice of lung cancer. I raise some minor points to be considered below.

1. (p.6, ll.1-4) Imaging examinations: There is no description of primary lung cancer.
2. (p.6, ll.5-10) Immunohistochemistry ... poorly differentiated NSCLC: This description should be made in more detail. What were the results of immunostaining of TTF-1, napsin A, CK5/6, p40? Although it is later described that histopathologic markers TTF-1, CK7, p40, and CDX2 were negative in p.8, l.7, these results only suggest that this tumor may not be adenocarcinoma derived from terminal respiratory unit, squamous cell carcinoma, invasive mucinous adenocarcinoma, and metastatic adenocarcinoma from the intestine. Evidence of poorly differentiated adenocarcinoma as they say is not sufficient. I suspect that this tumor may be putative large cell carcinoma, putative carcinosarcoma, and also may be neuroendocrine cell carcinoma. I hope the authors to present more information about the pathologic diagnosis and also representative histopathologic figure of the tumor.
3. (p.8, ll.20-21) This is similar with the previous studies that ...: Reference should be cited.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05088799

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: China

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
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SPECIFIC COMMENTS TO AUTHORS

The authors described a case report of the effect of crizotinib on a patient with poorly differentiated NSCLC with concurrent MET fusions, KIF5B-MET and MET-CDR2. The case was well described for the tracking of the treatment processes. The manuscript could be enhanced with some refinement. - At 'Author contributions', there is a name 'Chang J' who was not included in the author list. Is it a simple mistake? - Can authors provide the reason why nivolumab was not selected as a second line treatment? - page 3: 'poorly-differentiated' -> Because all other parts of the manuscript did not use a hyphen, it would be better to change it 'poorly differentiated' for consistency. - page 7: 'Response Evaluation Criteria in Solid Tumors v.1.1' -> Because the authors used 'RECIST 1.1' three rows below, it would be better to change the sentence as 'Response Evaluation Criteria in Solid Tumors v.1.1 (RECIST 1.1)' - page 8: 'This is similar with the previous studies that ICIs are less effective in NSCLC with EGFR mutation or EML4-ALK fusion.' -> References should be provided.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Peer-review model: Single blind

Reviewer's code: 03252941

Position: Editorial Board

Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors responded to my previous comments to some extent. They say that they cannot receive a full reply from their pathologists. After understanding the situation, I want to point out some issues. 1. AE1/AE3 (+) ... S-100 (-) (p.6, ll.3-4): Results of neuroendocrine markers, such as chromogranin, synaptophysin, and CD56, should be presented to exclude the possibility of neuroendocrine carcinoma/small cell carcinoma. By the way, CK18 (+) is described twice. Other minor points. 2. chromatography (p.3, l.15): This may be "tomography." 3. even received (p.3, l.17): despite receiving 4. Table 1: References of text and Table 1 should be unified. 5. Figure 2A is not referred to in the text. 6. Base the (p.6, l.14): Based on the Additional comment: If histological figures get available, please show them.

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Academic degree: MD

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Reviewer's Country/Territory: South Korea

Author's Country/Territory: China

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Review time: 1 Day and 17 Hours

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statements

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

All raised concerns are resolved. I have no further question.

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Author's Country/Territory: China

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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Thank you for providing a revised copy. The revised manuscript has been significantly improved worth to be published.