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Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Successful Treatment with Osimertinib in a Patient with Thr790Met-positive Non-Small-Cell Lung Cancer and Leptomeningeal Carcinomatosis Resistant to Gefitinib: A Case Report" (ID:74665). Those comments are valuable and very helpful for revising and improving our paper. We have studied the comments carefully and this manuscript has been revised. Revised portion are marked in **the revision model** in tracked revised manuscript. The responses to the reviewers' comments are as following. **Page number and line number are subject to the tracked version.** Because the manuscript file is generated automatically, there are some garbled words at the beginning and end of some paragraphs. We don't know how to remove them. In case, We upload the tracked version to the supplementary file

In addition, the first author, Liqing Xu (xlq17@outlook.com or xuliqingpku@163.com), did not receive the email about Notification on Copyright License Agreement. While, our other co-authors, Shenli Shen, Yingjin Wang, Yao Wu, Hongzhou Duan, has already accepted and signed the Copyright License Agreement. We have sent the email to [l.s.ma@baishideng.com](mailto:l.s.ma@baishideng.com) and [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com) about this problem. Could you please check and send



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## **PEER-REVIEW REPORT**

**Name of journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 74665

**Title:** Successful Treatment with Osimertinib in a Patient with Thr790Met-positive Non-Small-Cell Lung Cancer and Leptomeningeal Carcinomatosis Resistant to Gefitinib: A Case Report

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 00503561

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-02-11

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-02-25 01:31

**Reviewer performed review:** 2022-02-25 02:08

**Review time:** 1 Hour

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

## SPECIFIC COMMENTS TO AUTHORS

This is an important case report and the point would be that early detection of T760M in CSF by ctDNA NGS. The title could contain this portion.

**Response:** Thank you for your comments. The early detection of T790M in CSF by ctDNA NGS is really a core tip in this case report. We have added this portion in the title.

Changes in the text: We have added this portion- Early Detection of Thr790Met in CSF ctDNA by Next-generation Sequencing- in the title. (Page 1, Line 1-2)

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 74665

**Title:** Successful Treatment with Osimertinib in a Patient with Thr790Met-positive Non-Small-Cell Lung Cancer and Leptomeningeal Carcinomatosis Resistant to Gefitinib: A Case Report

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05478444

**Position:** Peer Reviewer

**Academic degree:** BSc, MSc, PhD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** Saudi Arabia

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-02-11

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-05-05 15:25

**Reviewer performed review:** 2022-05-09 05:59

**Review time:** 3 Days and 14 Hours

<b>Scientific quality</b>	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<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

<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

The following case report, entitled: Successful Treatment with Osimertinib in a Patient with Thr790Met-positive Non-Small-Cell Lung Cancer and Leptomeningeal Carcinomatosis Resistant to Gefitinib: A Case Report, presents important and interesting case study. Yet the following points should be addressed before further steps:

**Response:** Thank you for your detailed revision comments. They are really valuable for improving our manuscript. We have revised our paper point by point according to your comments.

Abstract: -Line 33: add LM after (Leptomeningeal).

Changes in the text: We have added the item -(LM)- after (Leptomeningeal). (Page 2, Line 35)

-Line 38: Mention name of the hospital

Changes in the text: We added the name of the hospital (Page 2, Line 40).

-Line 40: amend: EGFR mutation was detected by the genomic examination

Changes in the text: We have amended the preposition. (Page 2, Line 42).

-Line 48-49: resulting in a good response, add: (within ...months).

Changes in the text: We have added the time (Page 3, Line 53-54).

-Line 51: as the study proved the effect of Osimertinib in one patient, so amend: (patient) not (patients).

Changes in the text: We have amended plural to singular. (Page 3, Line 146-147).

-Line 51: amend (great clinical benefit) to more specific word, example showing the % of remission.

Changes in the text: We have added the variation frequency. (Page 3, Line 48-49).

Informed consent statement: Number or date of the Informed consent statement should be mentioned.

Changes in the text: We have added the date. (Page 2, Line 21-22).

Keywords: -Line 59-60: I am suggesting the following sequence: non-small cell lung cancer, EGFR mutation, circulating tumor DNA detection, leptomeningeal carcinomatosis, Osimertinib

Changes in the text: We have amended the sequence. (Page 3, Line 64-65).

Abbreviations: -It is important to be consistent when using abbreviations. Every time, first mention the full word then keep mentioning the abbreviation. -Add: Leptomeningeal: LM

Changes in the text: We have added the abbreviation and the following contents have also been modified accordingly. (Page 4, Line 81, 90, 92; Page 5, Line 104; Page 7, Line 148; Page 8, Line 168, 173).

-Line 93: (targeted oncogenes) should be amended to (target oncogenes).



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Changes in the text: We have amended (targeted oncogenes) to (target oncogenes). (Page 5, Line 105).

-Line 100: amend to: (meningeal carcinomatosis, which is resistant to gefitinib).

Changes in the text: We have changed into an attributive clause. (Page 5, Line 111).

-Line 144: specify for how long Osimertinib was used?

Changes in the text: We have added the time. (Page 7, Line 157).

-Line 167: amend: and could thus be more helpful for.

Changes in the text: We have added to (more). (Page 8, Line 185).

-Line 169: re-write this sentence: Moreover, this report is characteristic of lung cancer.

Changes in the text: We have amended that sentence. (Page 8, Line 187-188).

-Line 184: change benefits to (results).

Changes in the text: We have changed (benefits) to (results). (Page 9, Line 206).

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 74665

**Title:** Successful Treatment with Osimertinib in a Patient with Thr790Met-positive Non-Small-Cell Lung Cancer and Leptomeningeal Carcinomatosis Resistant to Gefitinib: 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:** 2022-02-11

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-05-11 23:44

**Reviewer performed review:** 2022-05-19 02:08

**Review time:** 7 Days and 2 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input checked="" type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection



<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

The current case report summarized the Successful Treatment with Osimertinib in a Patient with Thr790Met-positive Non-Small-Cell Lung Cancer and Leptomeningeal Carcinomatosis. I regret to give further positive comments due to the below reasons.

**Response:** Thank you for your comments. We have revised and explained your comments.

The signed consent provided is statement to agree for surgery, not for publication of the patient's material. Moreover, Institutional. Review Board statement is missing.

Response: We have uploaded the signed consent for publication of the patient's material. For the review board statement, 本例 case 免伦理 because the report does not involve clinical trials and new drugs.

The core information adds little value to the literature.

Response: We report a patient with EGFR Thr790Met-mutant NSCLC with meningeal carcinomatosis and resistance to gefitinib. From this case, we propose that the positive findings of CSF circulating tumor DNA as a liquid biopsy technology based on the detection of cancer-associated gene mutations may appear earlier than the imaging and CSF findings. Such an early finding may thus be helpful for therapy. We believe that this report can provide the experience of diagnosis and treatment for patients with meningeal metastasis of lung cancer.

The dosage of Osimertinib applied to the patient was not well explained.

Response: The dosage is mentioned in the article in page 7, line 160.

The follow-up period was too short.

Response: Thank you for your suggestions. The prognosis of patients with leptomeningeal metastasis of lung cancer is not good. In the current follow-up period, the patient's situation has improved. We consider that the patient could benefit from CSF-NGS and Osimertinib treatment. Of course, we will continue to follow up.

The effectiveness and safety of Osimertinib is not elucidated and compared with other potential medications.

Response: The patient in the report was suffered from lung cancer who failed to improve from gefitinib treatment. After the CSF ctDNA NGS showed leptomeningeal metastasis, we switched the patients to osimertinib according to previous literature evidence, and achieved good clinical results. This article is not a clinical trial or case-control study and cannot be compared with other treatment schemes.