

Peer Review File

Article information: <https://dx.doi.org/10.21037/pcm-21-24>

Review Comments

Reviewer A

Thank you for the opportunity to review the manuscript titled "Ineffective target therapy in non small cell lung cancer harboring BRAF G446R mutation: A case report and biological rationale".

This case report will provide additional information on the lack thereof benefit of BRAF and MEK inhibition in patients with a non-V660E BRAF mutation. The clinical data and the biological explanation for the absence of response were great. But the case report was full of grammatical and typographical errors and many sentences are redundant and peculiar. Editorial review by a native English writer/editor will benefit this case report immensely.

Response: English review was provided.

Reviewer B

This is a case report with no treatment efficacy of TKI Dabrafenib and Trametinib. 1. In the abstract, the authors need to clearly indicate the clinical significance and the unique contribution of this case report. There are too many reasons for no benefits from treatment. The authors need to explain why they linked it to non-V600E BRAF mutations.

Response: A biological explication for ineffectiveness was added in the abstract

2. Second, the authors need to provide more details of the case presentation in the abstract. In the conclusion part of the abstract, the authors may consider to provide suggestions on questions to be addressed with regard to the current case report.

Response: we specified that the present case report enlightens the need for appropriate evaluation of specific BRAF mutation before starting of TKI-based strategy.

3. Third, in the introduction paragraph of the main text, the authors did not provide insights on the clinical significance and potential unique contribution of this case report. It would be helpful to briefly review factors affecting the efficacy of combination treatment.

Response: in our opinion, the uniqueness of our cases depends on the rarity of the mutation and on the evaluation of concomitant mutations. Indeed, the only previous reported case received a different treatment rather than TKI.

4. Fourth, in the case presentation please provide detailed clinical characteristics of the patients such as co-morbid physical conditions and the main complaints of the patient.

Response: other relevant clinical comorbidity was added in the case presentation.

5. Fifth, in the discussion, please have comments on clinical issues to be addressed in related to treatment results of the case, as well as the unique contributions of this case report. Importantly, detailed comments on clinical implications from this case report are needed.

Response: Comments on clinical issues and implications from this case report were added in the discussion section.