Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled " Efficacy of afatinib in patients with rare EGFR (G724S/R776H) mutations and amplification in lung adenocarcinoma: a case report" (ID: 58038). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. The revised portion of manuscript and supplement material are marked in red. The main corrections in the article and responds to the reviewer's comments are as following:

Reviewer #1:
Scientific Quality: Grade E (Do not publish)
Language Quality: Grade D (Rejection)
Conclusion: Rejection
Specific Comments to Authors: The authors reported a case of NSCLC with rare EFGR mutations that responded to afatinib. I have a few comments about this report. #I admit that ONE experience with ONE patient in the clinical field is very important; in this sense, to compile a case report is sine qua non for the development of medicine. With this in mind, I read the paper. I admit that the EFGR mutations detected in this NSCLC patient must be RARE, and the experience where afatinib was effective for the treatment of such an NSCLC patient must be much RARER; this is ok, but to be rare is not necessarily important for a scientific paper. The PFS of this patient was more than 14 months after the afatinib treatment; this is ok, but what was this patient like thereafter? To know this 'thereafter' is very important to know the true effect of afatinib on this patient. Just 14 months is too short to make any conclusions about afatinib particularly because it is about a patient with lung malignancy. What is described in this paper seems, at first glance, seems new and surprising; but its content, in fact, is too little and superficial to draw something like a conclusion or even a lesson. With only one patient with only a follow-up of only 14 months, who can draw the right picture about the treatment of NSCLC patients, by afatinib, with that RARE EFGR mutations? Even though such a picture could be drawn, it could be even dangerous particularly because it is about the treatment (life or death) of the patients. #There are a countless number of grammatical errors throughout the MS. The following lists some of them (from the abstract). These need to be thoroughly corrected. -Abstract: To show the gene 'EGFR', some are EGFR, which is ok; but some are EGFR, which is not correct. -Abstract, background, line 3: 'treatment show good' >>> 'treatment shows good' -Abstract, background, line 5: 'some uncommon genomic mutation are' >>> 'some uncommon genomic mutations are' -Abstract, background, line 6, 'the response effect of some uncommon EGFR mutations to TKI remains unclear': This sentence is structurally clumsy and difficult to understand. It

would be easier to understand if it were ‘the effect of TKI on some uncommon EGFR mutations remains unclear’ -Abstract, case summary, ‘A 64-year-old woman…left pleural effusion’: This sentence ends half-way, i.e. it is composed of only the subject, and does not have any verbs. -Abstract, case summary, ‘rare EGFR G724S /R776H and amplification co-mutation’: What does this mean? It means ‘co-mutation comprised of rare EGFR G724S /R776H and amplification’? -Abstract, case summary, ‘Then the patient then’: One of ‘then’ is redundant. Abstract, case summary, ‘PFS’: What is this ‘PFS’? In every respect, an abstract should be self-sufficient. The appearance of this ‘PFS’ is too abrupt, and no full-spelling is given here.

Answer: Thank you for your suggest. Those comments are all valuable and very helpful for revising and improving our paper. And we also updated the patient prognosis data. On October 25, 2020, reexamination revealed the progress of the disease with multiple bone metastases (Fig. 4). Imaging studies show progressive disease (PD). So the patient's final PFS was 17 months. At the same time, we also check the spelling and other aspects of the full text to ensure the accuracy of the article in terms of description

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This is an informative and valuable study and is very useful to both clinicians and patients.

Answer: Thank you for your recognition of our work.

Reviewer #3:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This case describes a rare EGFR G724S/R776H mutations and amplification in a NSCLC responding to afatinib. The manuscript is very well written and illustrated. My recommendation is accept it for publication.

Answer: Thank you for your recognition of our work.