Reviewer’s report

Title: EGFR Exon 20 Insertion Mutations and Response to Osimertinib in Non-small-cell Lung Cancer

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Reviewer: Timothy Burns

Reviewer's report:

In the following manuscript, the authors describe their genotyping effort on 2316 Chinese patients to characterize the prevalence of EGFR mutant exon 20ins mutations in this population. They further describe the experience of six patients that received osimertinib for their exon 20ins disease. As only, two cases of response to osimertinib in exon 20ins have previously been reported in the literature and the characterization of exon 20ins patients in a Chinese population is lacking, this research article would be of significant benefit to research community. This article could be significantly improved if the following concerns were addressed.

1. Use of the foundation medicine cohort, may not give an accurate representation of the frequency of EGFRex20 ins in Caucasians patients as this only ordered in a small subset of patients. The use of a larger nationwide NGS effort would provide a more accurate picture of this disease. The IFCT cohort data is available and published and would serve as a better comparator. Leduc et al. Annals of Oncology 28: 2715-2724. 2017.

2. Supplementary Figure 1 and 2: Were any co-alterations significantly more or less common in EGFRex20 ins tumors? It looks like APC mutations maybe less common. Are the ERBB2, KRAS and BRAF mutations listed classic driver mutations or substitutions at other less common sites?

3. It would be helpful if the presence or absence of CNS disease was document for all patients? Was bone or liver disease present in these patients (already stated for patient 5)? What was the M1 stage of these patients?

4. Table 2 could be clearer. For example, for sex, patient number is listed but not percentage is probably more relevant.

5. The second published case of osimertinib response in an EGFRex20 mutation patient should be cited as well. Yang et al. Lung Cancer. 2018 Jul;121:1-4

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes
Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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Please indicate the quality of language in the manuscript:

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