## RESPONSE TO COMMENTS FROM REVIEWER A

**Reviewer A**

The authors report clinical efficacy and safety profile of an irreversible EGFR-TKI, lazertinib, in NSCLC patients with EGFR T790M mutation using real-world data. A real-world epidemiology may give new insights that overcome limitations in a clinical trial. However, the aim of the present study is not clearly described. In addition, STROBE statement did not work for the review.

**COMMENT #1**

The aim of the present study is not clear. What is the advantage of a real-world data? It is unclear what the authors wanted to know using a real-world data. The sample size did not exceed that of the Phase I/II study of Lazertinib. Although variety of the patient background in the real-world data potentially give a new information, the authors did not focus on this point

**RESPONSE #1**

Thank you for pointing out the important issue and fruitful comments. We collected and analyzed this data in the real-world clinical setting to compare and increase confidence in the clinical utility of Lazertinib in EGFR T790M mutation patients. Through this study, we emphasize the two things to the authors. First, clinical efficacy was similar or slightly better compared to the phase I/II study (LASER201, ORR of 55%), showing ORR of 72.8% in our study population. Second, in terms of safety profile, we observed 37.9% of the patient received dose modification during the treatment, which is mainly due to paresthesia. However, our study population showed that no impact on clinical outcome was observed in patients treated with a reduced dosage, 160mg, which suggests that similar clinical efficacy could be derived with appropriate adverse event management.

As highlighted by the reviewer, we tried to incorporate the additional analysis result based on the data which could be acquired from real-world settings, such as the type of EGFR detecting method **(cfDNA vs. tissue, Page 16, Line #238)**. In addition, we tried to share meaningful clinical experiences through a case who safely treated with Lazertinib after experiencing cardiac toxicity from Osimertinib **(Page 13, Line**

**#207).** In this revision, additional sentences emphasizing the safety result, which we would like to emphasize through our study but not observed in the trial outcomes are also added as below.

**Change in text:**

Page 16, Line #252: Through the data collected from the real-world setting, we observed unique findings which had not been highlight in the previous clinical trials.

Page 16, Line #258: The time of first symptom appearance also varied from 2 weeks to 15 months after the start of lazertinib therapy, and showed no correlation with other demographic factors such as gender, body weight, and body mass index.

**COMMENT #2.**

STROBE Statement did not work efficiently because page numbers and line numbers do not indicate corresponding page and line correctly. For example, page 3 does not include lane 30. Page 6 does not include Introduction. I could not check items listed.

**RESPONSE #2**

Thank you for the information. We re-wrote the STOBE statement, including the page and the line number, which is based on the page number of the Manuscript Word file. Please find the matched number based on the word file (not merged PDF file), which begins on page 1 from the title page.

The study presents results on the efficacy of lazertinib on NSCLC patients with an acquired EGFR T790M mutation.

In the end, this study, which is a retrospective study, is well conducted and well described. I have on major comment and two minor comments:

**COMMENT #1**

the authors must give more details on the methods used for the detection of cell-free and tissue-based mutations; moreover, they must discuss how the sensitivity of the detection of these mutations with these two different methods impacts the results and their interpretations

**RESPONSE #1**

Thank you for pointing out a very important issue. The cell-free DNA and tissue T790M evaluation from our study population was done with cobas EGFR mutation Test V2 (Roche Diagnostic, USA). Due to both tests conducted with the same method, the difference in clinical outcome showing inferior outcome in T790M plasma detected patients compared to T790M tissue detected patients in our study population (HR 0.43, P = 0.02) could be derived due to the clinical characteristics of patients. More in detail, as described in our discussion section **(Page #16, Line #248)**, this finding might be due to the cf-DNA being more frequently used in patients with greater tumor burden and general conditions unfit for repeat biopsy. As highlighted by the reviewer, we included the testing kit information in the method section below.

**Change in text:**

Page #8, Line #94 Testing for T790M mutation from both tissue or cell-free DNA was conducted with cobas EGFR mutation Test V2 (Roche Diagnostic, USA).

**COMMENT #2**

the authors should discuss more critically their results in the light of a possible switch between the use of osimertinib and lazertinib

**RESPONSE #2**

Thank you for the comment. We agree with the reviewer that since Lazertinib is placed as an alternative 3$^{rd}$ generation EGFR TKI to osimertinib, there are occasions in which Lazertinib could be used as the preferential choice of treatment. One good example could be a "Case of interest" in section 3.5. Aligned with the reviewer's comment, we included and modified the emphasizing sentences in the discussion section.

**Change in text:**

Page #18 Line #304: As lazertinib becomes accessible in some regions in the clinical setting, this case provides clinical evidence that an alternative treatment strategy of switching to lazertinib is safe and tolerable in patients with specific occasions such as experience cardiotoxicity to osimertinib.
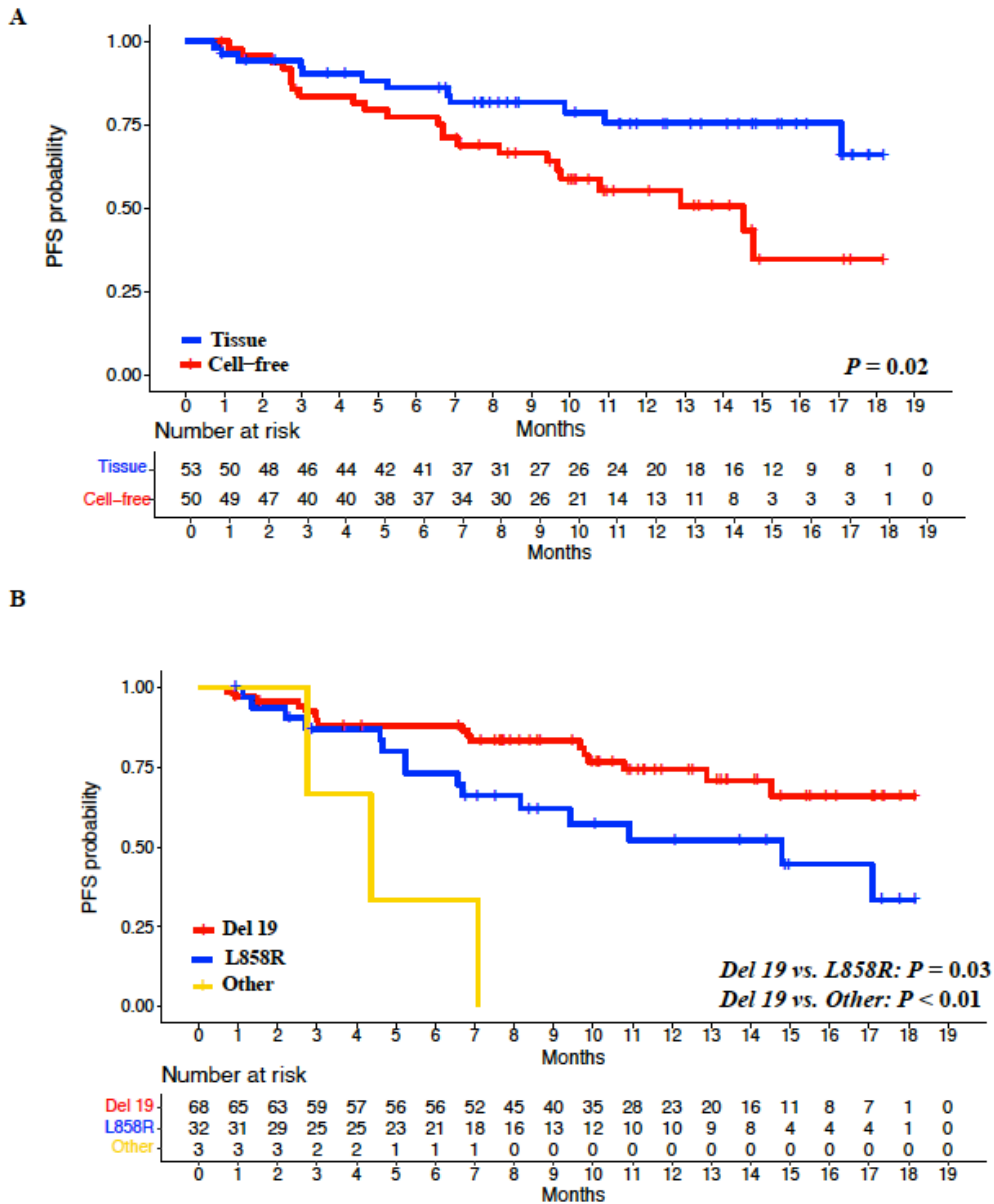
## COMMENT #3

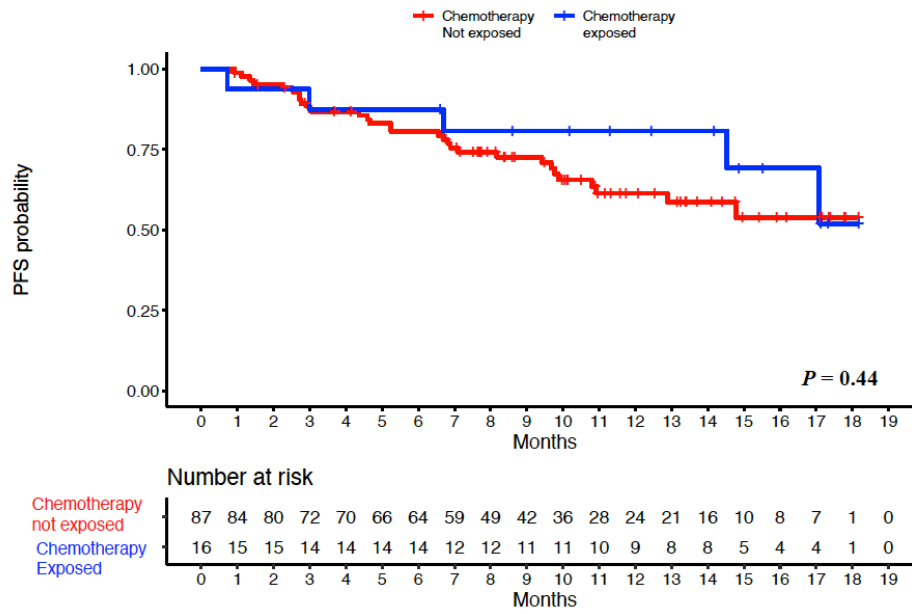the addition of the p-values in figures 2, S1 and S2 would help the reader

## RESPONSE #3

Thank you for the suggestion. Based on the reviewer's comment, we included P-values in the figures (2, S1 and S2) as below:

**Figure 2**

**Supplementary Figure 1**



**Supplementary Figure 2**