

Peer Review File

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Review Comments

Comment 1

In this study, the authors try to analyze the clinical benefit of combining erlotinib with bevacizumab through biomarker searching using data from the JO25667 study. This study aims to confirm the association with pVEGFA level, screening possible predictive biomarker candidates, and the underlying mechanisms of combination. However, several points need to be clarified.

The authors need to point out the primary biomarker analysis data between the two treatment groups before the treatment. After that, compare the biomarkers change in each group before and after treatment.

Reply: We thank the reviewer for this comment. As the aim of this study was to predict the therapeutic effect of erlotinib plus bevacizumab treatment from the pre-treatment biomarker candidates, no post-treatment biomarker specimens were collected. Therefore, unfortunately, we do not have any post-treatment biomarker data to include.

Changes in the text: No changes made to the text.

Comment 2: The authors described that median pVEGFA levels were 18.0 pg/mL in the EB treatment group and 18.8 pg/mL in the E group but suggested that pVEGFA levels have predictive value through statistical analysis (figure 2). However, there is no recommended cutoff value for clinical judgment. It seems this finding without beneficial for clinical reference.

Reply: We thank the reviewer for this comment. Although an association between pVEGFA and erlotinib plus bevacizumab treatment was suggested, we cannot find a meaningful cutoff value from this study, as stated in the Discussion section. This is a limitation of this study for which further investigation is needed.

Changes in the text: No changes made to the text.

Comment 3: The format of line 141 needs to be corrected.

Reply: Thank you for highlighting a potential issue with line 141. The format of this line appears to be correct in our version of the manuscript, so the issue may have arisen when the Word document was converted for sharing with the reviewer. We will check this again when we re-upload the manuscript to the submission website.

Changes in the text: No changes made to the text.