Reviewer's report

Title: Enhancement of gefitinib-induced growth inhibition and apoptosis by Marsdenia tenacissima extract in non-small cell lung cancer cells expressing wild or mutant EGFR.

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Reviewer: JIICHIRO SASAKI

Reviewer's report:

1) The authors used EGFR-TKI sensitive cell lines such as HCC827 and H292, the IC50s of gefitinib is less than 0.2 uM. However, they used 1 uM dose of gefitinib for experiments in this paper and showed about 30% induction of apoptosis using FACS analysis. These results indicated that EGFR-TKI and/or MTE had cell growth inhibition due to not only apoptosis but also cell cycle arrest or other type of cell deaths. Please show us the results of cell cycle analysis after each treatment and other type of cell death such as autophagy. It is well-known that the sequence of treatment by multiple agents may affect the cell cycle rather than the induction of apoptosis on cells.

2) Western blot analysis showed that MTE alone inhibited phosphorylation of EGFR. This finding is very important for mechanism of MTE on EGFR-TKI sensitive NSCLC. Please mention about this finding in Results and Discussion. Is MTE a kind of multiple kinase inhibitors?

3) MTE has the same enhancement effect with other EGFR-TKI? Please use erlotinib or afatinib instead of gefitinib in this situation.

4) We really need in vivo data.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.