

Reviewer 2 v.1

Comments to the Authors:

The article titled "Acquired compound mutations ALK I1171N, L1196M and G1202R mediate lorlatinib resistance in EML4-ALK rearranged malignant pleural mesothelioma: a case report" is an interesting and novel case of MPM where ALK fusion has been detected and third generation ALK inhibitor, lorlatinib, has been used for its treatment for the first time.

Given the rarity of ALCL of the oral cavity cases, the author's report adds to the current knowledge. The report is well written and well cited. I only have a few minor suggestions/comments to the authors.

1. Line 48, 'report described' should be 'report describes'
2. Line 49, 'response from' should be 'response with'.
3. Line 65, 'MPM cases is diagnosed' should be 'MPM cases has been observed'.
4. Line 134, 'with overall survival' should be 'with an overall survival'.
5. Line 136, 'our study was' should be 'our study is'.
6. Line 137, 'and described' should be 'and describes'.
7. Line 148-149, 'alectinib inhibition' should be 'alectinib mediated inhibition'.
8. Line 251, 'B-D' should be 'B-E' as the description is for figures B-E and not just B-D.
9. In Figure-2 legend, the authors have mentioned tumor size at all the stages except for (C) PR, I think they should include it so that the readers can see the reduction in tumor size.
10. In Figure-2, the authors have highlighted the 3604G and 3586C base positions with a complete vertical red column. Perhaps, it would be clearer to the readers if they could show the base 'A' in the 3604 and 3586 base positions to make it clear.

11. The patient was detected to have EML4-ALK fusion by targeted NGS and the authors suggest that the patient's tumor was majorly driven by the oncogenic EML4-ALK fusion. Expression of ALK protein is generally confirmed in lung cancer patients by Ventana ALK (D5F3) CDx Assay, FoundationOne CDx or Vysis ALK Break Apart FISH Probe Kit. I think it would add more value to the report if the authors also had the ALK confirmation in the diagnosis tissue biopsy samples.