

Reviewer 1 v.1

Comments to the Author

The case report by Jia Hu et al. describe the response of an EML4-ALK rearranged malignant pleural mesothelioma (MPM) patient treated with two different next generation ALK TKI. The case is interesting.

1) The main comment is about the nomenclature of mutations that needs to be adjusted to avoid confusion for the readers:

The term “compound mutation” has to be restricted to mutations detected on the same allele, i.e. in cis.

This seems to be the case for the L1196M/G1202R mutation at lorlatinib relapse. However this has not been investigated for the I1171N mutation so the term “compound” cannot be used here. The reviewer suggests using the term “multiple” mutations when several mutations are detected in one sample but the cis/trans status cannot be confirmed.

For instance, the sentences below (including the title and abstract) are wrong or imprecise and have to be reformulated:

“Acquired compound mutations ALK I1171N, L1196M and G1202R”

“Meanwhile, compound ALK I1171N, L1196M and G1202R mutations”

“speculate that these compound mutations synergistically”

“compound mutations involving ALK I1171N, L1196M and G1202R”

“potentially mediated by compound mutations ALK I1171N/L1196M and ALK I1171N/L1196M/G1202R”

“compound missense mutations in ALK kinase domain I1171N, L1196M and G1202R”

These are examples but in all the manuscript this has to be carefully corrected.

2) Precision about figure 2 would be necessary. The two red bars would suggest that both point mutations are present in 100% of the reads? Why did the authors add these red rectangular that seem to hide what is behind?

3) the authors should define what they used as “blood tumor markers”