Reviewer's report

Title: Genome wide single cell analysis of chemotherapy resistant metastatic cells in a case of gastroesophageal adenocarcinoma

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Reviewer: Tsz-Kwong Man

Reviewer's report:

- Major Compulsory Revisions
1. Thank you for the authors' responses to my original comments and clarification of the issues raised in the last review. For instance, in Fig. 5 the authors now show the FISH images of the ERBB2 and KRAS in the primary and metastatic lesions, which are crucial to the interpretation of the study. However, it is still difficult to correlate the images with their statement that ERBB2 was heterogeneously amplified in the primary tumor, but homogenously amplified in the metastatic lesion. For example, I can still see negative cells in the Fig. 5B, thought they were not highlighted. Can the authors please clarify this issue further? Also, even with the understanding that this is a case study, with such a small number of cells, can they really make the claim of enrichment without any statistics, such as % of amplified cells versus nonamplified cells?

2. The main unresolved issue is that the authors’ claim of ERBB2 amplified tumor cells enrichment after chemotherapy is heavily based on the fact that ERBB2 amplification was not detected in the bone metastasis sample before chemotherapy. However, because a small number of cells was analyzed, would it be possible that it is an artifact or sample bias that lead to the negative result? Perhaps they should discuss this further in the text and describe any controls they used to eliminate this possibility.

- Minor Essential Revisions
1. If it is due to scarcity of the biopsy material that the authors could not verify KRAS overexpression in the amplified cases. I think it is necessary to mention in the text, so that the readers would interpret the results cautiously.

2. Some minor points: A period is needed after the last sentence in the consent section. The semicolon should be replaced by a period after “resonance imaging” in the abbreviations section.

- Discretionary Revisions
None.

Level of interest: An article of importance in its field

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