Reviewer's report

Title: Capecitabine and irinotecan with bevacizumab 2-weekly for metastatic colorectal cancer: The phase II AVAXIRI study

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Reviewer: Ruchan Uslu

Reviewer's report:

To whom it may concern,

I have read and assessed the following manuscript by P. Garcia-Afonso et al. and here are my comments about the manuscript:

Capecitabine and irinotecan with bevacizumab 2-weekly for metastatic colorectal cancer: The phase II AVAXIRI study

1- This is a well-designed and well-written phase II study on treatment choices for metastatic colorectal cancer. The language of the manuscript is clear and easy to follow.

2- However, there are some issues that need to be addressed within the context of the trial. In the efficacy part of the manuscript, between lines 218-224, authors have found that the AVAXIRI regimen has similar outcomes on K-Ras mutant and wild type patients. But, the question why the clinicians should prefer beva instead of a EGFR inhibitor as a first line treatment for K-ras wild type patients is pending??

3- In the safety data part, between lines 237-242, some of adverse events (like multi-organ failures) are associated with capecitabine-irinotecan. It is not clear how they reached to this link, and how they distinguished this from disease progression??

4- In the discussion part, “As with the prognostic value of KRAS genotype study[29] we found progression-free survival and overall survival to be extended in KRAS wild-type genotypes over the mutant form”, this cannot be concluded from your data, since as you have addressed in the efficacy part, you could not demonstrate any difference between K-ras wild type and mutant patients??

Minor issues:

1- It will be better to discuss about the limitations of your study in the end of the discussion part.

Yours sincerely,

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests