Reviewer’s report

Title: BRAF mutant colorectal cancer: ErbB2 expression levels as predictive factor for the response to combined BRAFi/ErbB1 inhibitors

Version: 0 Date: 27 Nov 2019

Reviewer: Pashtoon Kasi

Reviewer's report:

Dear Authors,

I read your article with great interest.

BRAF-V600E mutant colorectal cancer constitute the worst kind of colorectal cancer. Outcomes are dismal and single agent RAF-inhibition efforts thus far have failed.

However, this article/research is grossly deficient if we don't take into account the recent developments in the field which the article does not mention or cite.

1. RAF+EGFR inhibition has been studied preclinically as well as in trials. The so called VIP (Vemurafenib+Irinotecan+Panitumumab or Cetuximab) is now in guidelines as well for 2nd line BRAF.
2. RAF+EGFR+MEK (the so called BEACON regimen just got published in NEJM). This is already in guidelines as well and should get FDA approval for 2nd line soon. ANCHOR trial evaluating it 1st line.

Also with respect to HER2:
1. Anti-HER2 (lapatinib+trastuzumab) already in guidelines
2. Anti-HER2 dual combination (Trastuzumab+Pertuzumab) already in guidelines and published both in Lancet Oncology.

A recent review in The Lancet on Colorectal Cancer highlights all these. Without this, the approach and drugs and the implications are not up to date with the current evolving standard of care.

While the experiments/findings are of value, they won't impact practice if the research is not up to date with the field and current guidelines.

I have suggested major revisions rather than a rejection. I hope you and your team would be able to incorporate these new findings and potentially experiments as well taking into accounts these new standards.

Good Wishes.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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I am able to assess the statistics

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