Reviewer’s report

Title: Clinicopathological and prognostic significance of HER-2/neu and VEGF expression in colorectal carcinomas

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Reviewer: THANAGARAJAN RAJKUMAR

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MS ID : 1162415342442403
Title : Clinicopathological and prognostic significance of HER-2/neu and VEGF expression in colorectal carcinomas
Authors: Li Qingguo, Daorong Wang, Jing Li and Ping Chen

Comments:
The Investigators have used IHC to study the expression of c-erbB2/HER2/neu and VEGF in 86 colo-rectal cancers and then tried to look for correlation with histopathological and clinical features, to ascertain the prognostic implications.

MAJOR COMPULSORY CORRECTIONS

1. The sample size is only 86 and includes a heterogeneous mix of site (colon = 48; rectum = 38) and stage (T1,T2 = 23 versus T3, T4 = 63). The biology of colon cancer is different from the rectal cancer; requiring sub set analysis, which will reduce the number of cases. Additionally, it is not clear whether there were any metastatic disease (M1) patients included. It is also not clear whether the cases enrolled for the study were consecutively seen patients or were selected. Over all the sample number will need to be enhanced substantially. The HER2 positivity is around 15 - 20% in colon cancer, which would mean that at least 300 samples minimum will be required to get around 50 HER2 positive colon cancers. Hence, ideally the sample size should be above 300 and preferably colon cancer only.

2. IHC has been done for c-erbB2/HER2/neu and VEGF. There is no mention as to which form of VEGF was studied (A, B, C or D). The photomicrographs look to be wrongly labelled – the strong membrane staining is seen in ‘b’ but is labelled as VEGF. It would be better to have cancers which are negative also included in the panel.

3. HER2/neu has been shown to regulate VEGF expression (Kumar and Yarmand-Bagheri, 2001). The current IHC study by Li et al., will not be able to assess this functionally and the concluding remark is unwarranted.

4. This study does not mention about the earlier study published by Ochs et al., (2004), in which HER2 and VEGF levels were studied using IHC in 109 colon cancers, with pretty similar results.

MINOR ESSENTIAL CORRECTIONS
1. There are many spelling mistakes throughout the manuscript, which will need to be corrected.

Recommendation: Needs major revision as suggested in the comments. Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions.

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

Quality of written English: Needs substantial correction before being published.

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.

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

**Quality of written English:** Needs some language corrections before being published

**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.