Reviewer's report

**Title:** Retrospective exploratory analysis of VEGF polymorphisms in the prediction of benefit from first-line FOLFIRI plus bevacizumab in metastatic colorectal cancer

**Version:** 3  **Date:** 27 February 2011

**Reviewer:** W. Charles Charles Conway

**Reviewer's report:**

Major Essential Revisions: None

Minor Essential Revisions

1) This paper needs a review with a keen eye to grammar and style. There are several areas that are poorly worded, missing words, and at times have grammatical errors. For example, in the first sentence in the background section, "has notably changed in last years," is not appropriately worded. Multiple other examples exist throughout the paper and must be fixed.

2) The background section is too long and needs to be shortened. The background should not include an extensive literature review; this is reserved for the discussion section. The background should be more focused, concentrating on reasons why you took on your study and a concluding sentence clearly indicating your hypothesis.

3) In the background, the SNP 1154 A/G is discussed in regard to the ECOG trial, yet not studied in this paper. It is important to discuss why you chose the particular SNP's you looked at, and if citing data on a SNP evaluated, discuss why you didn't use a particular SNP from that data cited.

4) Include citations for the ECOG performance status, Kohne prognostic score, RECIST criteria, and the NCI-CTCAE criteria.

5) Is there any data that could be cited that confirms VEGF SNP's in peripheral blood are the same as that in tumor samples? If so, please cite in your methods section under genotyping. If not, look into this and write another paper.

6) Add some subheadings to the Results section, such as, "toxicity," and, "treatment response," etc.

7) If a p value is not <.05, report it only as a, "trend."

8) In the results section, break up major findings with appropriate paragraphs.

9) The discussion needs better organization. Focus on your results, what you think they mean, compare with others' results, discuss the limitations of your study, and finish with a conclusion paragraph. The conclusion paragraph should
include conclusions on what your data means ONLY. Your conclusion contains a bunch of info unrelated to your study.

10) In the discussion, focus on what you think your data means. Certainly admit that prospective validation is necessary, but absolutely include a discussion of the possible importance of this data, and what might be driving it at the patient level. Do you think Bev only helps in 1498 C/C, or does it hurt patients with 1498 T/T, etc. Make a statement of your thoughts on the meaning of your data, attempt to support it with other literature, and comment on limitations. This is what a discussion section is for.

11) Did ECOG performance status maintain significance in the various analyses when grouped by, "0-1," and, "2 and higher?" This may be a better break point and if this alters the data, it should be included.

**Level of interest:** An article of importance in its field

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

**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