Reviewer's report

Title: VEGFR-3 and CXCR4 as predictive markers for treatment with fluorouracil, leucovorin plus either oxaliplatin or cisplatin in patients with advanced esophagogastric cancer: a comparative study of the Arbeitsgemeinschaft Internistische Onkologie (AIO).

Version: 2 Date: 14 June 2013

Reviewer: Alicia Okines

Reviewer's report:

- Major Compulsory Revisions
1. At present, this study is not compliant with REMARK guidelines. Please revise in line with these guidelines.

2. Abstract; your results show trends rather than statistically significant differences; this must be clearly stated. The results from the (presumably) post-hoc subgroup analysis of patients aged >60 must be stated to be an exploratory analysis. The study is underpowered by the small sample size and this limitation should be mentioned.

3. Background; this should state why you selected these particular biomarkers for this study; what was your hypothesis and why? Is this part of a wider biomarker analysis investigating other potential biomarkers (such as those involved in DNA repair or fluoropyrimidine metabolism, which might seem a more logical initial choice in a study of platinum plus fluoropyrimidine)?

4. Patients; please provide a patient flow diagram detailing why only 72 patients from the phase III study were included, full baseline characteristics (in particular previous surgery) and how they compare to the overall study population (e.g using Kaplan Meier curves). Also please state clearly the nature of the specimens (biopsies or resections).

5. Immunohistochemistry; please explain your choice of antibodies ideally referencing the studies that have used these successfully previously (e.g I see ref 17 used the same primary CXCR4 antibody).

6. Statistical analysis; please explain how you chose the scoring method, ideally referencing other studies which have used this method for these markers. Please state what p-value is considered significant (presumably <0.05) and any correction for multiple testing. State any pre-planned sub-group analyses and the clinic-pathological parameters selected.

7. Results; all survival curves should have the number of patients at risk below the curves. The results which are not statistically significant (p#0.05) should be clearly stated as such.

8. Discussion; limitations of your study, in particular the small sample size should be discussed.
- Minor Essential Revisions

1. Background; the result that oxaliplatin appeared more beneficial in patients aged >65 was obtained from a post hoc sub-group analysis therefore this must be stated or the sentence removed altogether.

2. Results; Your choice of a sub-group aged >60 years is not explained and should ideally be removed.

- Discretionary Revisions

1. Ideally please include a table detailing your compliance with REMARK guidelines.

2. Figure 2A and 2B are confusing and should ideally be removed; these show the same data as 2C and 2D but the choice of a different x-axis scale is misleading.

**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