Reviewer's report

Title: Efficacy of bevacizumab and chemotherapy in the first-line treatment of metastatic colorectal cancer: broadening KRAS-focused clinical view

Version: 2 Date: 23 June 2014

Reviewer: Sina Vatandoust

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General comments:

1. Previous studies have looked at the same question in the past (Rossi L 2013 and Hurwitz HI 2009) as well as clinical trials (as mentioned in Line 234-237); which makes the current study important only to those with closely related research interests and less interesting clinically.

2. This study is still interesting because of its large sample size; nevertheless the role of some other mutations (BRAF, NRAS, PIK3CA, other-KRAS mutations) have not been explored (although this has been alluded to by the authors as a limitation of the study)

Major Compulsory Revisions

1. Line 202-205: “similarly to PFS…” authors have mentioned that the risk was higher whilst the confidence intervals overlap: the p value should be provided, and if not significant it would be better to avoid the statement: “this risk was higher in patients with KRAS mutation…” (Line 204).

2. Line 263-265: “…patients who received in the first line…” is the difference is statistically significant?

3. Line 280-281: “this hazardous effect was stronger…” again this is not based on a statistically significant difference

4. This study has looked at patients who have received chemotherapy and therefore patients with poor performance and/or with co-morbidities who were not chemotherapy candidates have all been excluded: this is a source of bias (and is worth mentioning in the discussions) for this reason, any conclusions regarding prognostic value of the variables should be made cautiously. The authors need to clarify this in the discussion section

Minor Essential Revisions

1. Page 6 lines 101-109: Naming all different ethics committees is unnecessary

2. Line 140: RECIST: which version?

2. Line 211-214: (“thus, the trend …”) it would be better to moved this to
discussion

3. Line 287: (“…KRAS mutation in colorectal cancer…”) it would be interesting if the authors discussed any potential molecular explanations

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

No competing interest to declare.