Reviewer's report

Title: Genetic predictors of cetuximab-based treatment activity in metastatic colorectal cancer

Version: 1 Date: 14 December 2007

Reviewer: Stuart Schwartz

Reviewer's report:

Minor Essential Revisions:

1. With the FISH studies for EGFR amplification; it needs to be stated that paraffin sections are being used and what their thickness is.

2. In Table 1 define what is meant by partial response, object response and stable disease. All of this terminology must be kept consistent throughout the entire manuscript.

3. The description of the EGFR amplification appears to be written differently in the methods than the results. This needs to be consistent. What is an increased EGFR copy?

4. How often is the R521K mutation detected in the general population? Explain why this is a variant (polymorphism).

5. I do not think that the data present allows for as strong of conclusions as given by the authors.

Major Compulsory Revisions:

1. Overall the manuscript should be reviewed by a native English speaker and the manuscript should be edited.

2. The manners in which the results are presented in the abstract are somewhat confusing and should be rewritten to be clearer. How many responders are there? How many patients have a partial response? How many non-responders are there?

3. Again within the text it is difficult to follow the different treatment regimens; this needs to be made clearer.

4. When talking about the number of gene copies of EGFR, does this refer to the absolute number of copies of EGFR or of the ratio of EGFR/7 centromere. What if there are three copies of each (EGFR and the centromere). How is this classified.

5. In the results the authors say that there are only 2 responding patients with
KRAS mutations; but 3 are given in the next section. Why is this section included if most of the patients with KRAS mutations didn’t respond?

6. In many cancers (e.g. lung cancer) mutations in the EGFR tyrosine kinase domain (exons 18, 19 and 21) are studied, however in this study exons 6 to 14 are studied. Why the differences between the exons studied.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Not suitable for publication unless extensively edited

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'