Reviewer's report

Title: The human epidermal growth factor receptor (EGFR) gene in European patients with advanced colorectal cancer harbors infrequent mutations in its tyrosine kinase domain

Version: 1 Date: 11 August 2011

Reviewer: Karen-Lise Spindler

Reviewer's report:

Major compulsory revisions:

From the previous literature it is well known that the frequency of these mutations is very low. The relevance of the study is consequently questionable, and the reasons for performing the analysis and investigating these mutations are not obvious.

In the background section the authors state that the EGFR mutations are responsible for resistance to EGFR in general, and the role of KRAS mutations is not mentioned. It is important to distinguish between the monoclonal antibodies which have show efficacy in CRC and TKI which have not. This paragraph should therefore be rewritten.

The KRAS mutations are responsible for the majority of resistance to the EGFR MoAbs, and a relation between the KRAS status and small mutations would therefore be relevant.

The impact of the data here presented is unfortunately limited as also acknowledged by the authors. The sample size is too small to allow for an investigation of the association between mutational status and the clinical parameters which would be of interest. Furthermore, the functional importance of the mutations e.g effect on gene expression levels/ protein levels, responsiveness to EGFR inhibition etc. has not been mentioned in the discussion. The data would be of interest if a functional importance of these mutations was presented, but a purely descriptive report of low frequency mutations has limited impact.

The combined result and discussion section should be separated into two independent sections to allow for a relevant discussion of the value of the data, and the limitations of the study which have not been mentioned.

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 interest.