Reviewer’s report

Title: Clinicopathological features of KRAS, NRAS, BRAF and PIK3CA mutations in Japanese patients with metastatic colorectal cancer

Version: 2 Date: 21 November 2014

Reviewer: Anders Edsjö

Reviewer’s report:

Major Compulsory Revisions
None

Minor Essential Revisions
The research question should be clearly stated in the abstract.

The authors should describe the tumor material in higher detail. It should be clear whether primary tumors and/or lgl or distant metastases have been analyzed. To be able to assess whether the assay had a chance of detecting mutations, a knowledge of the percentage of neoplastic cells in the tumor samples is needed. This could either e.g. be clarified by the authors stating the lower limit accepted by the study.

The authors should also state the level of detection in terms of allele frequencies needed for the refractory mutation system-Scorpion assay used.

Discretionary Revisions
The yellow parts of figs. 1-2 are difficult to read if printed on a regular printer. It might be a good idea to test other combinations of colors or symbols.

A file with the genotype of all samples using HGVS nomenclature as supplementary material would be of interest to (some of) the readers.

The authors are advised to rephrase the passage on assay characteristics on line 247. Although used by others, the terms sensitivity is potential misleading as it has nothing to do with the generally accepted terms “sensitivity” and “specificity” used to characterize the ability of medical assays to detect the condition they are design to detect. A more appropriate term might be “level of detection” or “allele frequency needed to detect…”

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:

The reviewer has received compensation for consultant work and has also received an unrestricted research grant of the amount of 10 000 euro from Amgen. No other possible competing interests.