Reviewer’s report

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

Version: 2
Date: 30 December 2014

Reviewer: Maria Carmela Piccirillo

Reviewer’s report:

The authors performed a retrospective analysis of the prevalence KRAS, NRAS, BRAF and PIK3CA mutations in Japanese metastatic colorectal cancer patients, enrolled in a single centre. Moreover, they analyzed the clinicopathological features associated to the mutations and, finally, tried to correlate mutational status and anti-EGFR treatment effect, in the subgroup of patients who were candidate to, and effectively received, an anti-EGFR therapy as second or further line of therapy.

- Major Compulsory Revisions
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1. All the questions were well defined and methods of the analyses were well described. However, they never declared that the study was retrospective, while this must be clearly stated when describing the study design in both the abstract and full text.

2. The authors clearly stated some limitations of the study, such as the small sample size, the single-centre population, the risk of a selection bias (no all the consecutive patients enrolled, but only those evaluated for RAS status in the examined time). They also should clearly state that their analyses were explorative and hypothesis generating (no predefined hypothesis was reported). This could render reasonable the fact that they did not adjust the alpha error value for multiple comparisons.

- Minor Essential Revisions
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3. The statistical method applied to test the significance of the differences between the examined groups should be added to the footnotes of the tables n. 1, 2, and 4.

4. Some details are lacking in the statistical methods section:
   - The authors should explain the statistical method applied to compare median age between examined groups
   - The method to analyze objective response rates according to mutational status was not described and not inferable (logistic regression?)
- Discretionary Revisions
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5. The title and abstract convey what has been found, but I suggest to explain in the title the study design (A retrospective observational study of clinicopathological features...)

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests