Reviewer’s report

Title: KRAS mutations: variable incidences in a Brazilian cohort of 8,234 metastatic colorectal cancer patients

Version: Date: 1 February 2014

Reviewer: Grazia Palomba

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“KRAS mutations: variable incidences in a Brazilian cohort of 8,234 metastatic colorectal cancer patients”

The aim of the study is to assess the distribution of KRAS mutations in Brazilian metastatic colorectal cancer patients.

Major Compulsory Revisions

KRAS point mutations are highly prevalent in CRC and mostly occur in codons 12, 13, and 61. The profile of KRAS mutations was analyzed by direct sequencing of KRAS codons 12 and 13 only. Although not frequently mutated in CRC (5-6% of cases), codon 61 should have been analyzed (in this large patients’ collection, more than 400 cases could have been misclassified).

More information about the distribution of mutations, according to additional clinico-pathological characteristics of CRC patients, should be presented [mainly, anatomical site of primary tumor (right, transverse, left colon, etc.), disease stage, tumor grading].

The discussion about the importance of sexual hormones in the risk for CRC should be more concise. Previous studies have indeed investigated sex-related differences in the prognostic impact of KRAS and BRAF mutation in CRC. No significant association was found between KRAS mutations and sex. Further studies directly focused on the associations of hormonal factors with KRAS mutation status in CRC are awaited.

Minor Essential Revisions

Methods: why did the authors use the semi-nested PCR for the mutational analysis?

Results: In the first paragraph of the Results, the last sentence should be removed (it has been repeated twice the fact that a part of samples was not analyzed).

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the
statistics.

Declaration of competing interests:

I declare that I have no competing interests.