Reviewer’s report

Title: Treatment recommendations to cancer patients in the context of FDA guidance for next generation sequencing

Version: 0 Date: 04 Sep 2018

Reviewer: Alessandro Lagana

Reviewer's report:

In the manuscript titled "Treatment recommendations to cancer patients in the context of FDA guidance for next generation sequencing" by Dy et al, the authors present results from comprehensive genomic profiling by the OmniSeq test (OCP) performed on 646 patients and the physicians' choices following OCP recommendations.

The manuscript reports the use of the OCP test on patients with solid tumors at different stages and discusses benefits and limitations of this kind of genomic testing for the generation of treatment recommendations.

There are a few points that need to be addressed:

- The authors should provide more details about the OCP test implementation in the Methods section, i.e. about calling of mutations, copy number alterations and gene rearrangements, as well as provide the complete list of the genes assayed. Also, the authors state that the "OCP uses tumor tissue to detect […] somatic mutations". How are somatic mutations identified without a germline control? The authors should also provide more details on their source of actionable alterations, a complete table would be useful.

- The authors show the evidence used by OCP for drug recommendation on Table 1. It is not clear whether this table contains the complete set of evidence or only selected few items. Also, is Level 3 evidence just the combination of Level 1 and 2 just applied to different tumor types or is there another layer of information that is not reported in the manuscript? This is not clear. Table 3 is referenced on Page 7 with regards to Level 3 mutations, however the table does not contain any of the genes included in the text (e.g. TP53, ATM, PTEN…).

- In the description of Level 2 mutations on Page 6, the authors include Thyroid carcinoma among the 99 tests with L2 results. However, thyroid cancer is not present in Table 1. Similarly, KRAS mutations in lung cancer, reported in the same manuscript section, and L1/L2 mutations in prostate cancer, mentioned on Page 7, are not shown in Table 1. Where is the evidence that concern these mutations/cancers? The authors should address these discrepancies.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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