Reviewer’s report

Title: Sequencing and curation strategies for identifying candidate glioblastoma treatments

Version: 0 Date: 12 Nov 2018

Reviewer: Mauro Biffoni

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The authors describe the results of a comparative evaluation of different methods to identify actionable targets in a therapy-orphan, aggressive malignancy. They show that in 30 glioblastoma patients all but one tumors carried a genetic alteration suitable for targeted therapy when analysed by whole genome sequencing (WGS). Whole exome sequencing (WES) produced results with a good correlation with WGS in the evaluation of variant allele frequency. The two technics allowed the identification of at least one actionable target in all patients' samples. In a limited number of cases information from WGS/WES caused a therapeutic decision by the clinician, the time to have the information available for clinician was identified as a critical step for usefulness. By comparing sequencing with gene panels analyses they found that WGS was not able to identify a potential target in 2.5% of the cases whereas panels in 39.5%. Automated results curation was correlated with manual one but required few minute instead of months. The authors conclude that WGS/RNA sequencing will be reasonably a potential routine tool provided that costs and efficiency improve and automatic curation of results is used.

The manuscript is well written and only minor modifications are needed:

Authors should explain all acronyms the first time they are used.

The identification of Caris Molecular Intel as Panel 6 is missing in the section Patients and Methods-Comparison of Targeted Panels (page 11, row 34).

Page 13, row 20, reasons for exclusion of 6 patients should be described also in the text.

In Table 1 age should be expressed as median (range) rather than mean (SD), total number of patients indication would ease the reading.

Page 13, rows 47-52, the ploidy of four remaining tumors should be indicated, e.g. 2 were hypoploid and 2 hyperploid.

Some typing errors are present, e.g. EFGR for EGFR at page 15 row 46, vemurafinib for vemurafenib at page 17 row 29.

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

Yes
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.
I am able to assess the statistics

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