Reviewer's report

Title: ADAR2 editing activity in newly diagnosed versus relapsed pediatric high-grade astrocytomas

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Reviewer: Dannis Van Vuurden

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The authors have investigated the RNA editing profiles and ADAR2 expression of pediatric high grade gliomas at diagnosis and relapse, to seek whether differences in RNA editing occur upon disease progression. Hereto they have tested a small case series of 4 patients with diagnosis and relapse samples. In general, no large differences were observed in editing, but further reduction of ADAR2 expression was observed. In a case of infant GBM, that survived, striking restoration of RNA editing profiles and ADAR2 mRNA expression in the relapse tumor were observed.

Minor essential revisions

1. A major drawback of this study is the limited number of paired diagnosis and relapse patient tumor samples that was used, which can be explained by the rarity of the disease and the fact that surgery at relapse is infrequently performed. It is therefore not possible to draw statistically valid conclusions on the role of RNA editing at diagnosis and relapse. The authors acknowledge this in their abstract (‘Despite the low number…’) , but not in their manuscript. They should explain the scarcity of material. Would there be a possibility to extend the number of samples, for example in collaboration with other groups?

2. The authors state that only limited information is available on genetic and molecular alterations in pediatric high grade gliomas. They however should refer to an important paper in this field by Paugh et al: ‘Integrated molecular genetic profiling of pediatric high-grade gliomas reveals key differences with the adult disease’ ( JCO 2010; 28(18):3061-8).

3. The distinction between GBM (case 1,2 and 4) and supratentorial PNET with glial differentiation can be challenging. Has pathology been reviewed by two independent neuropathologists and has sPNET been ruled out?

4. Are the authors able to biologically explain the discrepancy of further ADAR2 reduction in case 1-3 at relapse and no substantial changes in RNA editing in this material? Do the different editing sites have different sensitivity to ADAR2 activity?

5. Would the authors be able to speculate on potential shortcomings of the control tissue they have used? Does brain contusion result in altered RNA editing profiles or ADAR expression?
6. The authors have mainly used US English. They therefore should change ‘favourable’ to ‘favorable’, ‘analysed’ to ‘analyzed’ and ‘summarised’ to ‘summarized’. Furthermore ‘immunohystochemistry’ (page ) should be ‘immunohistochemistry’ and on page 5 there is a typo in ‘reverse trancriptase-polymerase’.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests