Reviewer's report

Title: O6-Methylguanine-DNA methyltransferase protein expression by immunohistochemistry in brain and non-brain systemic tumors: systematic review and meta-analysis of correlation with methylation-specific polymerase chain reaction

Version: 1 Date: 18 November 2010

Reviewer: Bernd B Kaina

Reviewer's report:

Brell et al.: This is a careful review on MGMT immunohistochemistry (IHC) and methylation specific PCR (MSP), notably for gliomas but also for other tumor groups. Lots of data on MGMT expression have been published in the last years, and data are quite conflicting especially as to the predictive and progressive value of the different methods applied. This study arrives at the conclusion that MGMT IHC does not provide the same information as MSP regarding MGMT expression. Therefore, both methods are not interchangeable. The same conclusion was previously drawn by some other authors based on their glioma studies, such as Maxwell et al. (ref. 68). This study goes somewhat further since the Meta-analysis shows lack of concordance between IHC and MSP if relevant published studies were compared.

- Unfortunately, the authors do not draw a conclusion as to the usability of IHC as a predictive/prognostic marker. They should refer at least to the recent study of Preusser et al. (ref. 20) in which important limiting factors were identified such as inter-observer differences in specimen evaluation and the quality of the antibody.

- I also recommend to add some data comparing the clinical response with the IHC. Are Kaplan-Maier curves for gliomas available on the basis of IHC and are they as significant as those published for MSP?

- Finally, it would be interesting to compile those papers in which pretreatment (primary) tumors was compared with recurrences. This has recently been done for gliomas (Christmann et al., Int. J. Cancer, 127, 2106-2118). Are similar data available for MGMT IHC for gliomas and other tumor groups and is there any correlation between pretreatment tumors and recurrences in IHC and MSP?

- The last paragraph (Conclusions, p. 17) should end up with a recommendation regarding the use of both methods. If they are not interchangeable, should both methods be applied or is one of them better suited for the purpose of prediction of the patient’s response (see the comment above)?

Level of interest: An article of importance in its field

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.