Reviewer's report

Title: Carbonic anhydrase IX in oligodendrogial brain tumors

Version: 1 Date: 22 June 2007

Reviewer: Dirk Vordermark

Reviewer's report:

General
The paper contains interesting data on the expression of the tumor- and hypoxia-associated protein CA IX and its effect of prognosis in oligodendroglioma.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

p. 6, last sentence of paragraph "patients": The statement that 50% of those who died did so during the first 1.5 years is confusing and there is discrepancy regarding Fig. 2. In that Fig., a survival plateau for CA IX - and CA IX + patients, respectively, is reached at about 70% and 40%, but at 1.5 years the levels are about 90% for both groups? (Much more than 50% of non-survivors must have died later than after 1.5 years?!

p. 8, second paragraph: The authors describe how groups of CA IX - (negative and weak) and CA IX + were defined. It remains unclear if these groups also apply to Fig. 2. This should be clearly stated in the text and in the legend for Fig. 2. The survival curves give the expression that the CA IX - group contains less patients (n=14, completely negative primary tumors only ?)

p. 10 and p. 12, survival analysis: It should be stated what type of survival was analyzed (overall-survival, disease-specific survival?), what was considered an event in the Kaplan-Meier analysis. Also, the p value for the difference between CA IX - and CA IX + in the univariate analysis ("tended to associate"), some hard survival data (e. g. 2-year, 5-year survival rates) and the variables used in the multivariate analysis should be stated. It should be discussed which confounding factors might explain the significance of CA IX in multivariate but not univariate analysis.

The discussion focuses too much on the general properties of CA IX but should concentrate more on the situation in brain tumors. The authors only discuss their own previous experience in astrocytic tumors (e. g. association with tumor grade, tumor progression) but should consider other work as well (Birner, Clin Cancer Res 2004; Proescholdt, Neuro-Oncol 2005). Since CA IX is HIF-1-regulated, published data on HIF-1alpha expression should also be discussed (Birner, Cancer 2001). In this context it would be of interest to characterize the
Localization / pattern of CA IX expression in the present study (focal vs. diffuse).

Fig. 1: The images are of low quality in the version provided for review.

Fig. 2: The figure would be easier to read if follow-up time were presented in years and the survival in percent. The line pattern legend (- vs. --) is a bit confusing.

Table 1: The table should be inserted in the text file so it will integrated in the PDF of the published version - not as supplementary material only available online.

----------------------------- Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)-----------------------------

p. 3, introduction, 1st paragraph: I am not sure if the authors´ assumption is correct that prognosis and therapeutic options (nowadays) vary to a much greater extent in oligodendrogliomas than in astrocytomas. Astrocytic tumors are also frequently treated with temozolomide or nitrosureas, for instance. Please check and, if confirmed, give references.

Table 1: In the last line ("grade III") the percentage numbers are missing.

----------------------------- Discretionary Revisions (which the author can choose to ignore)-----------------------------

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

I am a co-inventor on a US patent application (April 20, 2006) regarding the detection of CA IX to predict tumor hypoxia.