Predictive value of the MGMT promoter methylation status in metastatic melanoma patients receiving first-line temozolomide plus bevacizumab in the trial SAKK 50/07

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The O6-methylguanine-DNA-methyltransferase (MGMT) promoter methylation status is a predictive parameter for the response of malignant gliomas to alkylating agents such as temozolomide. First clinical trials with temozolomide plus bevacizumab therapy in metastatic melanoma patients are ongoing, although the predictive value of the MGMT promoter methylation status in this setting remains unclear. We assessed MGMT promoter methylation in formalin-fixed, primary tumor tissue of metastatic melanoma patients treated with first-line temozolomide and bevacizumab from the trial SAKK 50/07 by methylation-specific polymerase chain reaction. In addition, the MGMT expression levels were also analyzed by MGMT immunohistochemistry. Eleven of 42 primary melanomas (26%) revealed a methylated MGMT promoter. Promoter methylation was significantly associated with response rates CR + PR versus SD + PD according to RECIST (response evaluation criteria in solid tumors) (p<0.05) with a trend to prolonged median progression-free survival (8.1 versus 3.4 months, p>0.05). Immunohistochemically different protein expression patterns with heterogeneous and homogeneous nuclear MGMT expression were identified. Negative MGMT expression levels were associated with overall disease stabilization CR + PR + SD versus PD (p=0.05). There was only a poor correlation between MGMT methylation and lack of MGMT expression. A significant proportion of melanomas have a methylated MGMT promoter. The MGMT promoter methylation status may be a promising predictive marker for temozolomide therapy in metastatic melanoma patients. Larger sample sizes may help to validate significant differences in survival type endpoints.