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Continuous low-dose temozolomide and celecoxib in recurrent glioblastoma.

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Abstract

Even after gross tumor resection and combined radiochemotherapy, glioblastomas recur within a few months. Salvage therapy often consists of rechallenging with temozolomide in a dose-intensified schedule. Previously, low-dose metronomic temozolomide in combination with cyclo-oxygenase 2 inhibitors has had a beneficial effect as first-line treatment for glioblastoma. We report our experience with this procedure in recurrent glioblastomas after standard treatment. From June 2007 to April 2009, 28 patients with recurrent glioblastoma received continuous low-dose temozolomide of 10 mg/m² twice daily and 200 mg celecoxib. Before therapy the recurrent tumor was resected in 19 of 28 patients. Microvessel density (MVD) was determined by immunohistochemistry in 19 patients, and MGMT promoter methylation status, using the pyrosequencing method, was determined in 17 patients. In 14/28 patients, positron emission tomography with [F-18]-fluoroethyl-L: -tyrosine (FET-PET) was performed. Tumor progression was defined by the Macdonald criteria on MRI every 8-12 weeks or by clinical deterioration. The median time to progression was 4.2 months. Progression-free survival (PFS) after 6 months was 43%. Except for a lymphopenia in one patient, there was no grade 3 or 4 toxicity. PFS did not correlate with MVD or MGMT status. A high FET uptake correlated with tumor control after 6 months under therapy ($P = 0.041$, t-test). Low-dose continuous temozolomide in combination with celecoxib seems to have activity in recurrent glioblastoma without relevant toxicity. High FET uptake correlated with a better outcome under metronomic therapy.

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