Phase II study of imatinib mesylate (Gleevec(R)) for recurrent meningiomas (North American Brain Tumor Consortium Study 01-08).


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Platelet-derived growth factor (PDGF) and its receptors (PDGFR) are frequently co-expressed in meningiomas, potentially contributing to their pathogenesis. The North American Brain Tumor Consortium (NABTC) conducted a phase II study to evaluate the therapeutic potential of imatinib mesylate (Gleevec(R)), a PDGFR inhibitor, in patients with recurrent meningiomas. Patients were stratified into benign (WHO grade I) meningiomas or atypical (WHO grade II) and malignant (WHO grade III) meningiomas. The primary endpoint was 6-month progression-free survival (6M-PFS). Patients requiring enzyme-inducing anti-epileptic drugs were ineligible. Patients received imatinib at a dose of 600 mg/day for the first 4-week cycle and then gradually increased to 800 mg/day for subsequent cycles, if there were no unacceptable toxicities. Plasma concentrations of imatinib and its active metabolite, CGP74588, were assessed. Twenty-three heavily pretreated patients were enrolled into the study (13 benign, 5 atypical, and 5 malignant meningiomas), of whom 22 were eligible. The study was closed prematurely due to slow accrual. Tissue was available only from a minority of patients but in these specimens there was uniform distribution of PDGFR, the drug target. Imatinib was generally well tolerated. Of 19 patients evaluable for response, 10 progressed at the first scan, and 9 were stable. There were no complete or partial responses (PR). Overall median PFS was 2 months (range 0.7-34 months); 6M-PFS was 29.4%. For benign meningiomas, median PFS was 3 months (range 1.1-34 months); 6M-PFS was 45%. For atypical and malignant meningiomas, median PFS was 2 months (range 0.7-3.7 months); 6M-PFS was 0%. Cycle 1 trough concentrations of imatinib and CGP74588 were 2129+/-1600 ng/ml and 517+/-326 ng/ml, respectively. Single-agent imatinib was well-tolerated but had no significant activity in recurrent meningiomas. Trough plasma concentrations of imatinib exceeded those associated with imatinib activity in CML.

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