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Abstract

Bevacizumab, a monoclonal antibody to vascular endothelial growth factor (VEGF), and irinotecan for treatment of malignant gliomas

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Background: The prognosis for recurrent malignant gliomas is poor, with a median survival <12 months, median progression-free survival <12 weeks and response rates <20%. Malignant gliomas have high concentrations of VEGF receptors, and the higher the VEGF receptor concentration, the worse the prognosis. Bevacizumab is a humanized IgG1 monoclonal antibody to VEGF, which is synergistic with chemotherapy for most malignancies. Irinotecan is a topoisomerase 1 inhibitor, and has modest activity against recurrent malignant gliomas. **Methods:** We report a FDA approved phase II trial of bevacizumab and irinotecan for the treatment of recurrent malignant gliomas. 32 patients were enrolled, 23 with grade IV tumors (glioblastoma multiforme) and 9 with grade III tumors (anaplastic astrocytomas or oligodendrogliomas). All the patients had progressive disease and every patient had received prior radiation therapy and chemotherapy. Patients were treated every other week with bevacizumab 10 mg/kg and irinotecan 125 mg/m² for patients not taking enzyme inducing anti-epileptic drugs or 340 mg/m² for patients taking enzyme inducing anti-epileptic drugs. **Results:** The regimen was well tolerated with no CNS hemorrhages or >grade 1 systemic hemorrhages. Four patients were taken off study for thrombotic complications, 2 pulmonary emboli, 1 deep venous thrombus, and one thrombotic stroke. Two patients were discontinued secondary to grade 2 proteinuria and three were discontinued because they required non-neurosurgical surgery, appendectomy, repair of anal fissures and hip stabilization. The response rate was 63% (19 PRs and 1 CR). The median progression-free survival is 24 weeks. The median overall survival has not been reached, and exceeds 6 months. There have been ten deaths due to disease progression. **Conclusions:** The combination of bevacizumab and irinotecan is safe and one of the most active regimens against malignant gliomas.

Author Disclosure

Employment or Leadership	Consultant or Advisory Role	Stock Ownership	Research Honoraria	Research Funding	Expert Testimony	Other Remuneration
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