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Cancer Therapy: Clinical

Bevacizumab Plus Irinotecan in Recurrent WHO Grade 3 Malignant Gliomas

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Purpose: Although patients with newly diagnosed WHO grade 3 malignant glioma have a more favorable prognosis than those with WHO grade 4 malignant glioma, salvage therapies following recurrence offer essentially palliative benefit. We did a phase II trial of bevacizumab, a monoclonal antibody to vascular endothelial growth factor, in combination with irinotecan for patients with recurrent grade 3 malignant glioma.

Experimental Design: Upon documentation of adequate safety among an initial cohort of nine patients treated with bevacizumab (10 mg/kg) and irinotecan every 14 days, a second cohort ($n = 24$)

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was treated with bevacizumab (15 mg/kg) every 3 weeks with irinotecan on days 1, 8, 22, and 29 of each 42-day cycle. For both cohorts, the dose of irinotecan was 340 mg/m² for patients on enzyme-inducing antiepileptic drugs (EIAED) and 125 mg/m² for patients not on EIAEDs. After each 6-week cycle, patients were evaluated with a physical examination and magnetic resonance imaging.

Results: The 6-month progression-free survival was 55% (95% confidence interval, 36-70%). The 6-month overall survival was 79% (95% confidence interval, 61-89%). Twenty patients (61%) had at least a partial response. Outcome did not differ between the two treatment cohorts. Significant adverse events were infrequent and included a central nervous system hemorrhage in one patient, and one patient who developed thrombotic thrombocytopenic purpura.

Conclusion: Bevacizumab and irinotecan is an active regimen with acceptable toxicity for patients with recurrent WHO grade 3 malignant glioma.

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