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### Phase II trial of bevacizumab and erlotinib in patients with recurrent malignant glioma.

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#### Abstract

Vascular endothelial growth factor (VEGF) and epidermal growth factor receptor (EGFR) signaling are established contributors to malignant glioma (MG) biology. We, therefore, evaluated bevacizumab, a humanized anti-VEGF monoclonal antibody, in combination with the EGFR tyrosine kinase inhibitor erlotinib, in this phase 2 study for recurrent MG patients ([www.ClinicalTrials.gov](http://www.ClinicalTrials.gov), NCT00671970). Fifty-seven patients (n = 25, glioblastoma [GBM]; n = 32, anaplastic glioma [AG]) were enrolled. The primary endpoint was 6-month progression-free survival (PFS-6). Overall survival (OS), radiographic response, pharmacokinetics, and correlative biomarkers were the secondary endpoints. Patients were stratified based on the concurrent use of enzyme-inducing antiepileptic drugs (EIAEDs). Bevacizumab (10 mg/kg) was given intravenously every 2 weeks. Erlotinib was orally administered daily at 200 mg/day for patients not on EIAEDs and 500 mg/day for patients on EIAEDs. PFS-6 and median OS were 28% and 42 weeks for GBM patients and 44% and 71 weeks for AG patients, respectively. Twelve (48%) GBM patients and 10 (31%) AG patients achieved a radiographic response. Erlotinib pharmacokinetic exposures were comparable between EIAED and non-EIAED groups. Rash, mucositis, diarrhea, and fatigue were common but mostly grades 1 and 2. Among GBM patients, grade 3 rash, observed in 32%, was associated with survival benefit, whereas elevated hypoxia-inducible factor-2 alpha and VEGF receptor-2 levels were associated with poor survival. Bevacizumab plus erlotinib was adequately tolerated in recurrent MG patients. However, this regimen was associated with similar PFS benefit and radiographic response when compared with other historical bevacizumab-containing regimens.

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