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Tumor Angiogenic and Hypoxic Profiles Predict Radiographic Response and Survival in Malignant Astrocytoma Patients Treated With Bevacizumab and Irinotecan

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Purpose: The combination of a vascular endothelial growth factor (VEGF) – neutralizing antibody, bevacizumab, and irinotecan is associated with high radiographic response rates and improved survival outcomes in patients with recurrent malignant gliomas. The aim of these retrospective studies was to evaluate tumor vascularity and expression of components of the VEGF pathway and hypoxic responses as predictive markers for radiographic response and survival benefit from the bevacizumab and irinotecan therapy.

Patients and Methods: In a phase II trial, 60 patients with recurrent malignant astrocytomas were treated with bevacizumab and irinotecan. Tumor specimens collected at the time of diagnosis were available for further pathologic studies in 45 patients (75%). VEGF, VEGF receptor-2, CD31, hypoxia-inducible carbonic anhydrase 9 (CA9), and hypoxia-inducible factor-2 α were semiquantitatively assessed by immunohistochemistry. Radiographic response and survival outcomes were correlated with these angiogenic and hypoxic markers.

Results: Of 45 patients, 27 patients had glioblastoma multiforme, and 18 patients had anaplastic astrocytoma. Twenty-six patients (58%) had at least partial radiographic response. High VEGF expression was associated with increased likelihood of radiographic response ($P = .024$) but not survival benefit. Survival analysis revealed that high CA9 expression was associated with poor survival outcome ($P = .016$).

Conclusion: In this patient cohort, tumor expression levels of VEGF, the molecular target of bevacizumab, were associated with radiographic response, and the upstream promoter of angiogenesis, hypoxia, determined survival outcome, as measured from treatment initiation. Validation in a larger clinical trial is warranted.

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