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Clinical Investigation

Safety and Efficacy of Bevacizumab with Hypofractionated Stereotactic Irradiation for Recurrent Malignant Gliomas

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Purpose

Preclinical studies suggest that inhibition of vascular endothelial growth factor (VEGF) improves glioma response to radiotherapy.

Bevacizumab, a monoclonal antibody against VEGF, has shown promise in recurrent gliomas, but the safety and efficacy of concurrent bevacizumab with brain irradiation has not been extensively studied.

The objectives of this study were to determine the safety and activity of this combination in malignant gliomas.

Methods and Materials

After prior treatment with standard radiation therapy patients with recurrent glioblastoma (GBM) and anaplastic gliomas (AG) received bevacizumab (10 mg/kg intravenous) every 2 weeks of 28-day cycles until tumor progression. Patients also received 30 Gy of hypofractionated stereotactic radiotherapy (HFSRT) in five fractions after the first cycle of bevacizumab.

Results

Twenty-five patients (20 GBM, 5 AG; median age 56 years; median Karnofsky Performance Status 90) received a median of seven cycles of bevacizumab. One patient did not undergo HFSRT because overlap with prior radiotherapy would exceed the safe dose allowed to the optic chiasm. Three patients discontinued treatment because of Grade 3 central nervous system intratumoral hemorrhage, wound dehiscence, and bowel perforation. Other nonhematologic and hematologic toxicities were transient. No radiation necrosis was seen in these previously irradiated patients. For the GBM cohort, overall response rate was 50%, 6-month progression-free survival was 65%; median overall survival was 12.5 months, and 1-year survival was 54%.

Discussion

Bevacizumab with HFSRT is safe and well tolerated. Radiographic responses, duration of disease control, and survival suggest that this regimen is active in recurrent malignant glioma.

Author Keywords: Malignant gliomas; Glioblastoma; Bevacizumab; Anti-angiogenesis; Intensity-modulated radiation therapy

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Discussion

Acknowledgements

References

ClinicalTrials.gov Identifier: NCT00595322.

This study has been presented in part at the 2007 Annual Meeting of the American Society of Clinical Oncology (Chicago, June 1–5, 2007) at the 49th Annual Meeting of the American Society for Therapeutic Radiology and Oncology (Los Angeles, October 28–November 1, 2007), at the 16th Annual Meeting of the International Society for Magnetic Resonance in Medicine (Toronto, May 3–9, 2008), and at the 46th Annual Meeting of the American Society of Neuroradiology (New Orleans, May 31–June 5, 2008).

Conflict of interest: Drs. Abrey and Gutin received research support and consultation fees from Genentech.



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