Concurrent Bevacizumab and Radiosurgery for Recurrent Malignant Glioma: Toxicity Results from a Prospective Pilot Study


Duke University Medical Center, Departments of Radiation Oncology and Neurosurgery, Durham, NC

BACKGROUND

Most patients with a malignant glioma recur after primary therapy. Bevacizumab has been shown in phase II trials to improve disease free survival in patients with recurrent glioma. Retrospective studies of stereotactic radiosurgery (SRS) and bevacizumab (BVZ) for recurrent glioma have also suggested improved outcomes.

METHODS

Patients with a recurrent unifocal grade III or IV malignant glioma who were no longer responsive to chemotherapy were eligible for this IRB-approved pilot study. All patients were imaged with MRI and CT for SRS planning. The contrast-enhancing lesion on T1-weighted MRI was expanded 1 mm to yield the planning target volume. Lesions <2 cm and 2-2.9 cm in size were prescribed 24 and 18 Gy in a single fraction, respectively. Lesions measuring 3-5 cm were prescribed 25 Gy in 5 fractions. Subjects received BVZ 10 mg/kg the first day of SRS and 14 days later. The primary endpoint of the study was toxicity. Secondary endpoints included progression-free and overall survival, cognitive function, and performance status. Adverse events were scored using the NCI Common Terminology Criteria. Patients underwent baseline cognitive testing which was repeated 1 week and 2 months after SRS using the Mini-Mental State Exam (MMSE) and Trail Making Tests A and B (TMT).

RESULTS

15 subjects were enrolled between January 2010 and January 2011, completing targeted accrual. Median age and KPS at the time of SRS were 53 years (range 25-66) and 90 (range 80-100), respectively. 14 of 15 patients included in the study were previously treated with a BVZ-containing regimen. Median time from primary diagnosis to salvage SRS was 19.6 months. No patient experienced a cerebrovascular accident or thrombotic event. No grade 4/5 adverse events were seen and one patient experienced grade 3 headache requiring hospitalization. There were 5 possible treatment-related grade 2 adverse events including neuropathy, cognitive disturbance, dizziness, and fatigue. TMT scores did not significantly decrease 1 week or 2 months following SRS versus baseline. MMSE scores decreased no more than one point in any patient at 2 months compared to baseline. Median survival from the time of SRS is 14.5 months (95% CI 6-16 months).

CONCLUSIONS

Treatment with stereotactic radiosurgery and BVZ in heavily pre-treated patients with a recurrent malignant glioma appears well-tolerated. Further follow-up in a larger patient cohort is needed to test the efficacy of this approach.