Phase II Trial of Radiosurgery to Magnetic Resonance Spectroscopy-Defined High-Risk Tumor Volumes in Patients with Glioblastoma Multiforme.


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Abstract

PURPOSE: To determine the efficacy of a Gamma Knife stereotactic radiosurgery (SRS) boost to areas of high risk determined by magnetic resonance spectroscopy (MRS) functional imaging in addition to standard radiotherapy for patients with glioblastoma (GBM).

METHODS AND MATERIALS: Thirty-five patients in this prospective Phase II trial underwent surgical resection or biopsy for a GBM followed by SRS directed toward areas of MRS-determined high biological activity within 2 cm of the postoperative enhancing surgical bed. The MRS regions were determined by identifying those voxels within the postoperative T2 magnetic resonance imaging volume that contained an elevated choline/N-acetylaspartate ratio in excess of 2:1. These voxels were marked, digitally fused with the SRS planning magnetic resonance image, targeted with an 8-mm isocenter per voxel, and treated using Radiation Therapy Oncology Group SRS dose guidelines. All patients then received conformal radiotherapy to a total dose of 60 Gy in 2-Gy daily fractions. The primary endpoint was overall survival.

RESULTS: The median survival for the entire cohort was 15.8 months. With 75% of recursive partitioning analysis (RPA) Class 3 patients still alive 18 months after treatment, the median survival for RPA Class 3 has not yet been reached. The median survivals for RPA Class 4, 5, and 6 patients were 18.7, 12.5, and 3.9 months, respectively, compared with Radiation Therapy Oncology Group radiotherapy-alone historical control survivals of 11.1, 8.9, and 4.6 months. For the 16 of 35 patients who received concurrent temozolomide in addition to protocol radiotherapeutic treatment, the median survival was 20.8 months, compared with European Organization for Research and Treatment of Cancer historical controls of 14.6 months using radiotherapy and temozolomide. Grade 3/4 toxicities possibly attributable to treatment were 11%.

CONCLUSIONS: This represents the first prospective trial using selective MRS-targeted functional SRS combined with radiotherapy for patients with GBM. This treatment is feasible, with acceptable toxicity and patient survivals higher than in historical controls. This study can form the basis for a multicenter, randomized trial.

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