Clinical Investigation

Investigating the Effect of Reirradiation or Systemic Therapy in Patients With Glioblastoma After Tumor Progression: A Secondary Analysis of NRG Oncology/Radiation Therapy Oncology Group Trial 0525

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Summary

Optimal treatment for glioblastoma patients who progress after standard treatment chemotherapy remains unknown. We analyzed data from Trial RTOG 0525 to investigate the effect of reirradiation or systemic treatment on survival after progression. Salvage treatment options were found to be highly variable. Patients who received no salvage treatment had significantly shorter survival than those treated after progression. There was no significant survival difference among patients receiving systemic therapy (alone or with radiation) or radiation alone.

Introduction

Optimal management for recurrent glioblastoma (GBM) has not been established. A plethora of monotherapy and combination therapies have been evaluated. Such approaches include surgery, reirradiation, systemic therapy either with chemotherapy and/or targeted therapeutics or antiangiogenic agents, tumor treatment fields, or some combination of these, as well as supportive care (1-6). A variety of chemotherapies have been evaluated for recurrent GBM, with modest results. Recently bevacizumab, an anti-vascular endothelial growth factor monoclonal antibody, was evaluated for recurrent GBM. Phase 2 studies demonstrated favorable 6-month progression-free survival and objective responses with bevacizumab for recurrent GBM, which led to its approval by the US Food and Drug Administration in 2009 for use in recurrent GBM (7-10). Currently bevacizumab is one of the most commonly used treatment options for patients with recurrent GBM in the United States. On the other hand, for patients with limited volume recurrence, reirradiation seems to provide similar overall survival (OS) in comparison with those treated with bevacizumab (11-13). Despite some evidence of improvement in progression-free survival, no significant increase in OS has been demonstrated with any particular approach (1, 14). Further investigations are needed to define the optimal choice of salvage therapy, and in particular the role of reirradiation and systemic treatment in patients with recurrent GBM.

Trial RTOG 0525 was a phase 3 clinical trial evaluating dose-dense versus standard-dose temozolomide for patients with newly diagnosed GBM (15). Patients were enrolled between January 2006 and June 2008, and primary study findings were published in 2013, where more details of the study design and results can be found (15). All patients received 60 Gy partial-brain irradiation in 2-Gy daily fractions. After progression, patients participating in this trial received variable salvage therapies (reported as nonprotocol therapy). The information on the type of nonprotocol therapy is available for analysis. The purpose of this study was to determine the impact on OS with different salvage therapies, including no treatment, reirradiation, systemic therapy, or radiation and systemic therapy, in those Trial RTOG 0525 participants. Information from this analysis may help generate new hypotheses for future clinical trials.

Methods and Materials

A total of 833 patients were enrolled and randomized in Trial RTOG 0525. We analyzed postprogression prognosis
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