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Clinical Investigation

Phase I Three-Dimensional Conformal Radiation Dose Escalation Study in Newly Diagnosed Glioblastoma: Radiation Therapy Oncology Group Trial 98-03

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Purpose

To evaluate in a Phase I trial the feasibility and toxicity of dose-escalated three-dimensional conformal radiotherapy (3D-CRT) concurrent with chemotherapy in patients with primary supratentorial glioblastoma (GBM).

Methods and Materials

A total of 209 patients were enrolled. All received 46 Gy in 2-Gy fractions to the first planning target volume (PTV_1), defined as the gross tumor volume (GTV) plus 1.8 cm. A subsequent boost was given to PTV_2, defined as GTV plus 0.3 cm. Patients were stratified into two groups (Group 1: PTV_2 <75

cm^3; Group 2: PTV_2 ≥75 cm^3). Four RT dose levels were evaluated: 66, 72, 78, and 84 Gy. Carmustine 80 mg/m^2 was given during RT, then every 8 weeks for 6 cycles. Pretreatment characteristics were well balanced.

Results

Acute and late Grade 3/4 RT-related toxicities were no more frequent at higher RT dose or with larger tumors. There were no dose-limiting toxicities (acute Grade ≥3 irreversible central nervous system toxicities) observed on any dose level in either group. On the basis of the absence of dose-limiting toxicities, dose was escalated to 84 Gy in both groups. Late RT necrosis was noted at 66 Gy (1 patient), 72 Gy (2 patients), 78 Gy (2 patients), and 84 Gy (3 patients) in Group 1. In Group 2, late RT necrosis was noted at 78 Gy (1 patient) and 84 Gy (2 patients). Median time to RT necrosis was 8.8 months (range, 5.1–12.5 months). Median survival in Group 1 was 11.6–19.3 months. Median survival in Group 2 was 8.2–13.9 months.

Conclusions

Our study shows the feasibility of delivering higher than standard (60 Gy) RT dose with concurrent chemotherapy for primary GBM, with an acceptable risk of late central nervous system toxicity.

Author Keywords: 3D-CRT; Dose escalation; Glioblastoma

Article Outline