Chemotherapy plus concomitant low-dose fractionated radiotherapy as second-line treatment for recurrent or progressive glioblastoma after temozolomide-based chemoradiation: A pilot study.

G. R. D’Agostino, B. Diletto, S. Manfrida, A. Mangiola, S. Chiesa, L. De Filippo, V. Frascino, F. Micciche, C. Anile and M. Balducci

Department of Radiation Oncology, Catholic University of the Sacred Heart, Rome, Italy; Department of Neurosurgery, Catholic University of the Sacred Heart, Rome, Italy

Abstract

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Background: Second-line treatment in recurrent or progressive glioblastoma (GBM) has not yet been defined. Since in vitro and preclinical studies demonstrated a hyper-radiosensitivity of human malignant glioma cell lines to low doses fractionated radiotherapy (LD-FRT) and a synergism with chemotherapy, we performed a pilot study to evaluate the feasibility and efficacy of this approach.

Methods: Eligibility criteria were: radiological diagnosis of recurrent or progressive GBM, previously treated by surgical resection followed by 3D-CRT (total dose 59.4 Gy) plus concomitant and adjuvant TMZ. Patients with recurrent or progressive disease during adjuvant TMZ received 30 cGy twice a day on days 1-2, 8-9, 15-16, q42, concurrently with fotemustine (40 mg/m² on days 1, 8, 15) and cisplatin (30 mg/m² on days 2, 9, 16), whereas in patients with recurrent/progressive disease occurring more than 6 months after the end of adjuvant TMZ a re-challenge with TMZ (150/200 mg/m²) concurrently with LD-FRT (40 cGy twice a day, over consecutive 5 days, q28) was attempted. Primary endpoints were toxicity (RTOG criteria) and efficacy (RECIST criteria); Progression Free Survival (PFS) and Overall Survival (OS) were also evaluated.

Results: From February 2008 to January 2011, 20 patients were enrolled. The median total dose of LD-FRT was 760 cGy (range, 240-1200). The associated chemotherapy was based on cisplatin and fotemustine in 7 patients and on TMZ in 13 patients. Hematologic toxicity was mild, with a G3-4 (leucopenia) observed in 5% of patients; no treatment related death was observed. One out of 20 patients (5%) had a complete response, 1 patient (5%) experienced a partial response (PR), while 5 patients (25%) had a stable disease (SD) lasting at least 8 weeks (Clinical Benefit 35%). The median PFS and OS from relapse were 5 and 7 months, respectively; survival rate at 6 months was 58.7 % with an OS at 1 year of 26.7 %. No differences were observed between the two schedules of chemotherapy.

Conclusions: These data suggest that chemotherapy plus LD-FRT as second-line treatment is safe and well tolerated, encouraging the prosecution of the study.