Protracted administration of low doses of temozolomide (TMZ) in the treatment of relapse glioblastoma (GBM) enhances the antitumor activity of this agent

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Background: The efficacy of temozolomide (TMZ) is strictly related to the possibility to reach and maintain high and prolonged cellular drug concentrations in the target tissue. Evidence exists demonstrating that the achievement of this goal and the subsequent activity of TMZ are categorically schedule dependent. Aim of the present randomized phase II study is to verify whether a treatment schedule with TMZ appropriately modified induces better response rates along with a decrease of mielotoxicity as compared to the conventional one.

Methods: Twenty patients (5 F/15 M), median age of 53 years (range 35–74), median Karnofsky PS 90 (range 70–100), with GBM in progression after surgery and adjuvant RT have been treated as follows: Schedule A - TMZ for 5 days in a 28-day cycle, at the dose of 150 mg/m$^2$/d at the first cycle and of 200 mg/m$^2$/d thereafter, up to a total of 8 cycles. Schedule B - TMZ for 7 days alternating with 7 days of rest up to a total of 12 cycles: the starting dose of TMZ at the first cycle was 50 mg/m$^2$/d with progressive serial dose escalations of 25 mg/m$^2$/d in the subsequent ones until the achievement of the dose of 150 mg/m$^2$/d at the 5th cycle, and then keeping this regimen until the 12th cycle.

Results: They are summarized in the table: Severe thrombocytopenia and stomatitis have been observed only in patients treated with Schedule A.

Conclusions: These preliminary results, which deserve to be confirmed in a larger sample size, indicate that the treatment with TMZ on alternate week basis is strongly interesting and promising. In spite of the modality and the small number of patients included in this study, which doesn't allow a direct comparison between two different treatments, it should be noted that schedule B achieved a 2-year OS and PFS rate of 40% and 20% respectively, compared to 10% and 0% of schedule A.

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