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Temozolomide 3 weeks on and 1 week off as first-line therapy for recurrent glioblastoma: phase II study from gruppo italiano cooperativo di neuro-oncologia (GICNO)

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The efficacy of temozolomide strongly depends on O⁶-alkylguanine DNA-alkyl transferase (AGAT), which repairs DNA damage caused by the drug itself. Low-dose protracted temozolomide administration can decrease AGAT activity. The main end point of the present study was therefore to test progression-free survival at 6 months (PFS-6) in glioblastoma patients following a prolonged temozolomide schedule. Chemo-naïve glioblastoma patients with disease recurrence or progression after surgery and standard radiotherapy were considered eligible. Chemotherapy cycles consisted of temozolomide 75 mg/m²/daily for 21 days every 28 days until disease progression. O⁶-methyl-guanine-DNA-methyl-transferase (*MGMT*) was determined in 22 patients (66.7%). A total of 33 patients (median age 57 years, range 31–71) with a median KPS of 90 (range 60–100) were accrued. The overall response rate was 9%, and PFS-6 30.3% (95% CI:18–51%). No correlation was found between the *MGMT* promoter methylation status of the tumours and the overall response rate, time to progression and survival. In 153 treatment cycles delivered, the most common grade 3/4 event was lymphopenia. The prolonged temozolomide schedule considered in the present study is followed by a high PFS-6 rate; toxicity is acceptable. Further randomised trials should therefore be conducted to confirm the efficacy of this regimen.

Keywords: clinical trials; glioblastoma; *MGMT*; prolonged temozolomide