Phase II study of dose-intense temozolomide in recurrent glioblastoma.


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Abstract Disclosures

Abstract

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**Background:** Most GBM patients relapse within 1 year from diagnosis. Among patients who progress on standard temozolomide, the optimal therapy is unknown. Resistance to temozolomide is partially mediated by the DNA repair enzyme, O\(^{6}\)-methylguanine-DNA methyltransferase (MGMT). Since MGMT may be depleted by prolonged temozolomide administration, dose-intense schedules may overcome resistance in patients with recurrent GBM.

**Methods:** This is a phase 2 single arm study of temozolomide 75-100 mg/m\(^2\)/day for 21 days of each 28-day cycle. Patients have GBM in first recurrence following standard therapy, including at least 2 cycles of adjuvant temozolomide. The primary endpoint is 6-month progression-free survival (PFS6).

**Results:** Forty-eight participants have been accrued, one of whom withdrew prior to treatment. There are 26 men (55%), median age 57 (range 25-74), median KPS 90 (range 60-100). Of 40 patients with MGMT methylation results, 7 are methylated (17.5%). There were 6 (13%) partial responses (PR). Eighteen patients (38%) achieved stable disease (SD). Median PFS was 10 weeks (95% CI: 8-17) and PFS6 23%. Median OS was 13 months (95% CI: 8-17) and PFS6 23%. Median OS was 13 months (95% CI: 8-17). Patients with methylated MGMT had median PFS 7.4 months (95% CI 1.9-15.6), and unmethylated promoters 2 months (95% CI 1.9-3.8; p=0.08). Median OS in methylated patients was 16 months (95% CI 16-Not yet reached), unmethylated 11.5 months (95% CI 8-Not yet reached; p=0.05). The probability of achieving PR/SD was higher in patients with MGMT methylation (p=0.03). Response, PFS, and OS did not depend on the number of prior temozolomide cycles or the time off temozolomide. Treatment was well tolerated with limited Grade 3 neutropenia (n=3) or thrombocytopenia (n=4).

**Conclusions:** Dose-intense temozolomide on a 21/28 day schedule is a safe regimen for patients with GBM in first recurrence. Updated efficacy results will be presented.