Phase II trial of Gliadel plus O6-benzylguanine in adults with recurrent glioblastoma multiforme.


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PURPOSE: This phase II trial was designed to define the efficacy of Gliadel wafers in combination with an infusion of O6-benzylguanine (O6-BG) that suppresses tumor O6-alkylguanine-DNA alkyltransferase (AGT) levels in patients with recurrent glioblastoma multiforme for 5 days and to evaluate the safety of this combination therapy.

EXPERIMENTAL DESIGN: This was a phase II, open-label, single center trial. On gross total resection of the tumor, up to eight Gliadel wafers were implanted. Bolus infusion of O6-BG was administered at 120 mg/m² over 1 hour on days 1, 3, and 5, along with a continuous infusion at 30 mg/m²/d. The primary end points were 6-month overall survival (OS) and safety, and the secondary end points were 1-year, 2-year, and median OS. RESULTS: Fifty-two patients were accrued. The 6-month OS was 82% [95% confidence interval (95% CI), 72-93%]. The 1- and 2-year OS rates were 47% (95% CI, 35-63%) and 10% (95% CI, 3-32%), respectively. The median OS was 50.3 weeks (95% CI, 36.1-69.4 weeks). Treatment-related toxicity with this drug combination included grade 3 hydrocephalus (9.6%), grade 3 cerebrospinal fluid (CSF) leak (19.2%), and grade 3 CSF/brain infection (13.4%).

CONCLUSION: The efficacy of implanted Gliadel wafers may be improved with the addition of O6-BG. Although systemically administered O6-BG can be coadministered with Gliadel wafers safely, it may increase the risk of hydrocephalus, CSF leak, and CSF/brain infection. Future trials are required to verify that inhibition of tumor AGT levels by O6-BG results in increased efficacy of Gliadel wafers without added toxicity.

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