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When Temozolomide Alone Fails: Adding Procarbazine in Salvage Therapy of Glioma

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Abstract:

Background: Since temozolomide (TMZ) entry into routine practice in the first-line management of glial tumors, post-TMZ recurrences present a growing challenge. Without standard chemotherapy for TMZ failure, care in such palliative settings requires consideration not only of efficacy but of toxicity and convenience. **Methods:** At our institution, a combination regimen has been used: oral alkylating agents procarbazine (PCB) (100-150 mg/m²/day) and TMZ (150-200 mg/m²/day) administered on days 1-5 of a 28-day cycle. This treatment has been initiated upon radiological and/or clinical disease progression, and continued until evidence of further progression or toxicity. We retrospectively reviewed our experience with this regimen. **Results:** Since November 2004, 17 patients (median age 53) were treated for histologically confirmed glioma (glioblastoma multiforme (GBM), N=12; Grade 3 glioma, N=3; Grade 2 glioma, N=2) after a median of 2 recurrences. TMZ was previously given either as adjuvant therapy (post-chemoradiotherapy maintenance in 8 of 13 cases) or as salvage monotherapy (4 cases). Of 16 evaluable cases, 14 (13 high grade tumors) showed O-6-methylguanine-DNA methyltransferase (MGMT) promoter methylation. Two patients achieved partial response and one had complete response by RECIST criteria. Disease progressed after a

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median of 4 cycles (range 1 to 11+), with an actuarial progression-free survival of 42% after 6 cycles. Grade 3/4 toxicity was rare, and no dose reductions were needed. One patient discontinued treatment due to procarbazine hypersensitivity. **Conclusion:** Combination PCB-TMZ is well-tolerated, with modest activity in TMZ-exposed glioma.

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