

Journal Article



Local intracerebral administration of O⁶-benzylguanine combined with systemic chemotherapy with temozolomide of a patient suffering from a recurrent glioblastoma

Journal	Journal of Neuro-Oncology
Publisher	Springer Netherlands
ISSN	0167-594X (Print) 1573-7373 (Online)
Subject	Medicine
Status	Online First™
Category	Clinical-Patient Studies
DOI	10.1007/s11060-006-9244-8
Online Date	Thursday, September 21, 2006

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Received: 19 May 2006 **Accepted:** 9 August 2006 **Published online:** 20 September 2006

Summary The DNA repair protein O⁶-methylguanine-DNA methyltransferase (MGMT) is a major determinant of methylating anticancer drug resistance. Inactivation of MGMT by pseudosubstrate inhibitors, such as O⁶-benzylguanine (O⁶BG), sensitizes tumor cells to O⁶-alkylating agents. However, systemic administration of O⁶BG causes depletion of MGMT in all tissues of the body. Therefore, dose reduction of O⁶-alkylating drugs administered together with O⁶BG is required in order to avoid unwished toxic side effects. To attenuate the increased systemic toxicity caused by MGMT inhibitors, local MGMT inactivation would be desirable. Here, we report on intracerebral treatment with O⁶BG of a patient suffering from glioblastoma. O⁶BG was administered weekly in the tumor cavity by means of an Ommaya reservoir. This application was well tolerated. Concomitant treatment with temozolomide (Temodal) was associated with transient tumor stabilization without detectable side effects. Although evidence is still lacking that local O⁶BG administration caused MGMT to be depleted in the residual tumor, the trial shows that intracerebral treatment with O⁶BG is feasible. It might be a safe strategy for improving glioma therapy by treatment with temozolomide (and presumably also other O⁶-alkylating drugs) concomitant with O⁶BG without augmenting drug-induced systemic side effects.

Keywords Glioblastoma - O⁶BG - Intracerebral administration - MGMT - Temozolomide



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