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MGMT promoter hypermethylation correlates with a survival benefit from temozolomide in patients with recurrent anaplastic astrocytoma but not glioblastoma

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Abstract

Aims

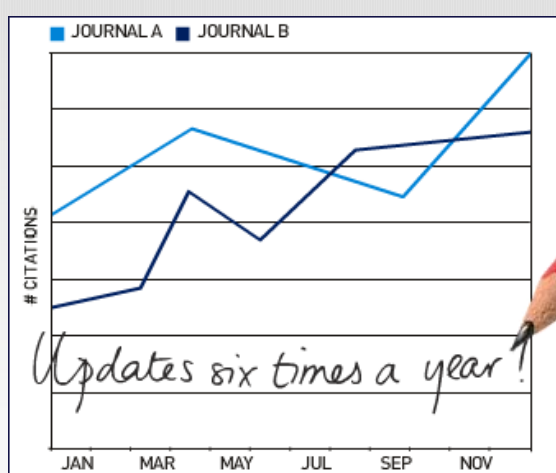
To investigate the correlation between O⁶-methylguanine-DNA-methyltransferase (MGMT) promoter methylation and benefit from temozolomide in patients with recurrent high-grade glioma.

Patients and methods

A real-time, quantitative, methylation-specific PCR assay was performed on

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archival tissue blocks from patients treated with temozolomide at the first recurrence.

Results

A subgroup of 38 patients who were chemotherapy-naive at recurrence was analysed (22 glioblastoma, 12 anaplastic astrocytoma [AA] and 4 anaplastic oligoastrocytoma [AOA]); none had 1p/19q loss. Among 10 (26%) patients with a hypermethylated MGMT promoter, none experienced disease progression within the first two treatment cycles compared with 12 of 28 (43%) patients with an unmethylated promoter ($p = 0.016$). By Cox multivariate analysis, tumour grade and MGMT promoter methylation correlated with time to progression ($p < 0.05$); MGMT promoter methylation correlated with superior overall survival in AA/AOA but not in glioblastoma.

Conclusions

MGMT promoter methylation predicted a survival benefit in patients with 1p/19q intact AA/AOA treated with temozolomide at recurrence.

Keywords: Extended dosing; High-grade glioma; MGMT; Recurrent; Temozolomide

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