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MGMT promoter methylation predicts overall survival after chemotherapy for 1p/19q-codeleted gliomas

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Abstract

Purpose: While MGMT promoter methylation (mMGMT) is predictive of response to alkylating chemotherapy and guides treatment decisions in glioblastoma, its role in grade 2 and 3 glioma remains unclear. Recent data suggests that mMGMT is prognostic of progression-free survival in 1p/19q-codeleted oligodendrogliomas, but an effect on overall survival (OS) has not been demonstrated.

Experimental design: We identified patients with newly diagnosed 1p/19q-codeleted gliomas and known MGMT promoter status in the National Cancer Database from 2010-2019. Multivariable Cox proportional hazards regression modeling was used to assess the effect of mMGMT on OS after adjusting for age, sex, race, co-morbidity, grade, extent of resection, chemotherapy, and radiotherapy.

Results: We identified 1,297 eligible patients, 938 (72.3%) of whom received chemotherapy in their initial course of treatment. The MGMT promoter was methylated in 1,009 (77.8%) patients. Unmethylated MGMT (uMGMT) was associated with worse survival compared to mMGMT (70% [95%CI 64-77%] vs. 81% [95%CI 78-85%], P<.001, adjusted hazard ratio [aHR] 2.35 [95%CI 1.77-3.14]). uMGMT was associated with worse survival in patients who received chemotherapy (63% [95%CI 55-73%] vs. 80% [95%CI 76-84%], P<.001, aHR 2.61 [95%CI 1.89-3.60]) but not in patients who did not receive chemotherapy (P=.38, HR 1.31 [95%CI 0.71- 2.42]). Similar results were observed regardless of WHO grade and after single- or multiagent chemotherapy.

Conclusions: Our study demonstrates an association between mMGMT and OS in 1p/19qcodeleted gliomas. MGMT promoter status should be considered as a stratification factor in future clinical trials of 1p/19q-codeleted gliomas that use OS as an endpoint.