ABSTRACT

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Survival outcomes associated with MGMT promoter methylation and temozolomide in gliosarcoma patients.

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PURPOSE: Gliosarcoma is an uncommon glioblastoma subtype, for which MGMT promoter methylation's relationship with response to temozolomide chemotherapy is unclear. We therefore examined this question using a national cohort.

METHODS: The National Cancer Database was queried for patients histopathologically diagnosed with gliosarcoma between 2010 and 2019. The associations between MGMT promoter methylation, first-line single-agent chemotherapy-presumed to be temozolomide herein-and overall survival (OS) were examined using log-rank tests and Cox regression, with correction for multiple testing ($p < 0.01$ was significant).

RESULTS: 580 newly-diagnosed gliosarcoma patients with MGMT status were available, among whom 33.6% were MGMT promoter methylated. Median OS for gliosarcoma patients that received standard-of-care temozolomide and radiotherapy was 12.1 months (99% confidence interval [CI] 10.8-15.1) for MGMT promoter unmethylated and 21.4 months (99% CI 15.4-26.2) for MGMT promoter methylated gliosarcomas ($p = 0.003$). In multivariable analysis of gliosarcoma patients-which included the potential confounders of age, sex, maximal tumor size, extent of resection, and radiotherapy-receipt of temozolomide was associated with improved OS in both MGMT promoter methylated (hazard ratio [HR] 0.23 vs. no temozolomide, 99% CI 0.11-0.47, $p < 0.001$) and unmethylated (HR 0.50 vs. no temozolomide, 99% CI 0.29-0.89, $p = 0.002$) gliosarcomas. MGMT promoter methylation was associated with improved OS among temozolomide-treated gliosarcoma patients ($p < 0.001$), but not in patients who did not receive chemotherapy ($p = 0.35$).

CONCLUSION: In a national analysis of gliosarcoma patients, temozolomide was associated with prolonged OS irrespective of MGMT status. These results provide support for the current practice of trimodal therapy for gliosarcoma.

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