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MGMT promoter methylation in 1p19q-intact gliomas

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Abstract

Objective: Standard-of-care for 1p19q-intact anaplastic gliomas is defined by the international randomized phase III CATNON trial, which found an overall survival (OS) benefit for adjuvant temozolomide (TMZ) when added to radiotherapy. Paradoxically, TMZ did not appear to benefit patients with IDH-wildtype gliomas, regardless of MGMT promoter status. The authors concluded that well-powered prospective study on the clinical efficacy of TMZ for patients with IDH-wildtype anaplastic gliomas (meeting criteria for glioblastoma) is warranted. Given that the prognostic and predictive role of MGMT status for grade 2-3 gliomas is unresolved, we determined the effect of MGMT status on OS in patients with 1p19q-intact gliomas in the National Cancer Database (NCDB).

Methods: We queried the NCDB from 2018 to 2019 for patients with diffuse (grade 2) and anaplastic (grade 3) IDH-wildtype or -mutant astrocytomas who received chemotherapy with follow-up through 2022. The Kaplan-Meier method and Cox proportional hazards regressions models were used to determine the association of MGMT with OS.

Results: We identified 1514 patients who were newly diagnosed with IDH-wildtype (n = 802, 33% methylated) or -mutant astrocytomas (n = 712, 48% methylated) and received chemotherapy during initial management. An unmethylated promoter was associated with poorer survival in patients with IDH-wildtype (3-year OS 34% [95%CI 29-39%] vs. 46% [95%CI 39-54%], p < .001, adjusted HR 1.53 [95%CI 1.24-1.89]) but not IDH-mutant astrocytomas (3-year OS 79% [95%CI 74-84%] vs. 80% [95%CI 75-86%], p =0 .81, HR 1.04 [95%CI 0.73-1.50]).

Conclusions: This ancillary analysis supports conclusions from the CATNON trial for adjuvant TMZ as standard-of-care for anaplastic astrocytomas (IDH-mutant and 1p19q-intact), irrespective of MGMT status. Determining the optimal strategy for diffuse gliomas that are IDH-wildtype will be particularly important. MGMT promoter methylation should be considered as a stratification factor in future clinical trials for these patients.

Keywords: 1p19q-intact; Chemotherapy; Glioma; MGMT.