MGMT promoter methylation in Gliosarcoma

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

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).

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 ($p = 0.35$).

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 [1].

1)
Kavouridis VK, Ligon KL, Wen PY, Iorgulescu JB. Survival outcomes associated with MGMT promoter methylation and temozolomide in gliosarcoma patients. J Neurooncol. 2022 Apr 26. doi: 10.1007/s11060-022-04016-5. Epub ahead of print. PMID: 35474499.