Prognostic or predictive value of MGMT promoter methylation in gliomas depends on IDH1 mutation.


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Abstract

OBJECTIVE: To explore whether the isocitrate dehydrogenase 1 (IDH1) or 1p/19q status determines the prognostic vs predictive role of O\(^6\)-methylguanine-DNA methyltransferase (MGMT) promoter methylation in the Neuro-Oncology Working Group of the German Cancer Society (NOA)-04 trial anaplastic glioma biomarker cohort.

METHODS: Patients (n = 183) of the NOA-04 trial with known MGMT and IDH1 status were analyzed for interdependency of the prognostic vs predictive role of MGMT promoter methylation from IDH1 or 1p/19q status and treatment, using progression-free survival (PFS) as an endpoint. An independent validation cohort of the German Glioma Network (n = 75) and the NOA-08 trial (n = 34) served as a confirmation cohort.

RESULTS: In tumors with IDH1 mutation, MGMT promoter methylation was associated with prolonged PFS with chemotherapy ± radiotherapy (RT) or RT-only groups, and is thus prognostic. In tumors without IDH1 mutation, MGMT promoter methylation was associated with increased PFS in patients treated with chemotherapy, but not in those who received RT alone as the first-line treatment, and is thus chemotherapy-predictive. In contrast, 1p/19q codeletions showed no such association with the prognostic vs predictive value of MGMT.

CONCLUSIONS: MGMT promoter methylation is a predictive biomarker for benefit from alkylating agent chemotherapy in patients with IDH1-wild-type, but not IDH1-mutant, malignant gliomas of World Health Organization grades III/IV. Combined IDH1/MGMT assessment may help to individualize clinical decision-making in neuro-oncology.

PMID: 24068788 [PubMed - as supplied by publisher]