Molecular predictors of progression-free and overall survival in patients with newly diagnosed glioblastoma: a prospective translational study of the German Glioma Network.


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Abstract

PURPOSE: The prognostic value of genetic alterations characteristic of glioblastoma in patients treated according to present standards of care is unclear.

PATIENTS AND METHODS: Three hundred one patients with glioblastoma were prospectively recruited between October 2004 and December 2006 at the clinical centers of the German Glioma Network. Two hundred fifty-eight patients had radiotherapy, 199 patients had temozolomide, 189 had both, and seven had another chemotherapy as the initial treatment. The tumors were investigated for TP53 mutation, p53 immunoreactivity, epidermal growth factor receptor, cyclin-dependent kinase CDK 4 or murine double minute 2 amplification, CDKN2A homozygous deletion, allelic losses on chromosome arms 1p, 9p, 10q, and 19q, O(6)-methylguanine methyltransferase (MGMT) promoter methylation, and isocitrate dehydrogenase 1 (IDH1) mutations.

RESULTS: Median progression-free (PFS) and overall survival (OS) were 6.8 and 12.5 months. Multivariate analysis revealed younger age, higher performance score, MGMT promoter methylation, and temozolomide radiochemotherapy as independent factors associated with longer OS. MGMT promoter methylation was associated with longer PFS (relative risk [RR], 0.5; 95% CI, 0.38 to 0.68; P < .001) and OS (RR, 0.39; 95% CI, 0.28 to 0.54; P < .001) in patients receiving temozolomide. IDH1 mutations were associated with prolonged PFS (RR, 0.42; 95% CI, 0.19 to 0.91; P = .028) and a trend for prolonged OS (RR, 0.43; 95% CI, 0.15 to 1.19; P = .10). No other molecular factor was associated with outcome.

CONCLUSION: Molecular changes associated with gliomagenesis do not predict response to therapy in glioblastoma patients managed according to current standards of care. MGMT promoter methylation and IDH1 mutational status allow for stratification into prognostically distinct subgroups.

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