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Optimal MGMT promoter methylation cut-off to predict better survival in glioblastoma patients undergoing gross-total resection

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Abstract

Background: O6-Methylguanine-DNA methyltransferase (MGMT) promoter percentage of methylation in gliomas has been proved to be the most important predictive factor in temozolomide (TMZ) response. Nevertheless, an agreement about the cut-off to discriminate between a "methylated" and "unmethylated" status has not been reached yet. Many reports have analyzed the correlation between methylated status cut-off and survival, but they lacked sample homogeneity. Our aim was to calculate a clinical significant cut-off considering a homogenous group of patients.

Methods: We retrospectively analyzed 96 patients who underwent a complete removal of glioblastoma in our Institution. All the patients underwent to radiation therapy plus concomitant TMZ and twelve cycles of adjuvant TMZ as described by Stupp. Receiver operating characteristic (ROC) curve analysis was performed and 21% was determined as the optimal cut-off.

Results: The median OS was significantly higher in methylated patients compared to unmethylated ones (median 48 months vs 22 months respectively 95% CI 30-42 vs. 15-19, P<0.001). No difference was observed for PFS. The multivariate analysis with Cox regression model identified MGMT methylation status as an independent predictive factor for OS (P<0.001).

Conclusions: We confirmed the prognostic role of MGMT methylation status even in a highly selective group of patients with the best outcome. We calculated a cut-off of 21% to be highly predictable of survival.