Combined analysis of TERT, EGFR, and IDH status defines distinct prognostic glioblastoma classes.


Abstract

OBJECTIVE: To identify the prognostic significance of TERT promoter mutations (TERTp-mut) and their associations with common molecular alterations in glioblastomas (GBMs).

METHODS: We sequenced the TERTp-mut in DNA from 395 GBMs and analyzed the results with their respective histology, genetic profile (IDH1 mutation, EGFR amplification, CDKN2A homozygous deletion, loss of chromosome 10, TP53 mutation), and overall survival (OS).

RESULTS: TERTp-mut were found in 299 of 395 GBMs (75.7%) and were associated with an older age (median 59.6 years for TERTp-mut vs 53.6 years for TERT promoter wild type [TERTp-wt], p < 0.0001). TERTp-mut was an independent factor of poor prognosis (OS = 13.8 vs 18.4 months), in both IDH-mutated (OS = 13.8 vs 37.6 months, p = 0.022) and IDH-wt GBMs (OS = 13.7 vs 17.5 months, p = 0.006). TERTp-mut was associated with IDH-wt, EGFR amplification, CDKN2A deletion, and chromosome 10q loss, but not with MGMT promoter methylation. In the TERTp-wt group, OS was twice longer in EGFR-wt than in EGFR amplification GBMs (OS = 26.6 vs 13.3 months; p = 0.005). In the EGFR-wt group, patients with TERTp-wt had a significantly better outcome (OS = 26.3 vs 12.5 months, p < 0.0001), whereas in the EGFR amplification group, patients with TERTp-mut survived longer (OS = 15.8 vs 13.3 months, p = 0.05). Taken together, the absence of both EGFR amplification and TERTp-mut is associated with longer survival in patients with GBM (26.5 months for patients with IDH-wt, 36.7 months for patients with IDH mutation).

CONCLUSIONS: The analysis of TERTp-mut, in combination with EGFR amplification and IDH mutation status, refines the prognostic classification of GBMs.

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Comment in

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