Prolonged survival with valproic acid use in the EORTC/NCIC temozolomide trial for glioblastoma.


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Abstract

OBJECTIVE: This analysis was performed to assess whether antiepileptic drugs (AEDs) modulate the effectiveness of temozolomide radiochemotherapy in patients with newly diagnosed glioblastoma.

METHODS: The European Organization for Research and Treatment of Cancer (EORTC) 26981-22981/National Cancer Institute of Canada (NCIC) CE.3 clinical trial database of radiotherapy (RT) with or without temozolomide (TMZ) for newly diagnosed glioblastoma was examined to assess the impact of the interaction between AED use and chemoradiotherapy on survival. Data were adjusted for known prognostic factors.

RESULTS: When treatment began, 175 patients (30.5%) were AED-free, 277 (48.3%) were taking any enzyme-inducing AED (EIAED) and 135 (23.4%) were taking any non-EIAED. Patients receiving valproic acid (VPA) only had more grade 3/4 thrombopenia and leukopenia than patients without an AED or patients taking an EIAED only. The overall survival (OS) of patients who were receiving an AED at baseline vs not receiving any AED was similar. Patients receiving VPA alone (97 [16.9%]) appeared to derive more survival benefit from TMZ/RT (hazard ratio [HR] 0.39, 95% confidence interval [CI] 0.24-0.63) than patients receiving an EIAED only (252 [44%]) (HR 0.69, 95% CI 0.53-0.90) or patients not receiving any AED (HR 0.67, 95% CI 0.49-0.93).

CONCLUSIONS: VPA may be preferred over an EIAED in patients with glioblastoma who require an AED during TMZ-based chemoradiotherapy. Future studies are needed to determine whether VPA increases TMZ bioavailability or acts as an inhibitor of histone deacetylases and thereby sensitizes for radiochemotherapy in vivo.

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