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Abstracts

ATNT-10. DOES VALPROIC ACID IMPROVE SURVIVAL IN GLIOBLASTOMA? A META-ANALYSIS OF RANDOMIZED TRIALS IN NEWLY DIAGNOSED GLIOBLASTOMA

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Several small uncontrolled retrospective case series as well as a post-hoc analysis of the registration trial for temozolomide in newly diagnosed glioblastoma (Weller et al., 2011) have indicated an association between valproic acid (VPA) use and improved outcome in patients with newly diagnosed glioblastoma. To confirm the hypothesis generated based on the analysis of the temozolomide registration trial, we performed a combined analysis of a survival association of AED use at the start of chemoradiotherapy with temozolomide in the pooled patient cohort (n = 1869) of four contemporary randomized clinical trials in newly diagnosed glioblastoma: AVAGlio (NCT00943826), RTOG-0825 (NCT00884741), CENTRIC (NCT00689221) and CORE (NCT00813943). Progression-free (PFS) and overall survival (OS) were compared between (i) VPA versus no AED, (ii) VPA versus enzyme-inducing (EI)-AED, or (iii) VPA versus other non-EI-AED (without VPA). Results of Cox regression models stratified by trial and adjusted baseline prognostic factors including O^6-methylguanine DNA methyltransferase (MGMT) promoter methylation status were interpreted. The same analyses were performed with levetiracetam (LEV). VPA use at the start of chemoradiotherapy was not associated with improved PFS or OS compared with patients receiving no AED (PFS: hazard ratio (HR) = 0.92, 95% confidence interval (CI) 0.75-1.13, p = 0.41; OS: HR = 1.00, 95% CI 0.80-1.25, p = 0.95), EI-AED (PFS: HR = 0.95, 95% CI 0.74-1.21, p = 0.62; OS: HR = 1.02, 95% CI 0.0.77-1.33, p = 0.93) or non-EI-AED (PFS: HR = 1.02, 95% CI 0.80-1.3, p = 0.92; OS: HR = 1.06, 95% CI 0.83-1.35, p = 0.67). Similarly, no association with outcome was seen for LEV use. This pooled analysis did not validate an association of VPA or LEV use with improved survival, challenging the need for a full phase III trial exploring the repurposing of VPA or LEV as add-on to the standard of care treatment of newly diagnosed glioblastoma.