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# Valproic acid as a radio-sensitizer in glioma: A systematic review and meta-analysis

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## Abstract

**Background:** Histone deacetylase inhibitors (HDACi) including valproic acid (VPA) have the potential to improve radiotherapy (RT) efficacy and reduce treatment adverse events (AE) via epigenetic modification and radio-sensitization of neoplastic cells. This systematic review and meta-analysis aimed to assess the efficacy and AE associated with HDACi used as radio-sensitizers in adult solid organ malignancy patients.

**Methods:** A systematic review utilized electronic searches of MEDLINE(Ovid), Embase(Ovid), The Cochrane Library, and the International Clinical Trials Registry Platform to identify studies examining the efficacy and AEs associated with HDACi treatment in solid organ malignancy patients undergoing RT. Meta-analysis was performed with overall survival (OS) reported as hazard ratios (HR) as the primary outcome measure. OS reported as median survival difference, and AEs were secondary outcome measures.

**Results:** Ten studies reporting on the efficacy and/or AEs of HDACi in RT-treated solid organ malignancy patients met inclusion criteria. All included studies focused on HDACi valproic acid (VPA) in high-grade glioma patients, of which 9 studies ($n$ = 6138) evaluated OS and 5 studies ($n$ = 1055) examined AEs. The addition of VPA to RT treatment protocols resulted in improved OS (HR = 0.80, 95% CI 0.67-0.96). No studies focusing on non-glioma solid organ malignancy patients, or non-VPA HDACi met the inclusion criteria for this review.

**Conclusions:** This review suggests that glioma patients undergoing RT may experience prolonged survival due to HDACi VPA administration. Further randomized controlled trials are required to validate these findings. Additionally, more research into the use of HDACi radio-adjuvant treatment in non-glioma solid organ malignancies is warranted.

**Keywords:** central nervous system neoplasm; glioma; histone deacetylase inhibitor; radiation-sensitizing agents; valproic acid.



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