

## ABSTRACT

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The effect of levetiracetam treatment on survival in patients with glioblastoma: a systematic review and meta-analysis.

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**BACKGROUND:** Levetiracetam (LEV) is an anti-epileptic drug (AED) that sensitizes glioblastoma (GBM) to temozolomide (TMZ) chemotherapy by inhibiting O6-methylguanine-DNA methyltransferase (MGMT) expression. Adding LEV to the standard of care (SOC) for GBM may improve TMZ efficacy. This study aimed to pool the existing evidence in the literature to quantify LEV's effect on GBM survival and characterize its safety profile to determine whether incorporating LEV into the SOC is warranted.

**METHOD:** A search of CINAHL, Embase, PubMed, and Web of Science from inception to May 2021 was performed to identify relevant articles. Hazard ratios (HR), median overall survival, and adverse events were pooled using random-effect models. Meta-regression, funnel plots, and the Newcastle-Ottawa Scale were utilized to identify sources of heterogeneity, bias, and statistical influence.

**RESULTS:** From 20 included studies, 5804 GBM patients underwent meta-analysis, of which 1923 (33%) were treated with LEV. Administration of LEV did not significantly improve survival in the entire patient population (HR 0.89,  $p = 0.094$ ). Significant heterogeneity was observed during pooling of HRs ( $I^2 = 75\%$ ,  $p < 0.01$ ). Meta-regression determined that LEV treatment effect decreased with greater rates of MGMT methylation (RC = 0.03,  $p = 0.02$ ) and increased with greater proportions of female patients (RC = -0.05,  $p = 0.002$ ). Concurrent LEV with the SOC for GBM did not increase odds of adverse events relative to other AEDs.

**CONCLUSIONS:** Levetiracetam treatment may not be effective for all GBM patients. Instead, LEV may be better suited for treating specific molecular profiles of GBM. Further studies are necessary to identify optimal GBM candidates for LEV.

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