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Effect of Levetiracetam(LEV) on Survival in Patients with Glioblastoma(GBM): a Meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None financial support.

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 January 2024 and was last updated on 24 January 2024.

INTRODUCTION

Review question / Objective This study is performed to systematically summarize the existing literature to: (1) determine whether LEV has a clinically generalizable survival impact and (2) If it is beneficial, identify the type of patient for whom it is more beneficial.

Condition being studied Levetiracetam (LEV) is a relatively new anti-epileptic drug that recently became one of the most commonly prescribed drugs for seizures in patients with GBM . However, clinical benefits of LEV may not be limited to seizure control. Studies have reported that LEV inhibits MGMT transcription in GBM via a p53-mediated corepressor complex of mSin3A and HDAC1 and enhances apoptosis with TMZ . Retrospective studies have shown promising survival benefits in GBM patients treated with LEV . However, Single-agency studies are subject to biases from small sample sizes, patient selection, and variations in clinical practice that create non-generalizable results. Furthermore, Current systematic review and meta-analysis has generated contrary fndings, making it unclear whether LEV is a viable strategy . we summarized and meta-analyzed the relevant literature in the past 15 years to provide a certain reference value for clinical treatment consensus and guidelines.

METHODS

Participant or population Inclusion criteria for patients: GBM patients over 18 years old who underwent craniotomy or biopsy, and Application of levetiracetam during the course of the disease. Articles were excluded if any of the following were met: (1)focuses on GBM cases not treated with surgery, recurrent GBM, or pediatric patients; (2)

does not stratify by GBM diagnosis and LEV treatment; or, (3) does not report relevant outcomes on survival or adverse events.

Intervention Intervention group（treatment group）: GBM patients treated with LEV.

Comparator Control group: GBM patients treated without LEV.

Study designs to be included Randomized controlled trials studies, non-randomized studies, prospective cohort studies and retrospective studies.

Eligibility criteria Our inclusion and exclusion criterias are all defined in the PICOS sections, no any additional criteria.

Information sources Embase®, PubMed®, Cochrane Library, Web of Science,CNKI.

Main outcome(s) Survival data for patients with glioblastoma, including PFS, OS, HR.

Quality assessment / Risk of bias analysis We adopted the Newcastle-Ottawa Scale (NOS), a general tool for literature quality evaluation to evaluate literature quality, mainly from three aspects: (1) selection of cases; (2) Comparability; (3) Evaluation of results; Full score is 9 point, more than 5 point means good quality. An assessment of reporting biases (such as publication bias) by constructing a funnel plot and using tests for funnel plot asymmetry was planned if there were at least ten studies included in the meta-analysis.

Strategy of data synthesis Binary outcomes were calculated as relative risk (RR). Statistical heterogeneity among studies was evaluated using Cochran's Q test and Higgins I2 statistics. If $I2 > 50\%$ or $p < 0.10$ (indicating significant heterogeneity among studies), the data were combined using a random effects model.

Subgroup analysis The subjects were divided into two subgroups, a male group and a female group, according to their gender.Subjects were divided into MGMT(+) and MGMT(-) groups according to their MGMT expression type.

Sensitivity analysis By excluding one document one by one, the remaining documents (n-1) are merged and analyzed, and by observing the changes in the merged results, it is assessed whether the original Meta-analysis results have changed significantly due to the influence of certain studies, so as to determine whether the original Meta-analysis results are stable.

Country(ies) involved China.

Keywords Glioblastoma, Levetiracetam , Survival, Temozolomide, meta-analysis.

Contributions of each author
Author 1 - Yongyi Zhang.
Author 2 - Zhongqian Sun.
Author 3 - Bin Zhang.
Author 4 - Junchen Zhang.