INPLASY PROTOCOL

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Corresponding author:
Hubin Duan

hubinduan68@163.com

Author Affiliation:
First Hospital of Shanxi Medical University

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The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Programmed cell death ligand 1 is a prognostic factor for glioblastoma: A systematic review and meta-analysis

Xiao, Y[1]; Hao, J[2]; Ren, X[3]; Yang, X[4]; Zhang, Y[5]; Wang, Z[6]; Zhu, X[7]; Bai, H[8]; Wang, H[9]; Hao, C[10]; Duan, H[11].

Review question / Objective: **The purpose of this study was to explore the relationship between programmed cell death ligand 1 (PD-L1) expression and prognosis of glioblastoma (GBM) by meta-analysis, so as to provide evidence of Evidence-based medical for the treatment and prognosis of GBM.**

Condition being studied: **Glioblastoma (GBM) is the most common primary malignant tumor of the central nervous system and has a poor prognosis with a short overall survival ranging from 8 to 14 months, the identification of a prognostic factor is essential to predict the prognosis of GBM patients accurately, Programmed death-ligand 1 (PD-L1) has shown great prognostic value in other solid cancers, but the prognostic value of PD-L1 expression in patients with GBM is still controversial. Therefore we conducted the present meta-analysis to clarify the association between the PD-L1 expression and the prognosis of GBM patients.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 July 2020 and was last updated on 18 July 2020 (registration number INPLASY202070079).

INTRODUCTION

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METHODS

Search strategy: We comprehensively searched for articles in Embase, Pubmed, The Cochrane Library, and Web of Science databases from the inception of each database to June 7, 2020. We designed one comprehensive search strategy, focusing on minimizing bias and maximizing sensitivity. The search strategy is designed as (glioblastoma OR GBM) AND('programmed cell death ligand 1' OR PD-L1 OR B7-H1 OR CD274) AND (prognosis OR 'prognostic value'). The reference list of included studies was scrutinized to identify any additional studies missed through the original search strategy.

Participant or population: The patients diagnosed with GBM.

Intervention: GBM patients with PD-L1 expression.

Comparator: GBM patients without PD-L1 expression.

Study designs to be included: Prospective, retrospective, or randomized clinical trial studies.

Eligibility criteria: The criteria for inclusion of eligible articles were listed as follows: (a) prospective or retrospective cohort studies investigating the correlation of PD-L1 expression with OS in patients with GBM. (b) Expressions of PD-L1 were detected by Immunohistochemical (IHC) Assay or RNA sequencing data from GBM specimens. (c) The results of articles should provide the hazard ratio (HR) and its 95% confidence intervals (95%CI) to estimate the relationship between PD-L1 expression and the OS of GBM patients, or the articles must provide the K-M curve, from which we could extract data about the HR. Furthermore, the following criteria were used to exclude irrelevant papers: (a) in-vitro or animal experiments. (b) the article was not written in English. (c) conference abstracts, reviews, correspondence, comments, and case reports.

Information sources: The database: Pubmed, web of science, embase, the cochrane library. If it have necessary, we will contact with authors.

Main outcome(s): The hazard ratios (HRs) and 95% confidence intervals (95%CIs) in overall survival (OS).

Quality assessment / Risk of bias analysis: The newsastle-ottawascale scale (NOS) was used to evaluate the quality of the literatures, articles with scores not less than 6 were regarded as high-quality . Publication bias was quantitatively analyzed by Begg's test and Egger's linear regression, and the reliability of meta-analysis results were tested by sensitivity analysis excluding individual studies. A p-value of <0.05 was considered significant publication bias.

Strategy of data synthesis: All of HRs and 95% CIs extracted from studies were analyzed by Stata 15.1 software, and the forest plot figures present the pooled HR and its 95%CI. An observed HR > 1 implied a worse prognosis; HR <1 indicated a better prognosis. A random-effects model was accepted when we observed high heterogeneity or extreme heterogeneity across studies; otherwise, a fixed-effect model was accepted when there was no high heterogeneity or extreme heterogeneity.

Subgroup analysis: Subgroup analysis was conducted, according to the region (Asia, other), patient type(GBM, recurrent GBM, grade IV glioma), indicator (protein, gene), cut-off availability(report, not report), sample size(>=100, =8, <8).

Sensibility analysis: The sensitivity analysis of the effect of PD-L1 expression on the OS was carried out by sequentially excluding studies.

Language: English.

Country(ies) involved: China.

Keywords: Programmed death-ligand 1 (PD-L1), prognostic factor, glioblastoma, overall survival, immunotherapy.

Contributions of each author:
Author 1 - Youchao Xiao - conception of the study, formal analysis, manuscript preparation and writing.
Author 2 - Jiaqi Hao - conception of the study, formal analysis, manuscript preparation and writing.
Author 3 - Xingguang Ren - conception of the study, formal analysis, manuscript preparation and writing.
Author 4 - Hubin Duan - academic instruction, funding acquisition, manuscript reviewing and editing.
Author 5 - Chunyan Hao - academic instruction, funding acquisition, manuscript reviewing and editing.
Author 6 - Huan Wang - academic instruction, funding acquisition, manuscript reviewing and editing.
Author 7 - Xin Yang - resources, software, literature quality evaluation.
Author 8 - Yu Zhang - resources, software, literature quality evaluation.
Author 9 - Xiaolin Zhu - data extraction, data curation, constructive discussions.
Author 10 - Zhangzhang Wang - data extraction, data curation, constructive discussions.
Author 11 - Hao Bai - data extraction, data curation, constructive discussions.