INPLASY

Prognostic significance of Lymphocyte-Activation Gene 3 (LAG3) in patients with solid tumors: A systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

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 16 August 2023 and was last updated on 16 August 2023.

INTRODUCTION

Review question / Objective We aimed to conduct a meta-analysis to provide a quantitative summary of the association between LAG3 expression and prognosis in patients with solid tumors. The survival outcomes were compared for patients with low or high expression of LAG3.

Condition being studied Patients diagnosed with solid tumors were included in this study. The expressions of LAG3 in tumor cells and/or TILs were reported, and patients were divided into two groups of high and low LAG3 expression. HRs and corresponding 95% CIs for LAG3 and survival outcomes were reported.

METHODS

Search strategy The Medical Subject Headings (MeSH) including in the search strategy were "neoplasms" and "LAG3", and the free terms were accessed in PubMed. Keywords and free terms were used in every possible combination by 2 Boolean operators ("AND" and "OR").

Participant or population Patients with solid tumors.

Intervention Patients with higher expression of LAG3.

Comparator Patients with lower expression of LAG3.

Study designs to be included Corhort studies and Randomized Clinical Trials.

Eligibility criteria (1) involved patients diagnosed with solid tumors; (2) The expressions of LAG3 in tumor cells and/or TILs were reported, and patients were divided into two groups of high and low LAG3 expression; (3) hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) for LAG3 and survival outcomes were reported; (4) randomized clinical trials, cohort studies, or case-control studies; (5) English language publication.

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Information sources The literature review was performed relying on three online databases: PubMed, EMBASE and the Cochrane Library until June 4th, 2023. The Medical Subject Headings (MeSH) including in the search strategy were "neoplasms" and "LAG3", and the free terms were accessed in PubMed. Keywords and free terms were used in every possible combination by 2 Boolean operators ("AND" and "OR"). Articles were individually evaluated and cross-checked by 2 reviewers. In addition, we manually scanned the reference list of excluded publications to indicate any additional viable non-duplicate studies. Any differences between the reviewers are resolved through discussion.

Main outcome(s) The primary outcome of this meta-analysis was overall survival (OS), and the secondary outcomes were disease-free survival (DFS), progression-free survival (PFS) and recurrence-free survival (RFS).

Additional outcome(s) The primary outcome of this meta-analysis was overall survival (OS), and the secondary outcomes were disease-free survival (DFS), progression-free survival (PFS) and recurrence-free survival (RFS).

Data management The 2 reviewers independently reviewed eligible studies and extracted the corresponding data to fill in pre-defined forms. The following data were extracted from each study: (I) publication data: authors, published year, and country; (II) study related data: study design, analysis method, expression level and location of LAG3,cut-off values of LAG3, the methods to evaluate LAG3 expression, and survival outcomes; (III) demographic data: sample size, cancer type, and treatment; (IV) outcome data: HRs and corresponding 95% CIs for overall survival (OS), disease-free survival (DFS), progression-free survival (PFS), and recurrence-free survival (RFS).

Quality assessment / Risk of bias analysis The quality of eligible cohort studies was evaluated using the Newcastle-Ottawa Quality Assessment Scale (NOS). We determined that studies with a score comparable to or higher than 6 were applicable to further meta-analysis. The Cochrane risk of bias tool was used to assess quality of randomized controlled trials (RCTs). The quality of each study was independently appraised by two reviewers. Any disagreement on quality assessment was resolved by discussion.

Strategy of data synthesis The pooled HRs and 95% CIs were calculated to evaluate the prognostic significance of LAG3 in patients with solid tumors, and random effects models were applied to calculate pooled effect sizes in order to decrease possible bias. The Cochrane Q test and I2 statistics were used to quantify the heterogeneity level, and an I2 greater than 50% is considered to have considerable heterogeneity.

Subgroup analysis Subgroup analyses were performed based on different types of tumor and LAG3 expression location.

Sensitivity analysis Sensitivity analyses were performed to further examine the stability of pooled estimates, in which the impact of each study on the overall estimates could be detected by omitting individual studies sequentially.

Language restriction English only.

Country(ies) involved China.

Other relevant information None

Keywords LAG3; solid tumor; prognosis; survival.

Dissemination plans None.

Contributions of each author

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