INPLASY PROTOCOL

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None declared.

The value of pretreatment prognostic nutritional index in predicting prognosis in lung cancer patients receiving immune checkpoint inhibitors-based treatment: A Systematic Review and Meta-Analysis

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Review question / Objective: **P:lung cancer patients receiving immune checkpoint inhibitors-based treatment I:lung cancer patients with high pretreatment prognostic nutritional index C:lung cancer patients with low pretreatment prognostic nutritional index O: Whether pretreatment prognostic nutritional index have value in predicting prognosis in lung cancer patients receiving immune checkpoint inhibitors-based treatment S:Meta-Analysis.**
Condition being studied: **Prognostic nutritional index (PNI) is an easily available index based on nutritional and immunological parameters, and has attracted much attention in recent years. PNI was calculated as: 10 × albumin (g/dl) + 0.005 × total lymphocyte count (per mm³). Since the introduction of PNI, many investigators have provided evidence that low PNI predicts cancer prognosis. Immune checkpoint inhibitors have substantially revolutionized the lung cancer therapeutic status by improving the survival of certain advanced or metastatic cancers. Although immune checkpoint inhibitors have shown incredible therapeutic efficacy and are largely well tolerated, they do not maintain a lasting response in all treated patients.A reliable biomarker will be helpful in predicting the therapeutic efficacy of immune checkpoint inhibitors and selecting potential patients benefiting from immune checkpoint inhibitors treatment.There have been several retrospective studies exploring the value of pretreatment prognostic nutritional index in predicting prognosis in lung cancer patients receiving immune checkpoint inhibitors-based treatment. But there are no meta-analysis related articles.The aim of this meta-analysis is to explore the prognostic value of the Prognostic nutritional index in lung cancer patients receiving treatment based on immune checkpoint inhibitors to explore the biomarker.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 April 2022 and was last updated on 15 April 2022 (registration number INPLASY202240087).

INTRODUCTION

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METHODS

Search strategy: Two investigators independently searched EMBASE, PubMed, Cochrane Library, American Society of Clinical Oncology (ASCO), European Society of Medical Oncology (ESMO), Wanfang and CNKI databases. In these databases, the following terms were used to search: prognostic nutritional index; PNI; immunotherapy; immune checkpoint inhibitor; programmed death ligand-1 inhibitor; programmed death-1 Inhibitor. These results include all published and unpublished studies, references to these documents are also read to avoid missing relevant studies. If there is disagreement about the results of the literature search and the quality of the literature, a third member of the team will review the results and discuss them to reach a consensus.

Participant or population: Lung cancer patients receiving immune checkpoint inhibitors-based treatment.

Intervention: Lung cancer patients with high pretreatment prognostic nutritional index.

Comparator: Lung cancer patients with low pretreatment prognostic nutritional index.

Study designs to be included: Retrospective study.

Eligibility criteria: (1) All patients in the clinical trial were diagnosed with lung cancer based on cytology or histology;(2) Patients in all of these clinical trials received treatments that included immune checkpoint inhibitors(ICIs); (3)All articles have prognostic survival outcomes associated with PNI in the articles, such as PFS or OS, and provide HRs with 95% confidence interval (CI) for these metrics. (4)Pretreatment PNI is data prior to receiving a regimen containing ICIs.

Information sources: EMBASE, PubMed, Cochrane Library, American Society of Clinical Oncology (ASCO), European Society of Medical Oncology (ESMO), Wanfang and CNKI databases.

Main outcome(s): Pretreatment PNI may effectively predict the prognosis of patients receiving immune checkpoints-based therapy for lung cancer. Patients with high pretreatment PNI may have better survival outcomes. Patients with low pretreatment PNI may predict a poorer prognosis.

Quality assessment / Risk of bias analysis: Two reviewers will independently assess risk of bias based on the following domains from recommendations from the Cochrane handbook: 1. Adequate sequence generation; 2. Allocation concealment; 3. Blinding; 4. Incomplete outcome data and how it was addressed; 5. Selective reporting of the outcome; 6. Any other biases. results of bias assessment will be presented in a figure and a graph indicating low, high or unclear risk of bias for each of the 6 items in each trial. Sensitivity analysis will be conducted based on the bias assessment to assess robustness of results.The chi-square test and the I^2 statistic were used to evaluate the statistical heterogeneity. When we observe significant heterogeneity($I^2 > 50\%$), we choose the random-effects model. When low($I^2 < 25\%$) or moderate heterogeneity ($25\% < I^2 < 50\%$) is observed, we use a fixed-effects model. We used Begg's and Egger's tests to assess article publication bias. We used sensitivity analysis to assess the robustness of pooled HR.

Strategy of data synthesis: STATA 16.0 statistical software was used to perform the analysis of the data. We chose survival outcomes (PFS and OS) as primary endpoints of our study. We use HRs and 95% CIs to evaluate the correlation between pretreatment PNI and survival outcomes in lung cancer patients receiving ICIs-based therapy. We used HR with 95% CI as a pooled analysis of survival outcomes and $P < 0.05$ is considered statistically significant.

Subgroup analysis: Subgroup analysis was performed according to the characteristics of the included studies such as country, sample size, PNI cut-off values, patient's treatment modality, and NOS score.

Sensitivity analysis: Sensitivity analysis was conducted using STATA software to determine the sensitivity of an article by the change in effect size after the removal of one of the articles.

Country(ies) involved: China.

Keywords: lung cancer; prognostic nutritional index; PNI; immunotherapy; immune checkpoint inhibitor; programmed death ligand-1 inhibitor; programmed death-1 Inhibitor.

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