INPLASY

Efficacy and Safety of PD-1/PD-L1 Blockade Combining Another Immunotherapy Versus PD-1/PD-L1 Blockade Alone in Patients with Solid Tumor: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - No financial support.

Review Stage at time of this submission - Data extraction.

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 July 2023 and was last updated on 16 July 2023.

INTRODUCTION

Review question / Objective This systematic review and meta-analysis will focus on the efficacy of combining PD-1/PD-L1 blockade with another immunotherapy versus the usage of PD-1/PD-L1 blockade alone in patients with advanced or metastatic solid tumor. Apart from clinical efficacy, the safety will also be taken into consideration to conclude whether the combination therapy would bring more clinical benefits to patients.

Condition being studied Patients with advanced or metastatic solid tumors will be included, such as melanoma, NSCLC and HNSCC. However, researches on patients with hematologic malignancies will be excluded.

METHODS

Participant or population Patients with advanced or metastatic solid tumors.

Intervention The combination of PD-1/PD-L1 blockade with another IO therapy, no matter it is immune checkpoint inhibitor or novel IO therapeutic agent.

Comparator The usage of PD-1/PD-L1 blockade alone.

Study designs to be included Phase 3 or phase 2 randomized controlled trials.

Eligibility criteria Studies on patients refractory to previous treatment or untreated are both eligible to be included. Receiving IO combination therapy as adjuvant, neoadjuvant or maintenance therapy are excluded. Trials carried out in the pediatric are not considered. IO therapies combining chemotherapy, radiotherapy, TKIs or anti-angiogenic agents are excluded.

Information sources PubMed, Embase, Scopus, Cochrane Library and ClinicalTrials.gov will be systematically researched. Online proceedings of annual conferences from 2018 to 2023 will also be

sourced, including ASCO, ESMO, CSCO and AACR.

Main outcome(s) Efficacy measured by incidence of objective response rate[ORR], hazard ratios[HR] with corresponding 95% confidence intervals[95%CI] for progression-free survival[PFS] and overall survival[OS]. Safety measured by incidence of any-grade and grade greater than or equal to 3 treatment-related adverse events[TRAEs].

Quality assessment / Risk of bias analysis The quality of the included studies was assessed using the Cochrane Risk of Bias Tool (2.0) for RCTs, which is based on the following five domains: risk of bias arising from the randomization process, risk of bias owing to deviations from the intended interventions, risk of bias from missing outcome data, risk of bias in the measurement of the outcome, and risk of bias in the selection of the reported results.

Strategy of data synthesis The STATA software will be used to perform data synthesis. Statistical heterogeneity and inconsistency will be evaluated using the statistic inconsistency index (I^2). An I^2 value greater than 50% is generally considered to indicate a substantial level of heterogeneity, and the random-effect model will be used. Otherwise, a fixed-effect model will be applied for data analysis.

Subgroup analysis Subgroup analysis of clinical outcomes based on the PD-L1 expression level of patients will be carried out. There will be subgroup analysis based on cancer type as well.

Sensitivity analysis Sensitivity analysis will be performed using the STATA software through observing the changes in outcomes after deletion of trials one by one.

Country(ies) involved China.

Keywords immunotherapy; immune checkpoint inhibitor; immune checkpoint blockade; PD-1 or PD-L1; cancer; randomized controlled trial.

Contributions of each author
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