INPLASY PROTOCOL

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Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest: **None.**

Retreatment with immune checkpoint inhibitors in solid tumors: a systematic review

Yang, K[1]; Li, J[2]; Zhao, L[3]; Sun, Z[4]; Bai, C[5].

Review question / Objective: **To investigate the efficacy and safety of retreatment with immune checkpoint inhibitors in patients with solid tumors.**
Condition being studied: **Immune checkpoint inhibitors (ICIs) have shown remarkable efficacy in multiple tumor types. Patients may discontinue ICIs due to trial design, progressive disease or unacceptable toxicity. However, the efficacy and toxicity of ICI retreatment are still unclear. Up to now, recommendations for the resumption of ICIs are largely based on consensus. Therefore, we conduct this systematic review to investigate the efficacy of retreatment with ICIs in patients with solid tumors.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 April 2020 and was last updated on 08 April 2020 (registration number INPLASY202040041).

INTRODUCTION

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trial design, progressive disease or unacceptable toxicity. However, the efficacy and toxicity of ICI retreatment are still unclear. Up to now, recommendations for the resumption of ICIs are largely based on consensus. Therefore, we conduct this systematic review to investigate the efficacy of retreatment with ICIs in patients with solid tumors.

METHODS

Participant or population: Patients with solid tumors.

Intervention: Retreatment with immune checkpoint inhibitors.

Comparator: Not applicable.

Study designs to be included: We will only include prospective studies.

Eligibility criteria: The eligibility criteria includes PICOS listed above.

Information sources: We will search (From January 2005 to April 2020): (1) Databases: MEDLINE, Embase, CENTRAL; (2) Trial registers: http://www.ClinicalTrials.gov ; (3) Conference abstracts: American Society of Clinical Oncology (ASCO), European Society of Medical Oncology (ESMO); (4) Reference lists of included records; Language restrictions were publications in English.

Main outcome(s): Overall response rate (ORR), disease control rate (DCR), incidence of grade 3/4 immune-related adverse events, overall survival (OS), progression-free survival (PFS).

Data management: A comprehensive literature search will be performed by two investigators independently. Studies will be selected based on the PICOS principle described above. Two authors will independently screen the titles/abstracts of all papers resulting from the literature search. The full texts of all eligible papers will be screened independently by two review authors. A standardised, pre-piloted form will be used to extract data from the included studies for assessment of study quality and evidence synthesis (Microsoft Excel). Any disprepancies during the literature selection and data extraction process will be solved by consensus (with a third author if necessary).

Quality assessment / Risk of bias analysis: The risk of bias of included studies will be independently assessed by two authors. Disprepancies will be solved by consensus (with a third author if necessary). Assessment tools to be used are listed as following: 1. RCTs: Cochrane risk of bias tool (Higgins JPT, Altman DG, Sterne, JAC (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0. The Cochrane Collaboration, 2011. Available from http://www.cochranehandbook.org.) 2. Non-randomized studies: Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) (Sterne JAC, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias innon-randomised studies of interventions. BMJ, 2016, 355) 3. Observational studies: Newcastle-Ottawa Scale (NOS) (Stang A. Critical evaluation of the NewcastleOttawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. European Journal of Epidemiology, 2010, 25(9):603-605).

Strategy of data synthesis: Information of included studies including study design, baseline patient characteristics, intervention, risk of bias (quality) assessment, and their primary outcomes will be collected and summarized in a table. If the study report insufficient statistical information to calculate effect measures, we will only describe the results of each study within the text qualitatively. If appropriate data is provided, we will perform a meta-analysis by using Stata 15.1. For time-to-event (i.e. survival) outcomes, we used Stata 15.1 to estimate pooled HRs and 95% CIs using the random effects model. For binary outcomes, we used Stata 15.1 to estimate pooled RRs

and 95% CIs using the random effects model.

Subgroup analysis: Not applicable.

Sensibility analysis: If a meta-analysis is conducted, sensitivity analysis will be performed by Stata 15.1 using the leave-one-out approach.

Language: Language will be restricted in English.

Country(ies) involved: China.

Dissemination plans: This study will be published on completion.

Keywords: Immune checkpoint inhibitor, retreatment, solid tumor.