INPLASY PROTOCOL

To cite: Shen et al. Effect of renin-angiotensin-aldosterone system inhibitors on survival outcomes in cancer patients treated with immune checkpoint inhibitors: a systematic review and meta-analysis. Inplasy protocol 2022110136. doi: 10.37766/inplasy2022.11.0136

Received: 25 November 2022

Published: 25 November 2022

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Support: **This work was supported by Center for New Drug Safety Evaluation and Research, China Pharmaceutical University.**

Review Stage at time of this submission: **Formal screening of search results against eligibility criteria.**

Conflicts of interest:
None declared.

Effect of renin-angiotensin-aldosterone system inhibitors on survival outcomes in cancer patients treated with immune checkpoint inhibitors: a systematic review and meta-analysis

Shen, JH[1]; Hou, H[2]; Liang, BW[3]; Guo, X[4]; Chen, L[5]; Wang, Y[6].

Review question / Objective: **Whether renin-angiotensin-aldosterone system inhibitors (RAASIs) will affect survival outcomes in cancer patients treated with immune checkpoint inhibitors (ICIs) ?**
Condition being studied: **Tumor immunotherapy.**
Eligibility criteria: **All available studies comparing survival outcomes between concomitant use of ICIs and RAASIs (intervention group) and ICI monotherapy or combined with other negative agents (comparator group) in cancer patients will be included.**
Information sources: **PubMed, EMBASE, Cochrane Library, Web of Science databases and major oncology conference proceedings.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 November 2022 and was last updated on 06 January 2023 (registration number INPLASY2022110136).

INTRODUCTION

Review question / Objective: **Whether renin-angiotensin-aldosterone system inhibitors (RAASIs) will affect survival outcomes in cancer patients treated with immune checkpoint inhibitors (ICIs) ?**

Condition being studied: Tumor immunotherapy.

METHODS

Participant or population: Cancer patients receiving ICIs with or without RAASIs.

Intervention: Patients concomitant use of RAASIs and ICIs.

Comparator: Patients receiving ICIs monotherapy or combined with other negative medications.

Study designs to be included: RCT, retrospective studies, prospective studies, post hoc analysis and meeting abstract with sufficient information will be included.

Eligibility criteria: All available studies comparing survival outcomes between concomitant use of ICIs and RAASIs (intervention group) and ICI monotherapy or combined with other negative agents (comparator group) in cancer patients will be included.

Information sources: PubMed, EMBASE, Cochrane Library, Web of Science databases and major oncology conference proceedings.

Main outcome(s): Overall survival (OS) and progression-free survival (PFS).

Quality assessment / Risk of bias analysis: Funnel plots with Egger's regression tests will be used to examine publication bias if there are more than 10 studies included in the meta-analysis. Quality assessment will be evaluated using the Newcastle-Ottawa Scale (NOS) for observational studies and the Cochrane risk of bias assessment tool for randomized control trials.

Strategy of data synthesis: Data synthesis will be performed on Hazard Ratios (HR) for OS and PFS. Cochrane Q tests and the I^2 index will be used to evaluate heterogeneity. If heterogeneity is significant (I^2 > 50%), a random-effects model will be used. Otherwise, a fixed-effects model will be calculated. Heterogeneity will be explored through subgroup analysis, meta regression, and sensitivity analysis. Stata (version 17.0, Stata Corp, College Station, TX, USA) will be used for all pooled analyses.

Subgroup analysis: Cancer type, ICIs type, time window of RAASIs use, RAASIs type, region, and analysis model are planned for subgroup analysis.

Sensitivity analysis: Sensitivity analysis will be performed to exam the stability of the results.

Language restriction: English.

Country(ies) involved: China Pharmaceutical University, Nanjing, Jiangsu Province, China, 211198.

Keywords: cancer; renin-angiotensin-aldosterone system inhibitors; immune checkpoint inhibitors; survival outcomes.

Contributions of each author:

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