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INPLASY

Treatment-related adverse events of immune checkpoint inhibitors in clinical trials: A systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - Not applicable.

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 29 August 2023 and was last updated on 29 August 2023.

INTRODUCTION

Review question / Objective To comprehensively assess the incidences and profiles of treatment-related adverse events of immune checkpoint inhibitors (ICI)-based cancer treatment combinations.

Condition being studied Trials have demonstrated the therapeutic effects of immune checkpoint inhibitors (ICI)-based cancer treatment combinations, and knowing the toxicity profiles of treatment-related adverse events is essential.

METHODS

Search strategy ((Immune Checkpoint Inhibitors[MeSH Terms]) OR (Checkpoint Inhibitors, Immune[Title/Abstract])) OR (Immune Checkpoint Inhibitor[Title/Abstract])) OR (Checkpoint Inhibitor, Immune[Title/Abstract])) OR (Immune Checkpoint Blockers[Title/Abstract])) OR (Checkpoint Blockers, Immune[Title/Abstract])) OR (Immune Checkpoint Blockade[Title/Abstract])) OR (Checkpoint Blockade, Immune[Title/Abstract])) OR (Immune Checkpoint Inhibition[Title/Abstract])) OR (Checkpoint Inhibition, Immune[Title/Abstract])) OR (PD-L1 Inhibitors[Title/Abstract])) OR (PD L1 Inhibitors[Title/Abstract])) OR (PD-L1 Inhibitor[Title/Abstract])) OR (PD L1 Inhibitor[Title/Abstract])) OR (Programmed Death-Ligand 1 Inhibitors[Title/Abstract])) OR (Programmed Death Ligand 1 Inhibitors[Title/Abstract])) OR (PD-1-PD-L1 Blockade[Title/Abstract])) OR (Blockade, PD-1-PD-L1[Title/Abstract])) OR (PD 1 PD L1 Blockade[Title/Abstract])) OR (CTLA-4 Inhibitors[Title/Abstract])) OR (CTLA 4 Inhibitors[Title/Abstract])) OR (CTLA-4 Inhibitor[Title/Abstract])) OR (CTLA 4 Inhibitor[Title/Abstract])) OR (Cytotoxic T-Lymphocyte-Associated Protein 4 Inhibitors[Title/Abstract])) OR (Cytotoxic T Lymphocyte Associated Protein 4 Inhibitors[Title/Abstract])) OR (Cytotoxic T-Lymphocyte-Associated Protein 4 Inhibitor[Title/Abstract])) OR (Cytotoxic T Lymphocyte Associated Protein 4 Inhibitor[Title/Abstract])) OR (PD-1 Inhibitors[Title/Abstract])) OR (PD 1 Inhibitors[Title/Abstract])) OR (PD-1 Inhibitor[Title/Abstract])) OR (Inhibitor, PD-1[Title/Abstract])) OR

(PD 1 Inhibitor[Title/Abstract])) OR (Programmed Cell Death Protein 1 Inhibitor[Title/Abstract])) OR (Programmed Cell Death Protein 1 Inhibitors[Title/Abstract])) OR (nivolumab[Title/Abstract])) OR (pembrolizumab[Title/Abstract])) OR (atezolizumab[Title/Abstract])) OR (ipilimumab[Title/Abstract])) OR (camrelizumab[Title/Abstract])) OR (toripalimab[Title/Abstract])) OR (tislelizumab[Title/Abstract])) OR (sintilimab[Title/Abstract])) OR (durvalumab[Title/Abstract])) OR (envafolimab[Title/Abstract])) OR (cemiplimab[Title/Abstract]).

Participant or population Patients with cancer at varies sites.

Intervention Ipilimumab, pembrolizumab, nivolumab, tremelimumab, atezolizumab, durvalumab, avelumab, camrelizumab, cemiplimab, tislelizumab, toripalimab, sintilimab, adebrelimab, and sugemalimab.

Comparator None.

Study designs to be included Randomized controlled trials.

Eligibility criteria The following selection criteria were used: (1) studies designed as RCTs and published in English; (2) trials included patients were concurrently received 2 categories of treatments, and at least one therapy was ICIs (ipilimumab, pembrolizumab, nivolumab, tremelimumab, atezolizumab, durvalumab, avelumab, camrelizumab, cemiplimab, tislelizumab, toripalimab, sintilimab, adebrelimab, and sugemalimab); (3) trials reporting tabulated data of trAEs, irAE, or specific AEs; and (4) sample size of trials was greater than ten.

Information sources PubMed, EmBase, and the Cochrane library.

Main outcome(s) All grade and grade 3 or more treatment-related adverse events, immune-related adverse events, and any specific adverse events.

Quality assessment / Risk of bias analysis The Cochrane risk of bias tool was used to assess the methodological quality according to random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases.

Strategy of data synthesis The random-effect models with a logit transformation were applied to pool the overall incidences and profiles of AEs, and the restricted maximum likelihood estimation was used to fit all models via a classic continuity correction of 0·5 for zero cells and sample sizes. The effect estimates were calculated using incidences with 95% confidence interval (CI), and a division method was used to calculate incidence.

Subgroup analysis Further exploratory analyses were performed to identify whether the incidences of all-grade and grade 3 or higher trAEs, irAEs, and specific AEs are differing based on the type of ICIs, and combined therapies.

Sensitivity analysis Not applicable.

Language restriction English.

Country(ies) involved China.

Keywords immune checkpoint inhibitors; adverse events; cancer; systematic review; meta-analysis.

Contributions of each author

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