INPLASY PROTOCOL

To cite: Liu et al. Immune-related and treatment-related adverse events in patients with gastrointestinal cancer: a systematic review and meta-analysis. Inplasy protocol 202230147. doi: 10.37766/inplasy2022.3.0147

Received: 25 March 2022

Published: 25 March 2022

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Support: **CSCO research fund.**

Review Stage at time of this submission: **Completed but not published.**

Conflicts of interest:
None declared.

Immune-related and treatment-related adverse events in patients with gastrointestinal cancer: a systematic review and meta-analysis

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Review question / Objective: **To summarize and evaluate adverse events (AEs) in patients with gastrointestinal cancer (GIC) following the use of different immune checkpoint inhibitor (ICIs) regimens.**
Condition being studied: **According to global oncology epidemiology, the number of new cases of GIC (including colon, stomach, rectal and esophageal cancers) was 3.57 million and the number of new deaths associated with GIC was 2.23 million, remaining a major public health challenge. At present, the main treatments for GIC include surgical resection, chemotherapy, radiotherapy, and biomolecular targeted therapy. Immune checkpoint inhibitors (ICIs) can induce tumor cell death by regulating the proliferation and activation of T cells thus have been approved to treat a variety of tumors including GIC. However, the adverse events (AEs) of the ICIs have gradually been observed since they can affect multiple systems and organs of the human body. Considering the increasing use of the immune related in clinical practice, and different AEs, we will conduct a systematic review and meta-analysis of clinical trials with different ICI regimens in patients with GIC, and further summarize the AE characteristics of different ICIs regimen in patients with GIC.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 March 2022 and was last updated on 25 March 2022 (registration number INPLASY202230147).

INTRODUCTION

Review question / Objective: **To summarize and evaluate adverse events (AEs) in patients with gastrointestinal cancer (GIC) following the use of different immune checkpoint inhibitor (ICIs) regimens.**

Rationale: **To describe the AEs of GIC patients using ICIs regimens, we will conduct a systematic search in 8**

databases: PubMed, Embase, Web of Science, Emcare, CNKI, Wanfang, VIP, and CBM using search terms related to ICIs, GIC, and randomized controlled trials design. There will be no limitation of time and language of publications. After the removal of duplicates, two investigators will screen the articles on the basis of the titles and abstracts, and the third senior author will make the judgment if dispute arises. We will extract the following study information independently by two investigators using a predefined data extraction form: 1) General characteristics of studies; 2) population characteristics; 3) Study methods; 4) Intervention information (drugs type, dose, frequency, and duration of intervention); 5) Outcomes (safety indicators that this systematic review will focuse on); 6) Study conclusions. Controversy will be resolved by discussion and by assistance of a third reviewer if necessary. For data analysis, we will use R software (4.1.1) to perform single arm meta-analysis (random effects model); and we will use SPSS (22.0) to perform chi-square test to compare the difference between pooled estimates from meta-analysis of different treatment groups.

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METHODS

Participant or population: Patients with GIC (including esophageal cancer, gastric cancer, colorectal cancer), and patients' age, gender, race, and previous treatment methods will not be limited.

Intervention: ICI monotherapy, dual ICIs therapy, or ICI combined with other therapies (chemotherapy, targeted drugs).

Comparator: No limitation.

Study designs to be included: Randomized controlled trials (RCTs).

Eligibility criteria: The study population will focus on patients with GIC (including esophageal cancer, gastric cancer, colorectal cancer), and there will be no limitation on age, gender, race, and previous treatment methods. Eligible interventions will include ICI monotherapy, dual ICIs therapy, or ICI combined with other therapies (chemotherapy, targeted drugs). We will include RCTs in which the intervention method includes any of the above schemes, no matter what the control was. We will exclude: case-control studies, cohort studies, cross-sectional studies, case series, case reports, reviews, correspondence and other research types; studies that were not reported in Chinese or English; studies which not reported any adverse events.

Information sources: We will conduct a systematic search in the databases of PubMed, Embase, Web of Science, Emcare, CNKI, Wanfang, VIP, and CBM.

Main outcome(s): Primary Outcome: Adverse events (AEs) after receiving ICI monotherapy, dual ICIs therapy, and ICI combined with other regimens (AEs of any grade; AEs of grade 3 or higher). The AEs will be categorized as treatment-related AEs (TRAEs) and immune-related AEs (irAEs). In general, TRAEs include irAEs.

Quality assessment / Risk of bias analysis: No quality assessment is involved.

Strategy of data synthesis: Risk ratio (RR) will be used to combine the outcome data. If there is 0 event in the control group, we will use Revman (5.3) peto odds to obtain the OR value, and then convert it into RR value using the formula: RR = OR/((1-P0) + (P0*OR)) (P0 is the incidence rate of disease in the non-exposed population).

Subgroup analysis: Subgroup analysis of ICI will combine with different treatment methods.

Sensitivity analysis: No sensitivity analysis is involved.

Country(ies) involved: China.

Keywords: Immune checkpoint inhibitors; treatment-related adverse events; immune-related adverse events; gastrointestinal cancer.

Contributions of each author:

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