INPLASY PROTOCOL

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None declared.

Cutaneous adverse events in patients treated with ICIs monotherapy and combination therapy: A pharmacovigilance and meta-analysis study

Zhang, HY[1].

Review question / Objective: **P: patients diagnosised with tumor I: ICI monotherapy or combination therapy with chmotherapy/targeted therapy/ICIs C: none O: incidence of dermatologic adverse events.**
Condition being studied: **The use of immune checkpoint inhibitors (ICIs) has ushered in a new era of cancer treatment, and achieved tremendous success in various cancer types. It was well known that ICI could lead to a variety of immune-related adverse events (irAEs).Among the various irAEs, cutaneous adverse event (AE) is one of the most frequently observed,especially skin rash, pruritus, and vitiligo, which was also suggested to be an adverse effect associated with patient survival. Stevens -Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but life threatening dermatologic adverse reactions. Thus, it is important to recognize and manage these events appropriately, and try to avoid discontinuation of immunotherapy if possible. To our knowledge, the present study is the largest and most extensive analysis of dermatologic adverse events associated with ICIs collected data from clinical trials.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 July 2022 and was last updated on 12 July 2022 (registration number INPLASY202270069).

INTRODUCTION

Review question / Objective: **P: patients diagnosised with tumor I: ICI monotherapy or combination therapy with chmotherapy/ targeted therapy/ICIs C: none O: incidence of dermatologic adverse events.**

Rationale: **Immune checkpoint inhibitors (ICIs) and their combination therapy with other cancer treatments are now the mainstream, which are also accompanied by various immune related adverse events (irAEs). Cutaneous adverse events are the most common irAEs, uncovering its**

characteristics and frequency requires a synthesis of global data.

Condition being studied: The use of immune checkpoint inhibitors (ICIs) has ushered in a new era of cancer treatment, and achieved tremendous success in various cancer types. It was well known that ICI could lead to a variety of immune-related adverse events (irAEs).Among the various irAEs, cutaneous adverse event (AE) is one of the most frequently observed,especially skin rash, pruritus, and vitiligo, which was also suggested to be an adverse effect associated with patient survival. Stevens -Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but life threatening dermatologic adverse reactions. Thus, it is important to recognize and manage these events appropriately, and try to avoid discontinuation of immunotherapy if possible. To our knowledge, the present study is the largest and most extensive analysis of dermatologic adverse events associated with ICIs collected data from clinical trials.

METHODS

Search strategy: The following terms were used: (Nivolumab or Opdivo or Pembrolizumab or Lambrolizumab or Keytruda or Cemiplimab or Pidilizumab or Camrelizumab or SHR-1210 or JS001 or Sintilimab or Durvalumab or MEDI4736 or atezolizumab or Avelumab or Bavencio or Tremelimumab or Ticilimumab or Ipilimumab) and (Carcinoma or Neoplasia or Tumor or Cancer or Malignancy).

Participant or population: Patients diagnosised with tumor.

Intervention: ICI monotherapy or ICI combination therapy with chemotherapy/ targeted therapy/ICIs.

Comparator: None.

Study designs to be included: Randomized controlled clinical trials or single/ multicenter research.

Eligibility criteria: Studies fulfilled the criteria below were included: (1) studies included either ICI monotherapy or ICI combination therapy with chemotherapy/ targeted therapy/ICIs in patients diagnosed with malignancies; (2) Studies investigated the following cutaneous adverse events: vitiligo, bullous dermatitis, Palmar-plantar erythrodysesthesia syndrome, rash maculopapular, drug eruption, erythema multiform, rash acneiform, skin exfoliation, skin ulceration, urticarial, Stevens-Johnson syndrome, toxic epidermal necrolysis; (3) Randomized controlled clinical trials or single/multicenter research. When more than 1 publications reported the same trial, the article with the longer follow-up time wasselected.

Information sources: Pubmed, Embase and The Cochrane Library database was systematically searched.

Main outcome(s): Incidence of dermatologic adverse events in different ICI treatment regimens.

Additional outcome(s): None.

Quality assessment / Risk of bias analysis: Using the Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium (also known as PROTECT) checklist tool.

Strategy of data synthesis: The proportion of selected cutaneous irAEs and its 95%CI of each ICIs treatment regimen was evaluated. This meta-analysis was conducted using R statistical soft-ware (packages metafor, R studio). Both fixed-effect model and random-effects model were used for estimating event rates and their corresponding 95% confidence intervals.

Subgroup analysis: None.

Sensitivity analysis: sensitivity analysis was conducted by R using the "metainf" package.

Language: In English only.

Country(ies) involved: China.

Keywords: immunotherapy, dermatologic adverse events, incidence.

Contributions of each author:

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