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Reported Adverse Drug Reactions of Immune Checkpoint Inhibitors in the Eudravigilance Database

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Abstract

Introduction: Immune checkpoint inhibitors (ICIs) represent a revolution in the treatment of cancer patients. More than 40% of cancer patients in the United States of America (USA) are currently being treated with ICI. Up until now, ICIs approved by the Food and Drug Administration (FDA) for antitumor treatment include pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, cemiplimab, and ipilimumab.

Objectives: The main objective of the study is to identify any potential signal among reported cases of adverse events of immune checkpoint inhibitors in the Eudravigilance database and the factors influencing such as the age of the patient, the outcome of the case, gender ratio, seriousness, and reporter group.

Materials and Methods: In this study, Eudravigilance database has been used to identify potential signals for immune checkpoint inhibitors. Signals of suspected adverse events for immune checkpoint inhibitors have been evaluated using Proportional Reporting Ratio (PRR). Further, Reporting Odds Ratio (ROR) has been used to evaluate the association between the drug and the adverse event.

Results: A total of 19,712 adverse events were reported for ICI during the 2016-2020 period in the Eudravigilance database. The drug associated with most of the events was Nivolumab (7,628),

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followed by Pembrolizumab (6153). PRR values > 1 have been identified for Pembrolizumab for the following System Organ Class (S.O.C) and Preferred Terms (P.T); PRR of 1.26 for cardiac disorders, 1,76 for general disorders and administration site disorders, 2.1 for immune system disorders,1.9 for cytokine storm, 2.32 for drug ineffective, therapeutic response decreased, 2.6 for product issues, 1.2 for drug intolerance or withdrawn.

Conclusion: The real incidence rate of the adverse events cannot be determined with certainty because of the underreporting which is the major disadvantage of passive surveillance systems. Moreover, confounding factors such as genetics, weight, age, gender, comorbidities, combination therapy, and underlying clinical conditions might influence the prevalence of an adverse event reported after an ICI. Specific studies investigating causality must be implemented.

Keywords: immune checkpoint inhibitors, reported events, adverse events, eudravigilance