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Modulo per la sottomissione abstract di ricerca CLINICA

Titolo (massimo 15 parole)

Immune checkpoint inhibitor cardiac toxicity: analysis of WHO international global database of suspected adverse drug reactions

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Testo (massimo **250 parole**, preferibilmente in italiano (accettato anche in inglese), suddiviso in Introduzione, *Metodi, Risultati, Conclusioni* e *Finanziamento*

Immune checkpoint inhibitor(ICI) cardiotoxicity is an emerging issue as shown by case reports of severe, sometimes fatal, cardiac adverse drug reactions(ADRs). However, in the post-marketing setting, ICI cardiotoxicity has been poorly studied.

We retrieved individual case safety reports(ICSRs) of cardiac ADRs associated with ipilimumab/pembrolizumab/nivolumab/atezolizumab/avelumab/durvalumab from VigiBase®, the WHO global database of suspected ADRs, to assess patients' clinical features, treatment characteristics, cardiac ADR patterns and severity.

The proportion of ICSRs reporting cardiac ADRs related to ICIs accounted for up to 3.2% of all ICI-associated ICSRs in the database. Among 806 ICSRs of ICI-associated cardiac ADRs, 615(76.3%) were serious and 147 (18.2%) fatal. Of these, 102(69.4%) involved male patients and median patient age was 67(17-94) years. ICI treatment in patients ≥65years was more frequently associated with myocarditis and fatal cardiac ADRs compared to all other drugs in the database (logOR 3.3, 99%CI 2.7-3.8, and logOR 0.9, 99%CI 0.6-1.3, both p<0.01, respectively). Cardiac ADRs on ipilimumab plus nivolumab combination therapy showed the highest fatality rate(13 lethal cardiac ADRs out of 65 cardiac ADRs reported), with latency shorter than fatal cardiac ADRs with either agent alone(median 2.4weeks versus 5.1weeks with ipilimumab and 3weeks with nivolumab). Tumor type, treatment duration, pre-existing cardiac and autoimmune diseases did not emerge as risk factors for death from ICI cardiotoxicity.

In clinical practice cardiotoxicity is infrequently reported with ICI treatment. However, when it occurs, it is mostly associated with serious and fatal outcomes which seem to occur earlier with ipilimumab plus nivolumab combination therapy.

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Visto superiore (prego indicare Nome e Cognome del superiore)

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Invio Abstract