

MYOCARDITIS-MYOSITIS-MYASTHENIA GRAVIS OVERLAP SYNDROME: AN EMERGING SEVERE ADVERSE REACTION AMONG IMMUNE CHECKPOINT INHIBITORS. ANALYSIS OF REPORTS IN THE SPANISH ADVERSE REACTIONS DATABASE (FEDRA)

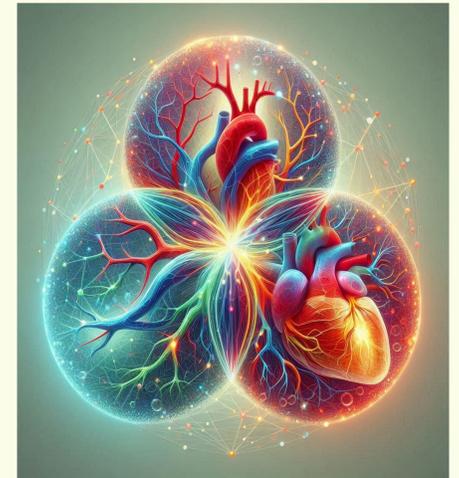
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BACKGROUND AND IMPORTANCE

- Immune Checkpoint Inhibitors are increasingly being used in oncology.
- Their **summaries of drug characteristics** include myositis, myocarditis and myasthenia gravis, but **not myositis-myocarditis-myasthenia gravis overlap syndrome**.
- Suspected adverse drug reactions (ADR) documented in FEDRA database provides a valuable resource for post-marketing pharmacovigilance assessment.
- Following four local reports of this syndrome linked to nivolumab, nivolumab+ipilimumab and pembrolizumab (including two mortal cases), FEDRA database was used to perform a pharmacovigilance analysis of this adverse drug reaction.



AIM AND OBJECTIVES

To analyse the outcome and reporting trend of **myocarditis-myositis-myasthenia gravis overlap syndrome** in reports of suspected ADR of nivolumab, pembrolizumab and ipilimumab in FEDRA and their correlation with those published in PubMed.

MATERIALS AND METHODS

We performed a **descriptive study** based on pharmacovigilance data retrieved from Individual Case Safety Reports identified in FEDRA from 2011 (marketing year of ipilimumab) to september 2025, of **suspected ADR reports** for pembrolizumab, nivolumab and ipilimumab using all MedDRA Preferred Terms that could identify a case of the overlap syndrome.

We have also searched in **Pubmed** for published **articles** with the term “**myocarditis-myositis-myasthenia gravis overlap syndrome**”.

RESULTS

DRUG cases (mortal cases)	2011-2019	2020	2021	2022	2023	2024	2025	TOTAL
Pembrolizumab	0	2(1)	0	2(2)	2(1)	2(1)	10 (4)	18 (9)
Nivolumab	0	0	0	0	0	0	2 (2)	2 (2)
Nivolumab+Ipilimumab	0	0	0	1(1)	1	1	5(1)	8 (2)
								28 (13)

	2020	2021	2022	2023	2024	2025	TOTAL
Number of articles with the term	2	4	2	7	6	16	37

CONCLUSIONS

- **Myositis-myocarditis-myasthenia gravis overlap syndrome** is a rare but life-threatening emerging adverse drug reaction to Immune Checkpoint Inhibitors, with a high mortality rate, that should be taken into account by clinicians in the management of these drugs.
- Pharmacovigilance is crucial in identifying new adverse drug reactions, promoting patient safety and the rational use of medicines.
- There is an urgent need to encourage consumers and health care professionals to report to National Pharmacovigilance Systems.

