

CARDIOTOXIC EFFECTS OF IMMUNE CHECKPOINT INHIBITORS IN 599 PATIENTS

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Background:

Checkpoint-inhibitor immunotherapies have had a profound effect in the treatment of cancer by inhibiting down-regulation of T-cell response to malignancy. The cardiotoxic potential of these agents is described in both murine models causing cardiomyopathy and myocarditis, and in case reports of pericarditis, pericardial effusion, cardiomyopathy, and new arrhythmias. In this retrospective cohort, we screened medical records of patients treated with checkpoint-inhibitor immunotherapy for cardiotoxic events.

Methods:

Medical records of patients who underwent immunotherapy with durvalumab, ipilimumab, nivolumab, and pembrolizumab were reviewed for: coexisting conditions (hypertension, diabetes mellitus, tobacco use), concurrent cardiac medications, and new diagnoses of heart failure, atrial fibrillation, ventricular fibrillation/tachycardia, myocarditis, pericardial effusion, and hypertensive urgency.

Results:

Review of 599 medical records revealed the following events: 3 ventricular fibrillation/ventricular tachycardia, 13 pericarditis, 12 atrial fibrillation with rapid ventricular rate, 1 myocarditis, 9 heart failure.

Conclusions:

Our study revealed 38 significant cardiac events, the most frequent being pericarditis (2.2%) and atrial fibrillation (2.0%). While these results do not necessarily point to causation, they suggest that patients on checkpoint inhibitors may require closer cardiac monitoring. Further collaborative investigation is required.

Table 1. Incidence of Adverse Cardiac Events with Immunotherapy							
	Atrial Fibrillation with RVR	HFpEF	HFrfEF	Hypertensive Urgency	Myocarditis	Pericarditis	VF/VT
<i>Durvalumab</i> (n = 41)	1 (2.4%)	0	1 (2.4%)	0	0	0	0
<i>Ipilimumab</i> (n = 56)	0	0	0	0	0	0	0
<i>Nivolumab</i> (n = 258)	4 (1.6%)	0	1 (0.4%)	0	0	5 (1.9%)	1 (0.4%)
<i>Pembrolizumab</i> (n = 244)	7 (2.9%)	2 (0.8%)	4 (1.6%)	0	1 (0.4%)	8 (3.3%)	2 (0.8%)
<i>Endometrial Cancer</i> (n = 2)	0	0	1 (50%)	0	0	0	0
<i>Esophageal Cancer</i> (n = 4)	1 (25%)	0	0	0	0	0	0
<i>Non-Small Cell Lung Cancer</i> (n = 265)	10 (3.8%)	0	3 (1.1%)	0	0	12 (4.5%)	2 (0.8%)
<i>Small Cell Lung Cancer</i> (n = 41)	1 (2.4%)	0	3 (7.3%)	0	1 (2.4%)	1 (2.4%)	1 (2.4%)
<i>Other*</i> (n = 287)	0	0	0	0	0	0	0
Total (n = 599)	12 (2.0%)	2 (0.3%)	7 (1.2%)	0	1 (0.2%)	13 (2.2%)	3 (0.5%)

*Other malignancies reported included: solid organ, leukemia, lymphoma, melanoma, mesothelioma, multiple myeloma, neuroendocrine, ovarian, and parotid.
Abbreviations: RVR: rapid ventricular response, HFpEF/HFrEF – heart failure with preserved ejection fraction/ reduced ejection fraction, VF/VT – ventricular fibrillation/ tachycardia.

Table 2. Demographics of Patients with and without Adverse Cardiac Events with Immunotherapy		
	Cardiac Events	No Cardiac Events
<i>Age</i>	66±9	65±11
<i>Race</i>	74% Caucasian, 26% African American	88% Caucasian, 10% African American, 2% Other
<i>Gender</i>	55% Female	35% Female
<i>Body mass index</i>	25±6	26±7
<i>History of Symptomatic Heart Failure/Diabetes/Hypertension</i>	22%/ 7%/ 52%	4%/ 17%/ 33%