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 list of malignancies that can be treated with these antibodies continues to grow and includes bladder cancer, melanoma, lung cancer, renal cell cancer, head and neck cancers, hepatocellular carcinoma, and more. The cardiotoxic potential of these agents has been described in murine models where it was found to lead to cardiomyopathy and myocarditis. More recently, there have been clinical case reports of cardiomyopathy as well as pericarditis, pericardial effusion, and new arrhythmias. In this retrospective cohort, we screened medical records of patients treated with checkpoint-inhibitor immunotherapy for cardiotoxic events.

METHODS

- Medical records from Wake Forest Baptist Medical Center were screened for patients who underwent immunotherapy with durvalumab, ipilimumab, nivolumab, and pembrolizumab.
- Patient charts were then systematically reviewed for coexisting conditions (hypertension, diabetes mellitus, heart failure), concurrent cardiac medications, new or worsening heart failure, and new diagnoses of atrial fibrillation, ventricular fibrillation/tachycardia, myocarditis, pericardial effusion, and hypertensive urgency.

RESULTS

- N = 599
- A total of 38 adverse cardiac events identified (Table 1).
- Demographics reported in Table 2
- Pre-treatment and treatment echocardiogram data available from 45 patients with an average decrease in EF of -1.9%

Table 1. Incidence of Adverse Cardiac Events with Immunotherapy

	Afib-RVR	HFpEF	HFrEF	Myocarditis	Pericarditis	VF/VT
Durvalumab (n = 41)	1 (2.4%)	0	1 (2.4%)	0	0	0
Ipilimumab (n = 56)	0	0	0	0	0	0
Nivolumab (n = 258)	4 (1.6%)	0	1 (0.4%)	0	5 (1.9%)	1 (0.4%)
Pembrolizumab (n = 244)	7 (2.9%)	2 (0.8%)	5 (2.0%)	1 (0.4%)	8 (3.3%)	2 (0.8%)
Endometrial Cancer (n = 2)	0	0	1 (50%)	0	0	0
Esophageal Cancer (n = 4)	1 (25%)	0	0	0	0	0
Non-Small Cell Lung Cancer (n = 265)	10 (3.8%)	0	3 (1.1%)	0	12 (4.5%)	2 (0.8%)
Small Cell Lung Cancer (n = 41)	1 (2.4%)	0	3 (7.3%)	1 (2.4%)	1 (2.4%)	1 (2.4%)
Other * (n = 287)	0	0	0	0	0	0
Total (n = 599)	12 (2.0%)	2 (0.3%)	7 (1.2%)	1 (0.2%)	13 (2.2%)	3 (0.5%)

Table 2. Demographics of Patients with and without Adverse Cardiac Events with Immunotherapy

	Cardiac Events	No Cardiac Events
Age	66±9	65±11
Race	74% Caucasian, 26% African American	88% Caucasian, 10% African American, 2% Other
Gender	55% Female	35% Female
Body Mass Index	25±6	26±7
History of HF/DM/HTN	22%/ 7%/ 52%	4%/ 17%/ 33%

Abbreviations: *HF – heart failure, DM – diabetes myelitis, HTN – hypertension.*

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.*

CONCLUSION

Our study revealed 38 significant cardiac events, the most frequent being pericarditis (2.2%) and atrial fibrillation (2.0%). Given the similar sample size between nivolumab and pembrolizumab, it's interesting to note nearly a doubling of adverse cardiac events in the pembrolizumab arm. Those who had a higher rate of adverse cardiac events had a higher percentage of prior hypertension and heart failure. It is likely that we have under-reported adverse events given that numerous patients moved or passed away outside of our hospital network. 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.

REFERENCES

Available upon request.

Disclosures: There are no financial conflicts of interest.