Characterization of immune checkpoint inhibitor-related cardiotoxicity in lung cancer patients from a rural setting

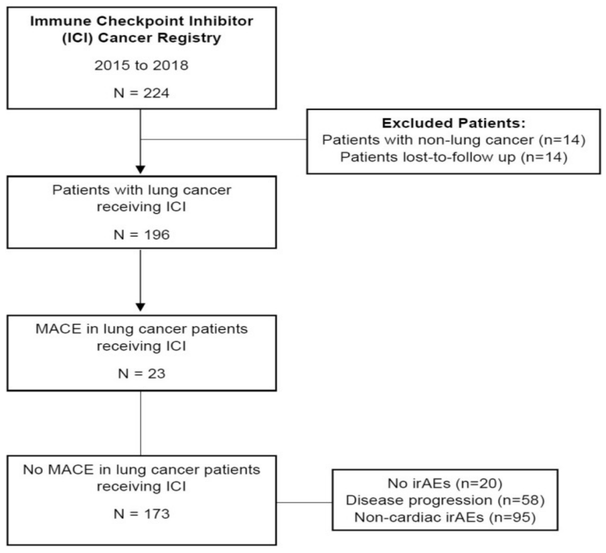
Melissa Y.Y. Moey, Anna N. Tomdio, Justin D. McCallen, Lauren Vaughan, Abdul R. Naqash, Cynthia Cherry, Blase A. Carabello and Paul R. Walker

Vidant Medical Center/East Carolina University, Greenville, North Carolina

INTRODUCTION

- Immune checkpoint inhibitor (ICI)-related cardiotoxicities (iRCs) are rare. However, recent literature have described major adverse cardiac events (MACE) such as myocarditis, pericardial disorders, cardiomyopathies and dysrhythmias as potential fatal adverse effects in patients receiving ICIs[1].
- The cardiotoxic profile of ICIs is not well defined. Our study aimed to characterize iRCs in lung cancer patients of a rural population at a tertiary care center.

METHODS



RESULTS

Figure 1A. Percentage of suspected types of iRC.

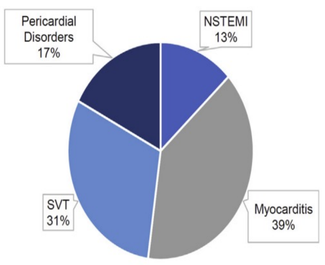


Figure 1B. Percentage of different grade toxicities.

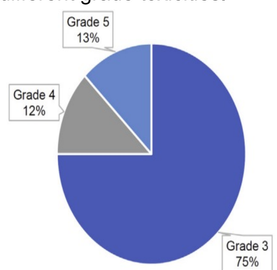


Table 1. Demographics and baseline characteristics of control and patients with ICI-related cardiotoxicities (iRC).

	No MACE	MACE	*p value*
Total Number of Patients (n, %)	174 (88%)	23 (11%)	
Age (years ± SD)	64.3 ± 0.79	68.71 ± 1.8	0.064
Gender			
Male (n, %)	99 (57%)	15 (65%)	0.456
Female (n,%)	74 (43%)	8 (35%)	
Ethnicity			
Black (n, %)	66 (38%)	5 (21%)	0.108
White (n, %)	107 (62%)	18 (78%)	
Type of Lung Cancer			
NSCLC (n, %)	158 (91%)	20 (87%)	0.509
SCLC (n, %)	15 (9%)	3 (13%)	
Immune Checkpoint Inhibitor			
Nivolumab (n, %)	119 (68%)	19 (83%)	0.17
Pembrolizumab (n, %)	44 (25%)	4 (17%)	0.41
Atezolizumab (n, 0%)	11 (6%)	0 (0%)	0.41
Other Chemotherapy			
Anti-topoisomerase (n, %)	66 (38%)	9 (39%)	---
Anti-VEGF (n, %)	13 (7%)	0 (0%)	---
Alkylating agents, (n, %)	139 (80%	21 (91%)	---
Anti-metabolites (n, %	68 (40%)	11 (48%)	---
Taxane (n, %)	11 (6%)	6 (26%)	---
Past Medical History			
DM	44 (25%)	7 (30%)	0.61
HTN	111 (64%)	12 (52%)	0.28
HLD	56 (32%)	4 (17%)	0.14
AF	15 (9%)	3 (13%)	0.48
CKD	9 (5%)	1 (4%)	0.86
CAD	27 (16%)	8 (35%)	0.02
Medications			
Steroids	66 (38%)	18 (78%)	< 0.01
BB	52 (30%)	15 (65%)	< 0.01
CCB	34 (20%)	4 (17%)	0.80
Diuretics	46 (26%)	13 (56%)	0.99
ACE-I/ARB	41 (24%)	5 (22%)	0.84
Statins	58 (33%)	12 (52%)	0.076

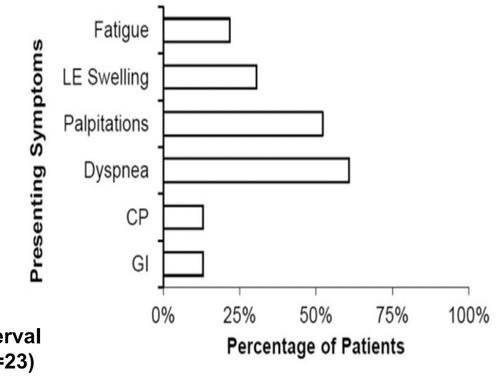
Abbreviations: ACE-I: angiotensin converting enzyme inhibitors, AF: atrial fibrillation, ARB: angiotensin receptor blocker, BB: beta-blockers, CCB: calcium channel blockers, CKD: chronic kidney disease, DM: diabetes mellitus, iRC: immune-related cardiotoxicity, HLD: hyperlipidemia, HTN: hypertension, NSCLC: non-small cell lung cancer, SCLC: small cell lung cancer, VEGF: vascular endothelial growth factor

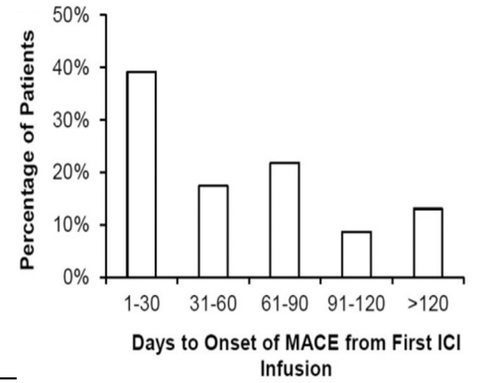
Table 2. Comparison of laboratory values in lung cancer patients with no MACE (174) versus with a MACE (n=23)

	No MACE	MACE	*p value*
Baseline Laboratory Values			
WBC, K/uL	8.86 ± 5.1	8.92 ± 5.4	0.003
Hemoglobin, g/dl	11.9 ± 7.4	10.6 ± 1.6	<0.001
Hematocrit, %	35.9 ± 15	32.5 ± 5.1	<0.001
Platelets, K/uL	282 ± 117	239 ± 117	0.005
Creatinine, mg/dl	1.06 ± 0.9	0.91 ± 0.3	<0.001
Neutrophil:lymphocyte ratio (NLR)	8.1 ± 9.0	10.9 ± 8.3	0.022
CRP, mg/l	37.5 ± 48.1	42.1 ± 46.0	0.546
Troponin, ng/ml	0.02 ± 0.01	0.03 ± 0.01	

Table 3. Comparison of laboratory values, ejection fraction, PR interval and QTc interval at baseline and at the time of suspected MACE (n=23)

	Baseline	MACE	*p* value
Laboratory Values			
CRP, mg/l	35 ± 4.1	99 ± 14	< 0.01
NLR	7.7 ± 0.54	20.78 ± 4.5	< 0.01
Troponin I (ng/mL)	0.03 ± 0.01	0.98 ± 0.36	< 0.01
Echocardiogram			
Ejection Fraction (%)	50.5 ± 16.2	46.2.3 ± 16.8	0.495
		Δ 4.22 ± 6.00	
Electrocardiogram			
PR Interval (ms)	171.1 ± 29.9	155.9 ± 30.6	0.031
		Δ -19.6 ± 8.2	
QTc Interval (ms)	442.4 ± 37.9	466.1 ± 34.8	0.036
		Δ 26.8 ± 12.0	





DISCUSSION

- iRCs are rare though can manifest as a spectrum of cardiotoxicities[1,2]. Majority of these toxicities appear to be grade 3 toxicities (severe undesirable adverse reaction requiring hospitalization or invasive intervention)[6].
- Elevated NLR is an inflammatory marker that has been associated with poor prognosis in cancer[3,4] as well as mortality in cardiovascular disease[5]. We demonstrate an increased NLR in correlation with an elevated CRP during the time of suspected iRC, suggesting its utility in diagnosing iRC.
- iRCs may be underrepresented in clinical trials and further studies describing this syndrome (ECG and echocardiographic findings), diagnostic work up and surveillance are warranted.
- Larger datasets to identify potential predictors that may guide optimal management of these events are encouraged.

ACKNOWLEDGEMENTS

I would like to thank the organizers of the 2022 Distinction Day for this opportunity. Additionally, I wish to thank Dr. Johanna Hannan and Dr. Kori Brewer for leading the RDT. Finally, I wish to thank Dr. Li Yang and Mona Marie for their additional support in my research throughout medical school.

REFERENCES

1. Lyon AR, Yousaf N, Battisti NML et al. Lancet Oncol 19(9):e4470e458, 2018
2. Varricchi G, Galdiero MR, Tocchetti. Circulation 136:1989-1999, 2017
3. Lalani AA, Xie W, Martini DJ et al., J Immunother Cancer 6(1):5, 2018
4. Zer A, Sung MR, Walia P et al., Clin Lung Cancer 19:426-434, 2018
5. Bhat T, Teli S,Rijal J et al. Expert Rev Cardiovasc Ther 11:55-9, 2013
6. CTCAE. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm

DISCLOSURES

The primary author and study authors have no disclosures to declare.