



Society for Immunotherapy of Cancer

Advances in Cancer Immunotherapy™

Immune Checkpoint Inhibitor Myocarditis

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#LearnACI

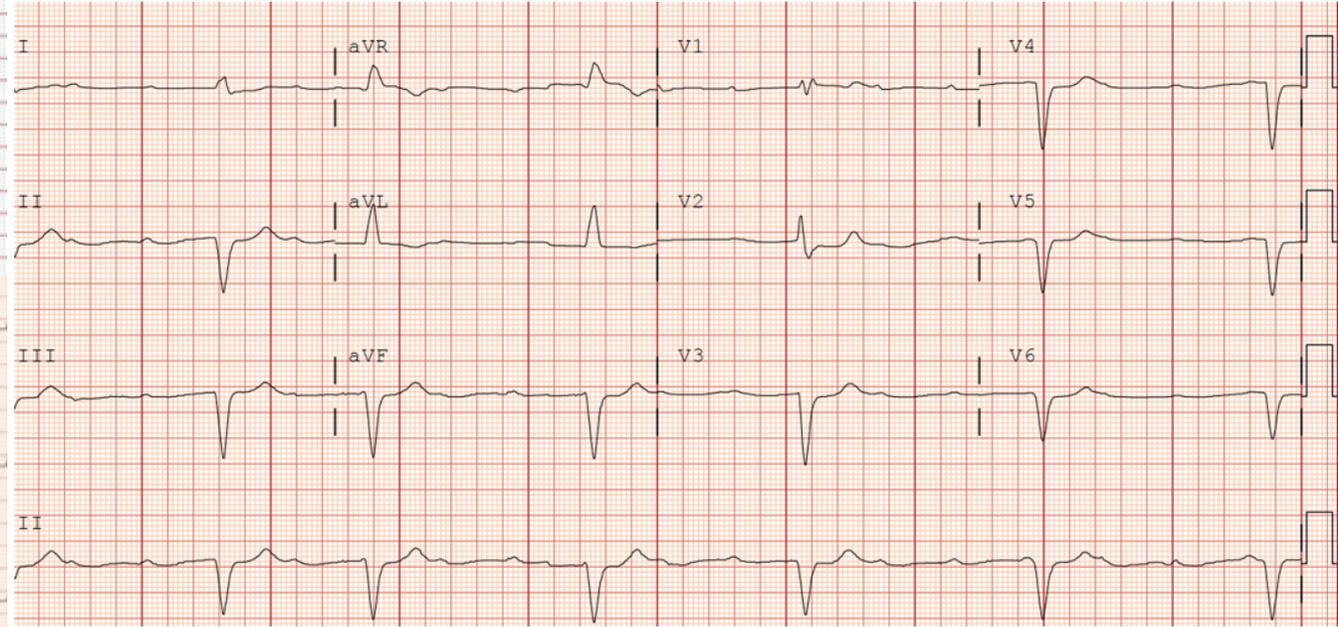
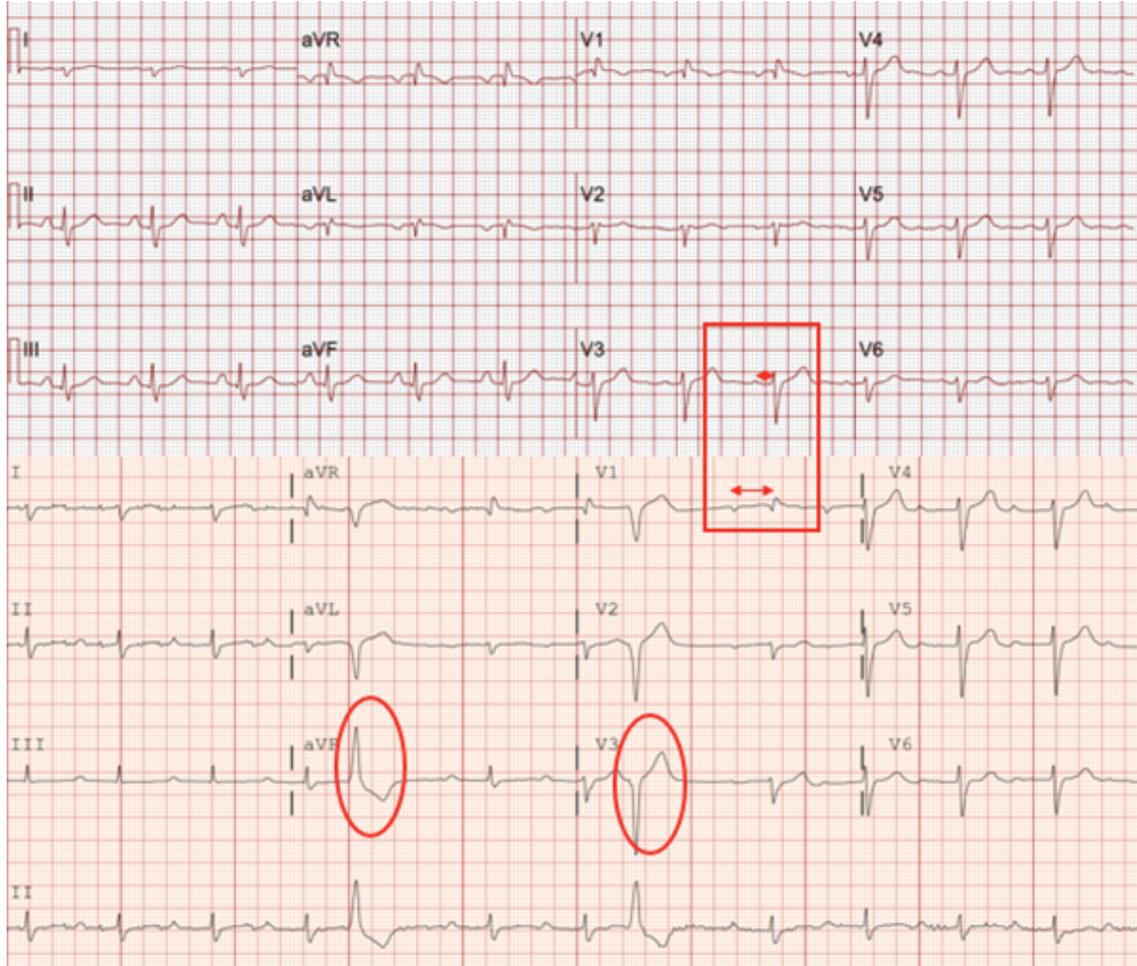
Disclosures

- Cancer Prevention & Research Institute of Texas, National Institute of Health, Sabin Family Fellowship, Patient Education Resource, Replimmune, Kiniksa
- I will be discussing non-FDA approved indications during my presentation.

Case Presentation

- 65 year old man with renal cell carcinoma recently started pembrolizumab
- Patient presents with dyspnea 10 days after second dose of pembrolizumab
- No previous cardiovascular disease history
- Previously physically active with good exertional capacity > 4 METs

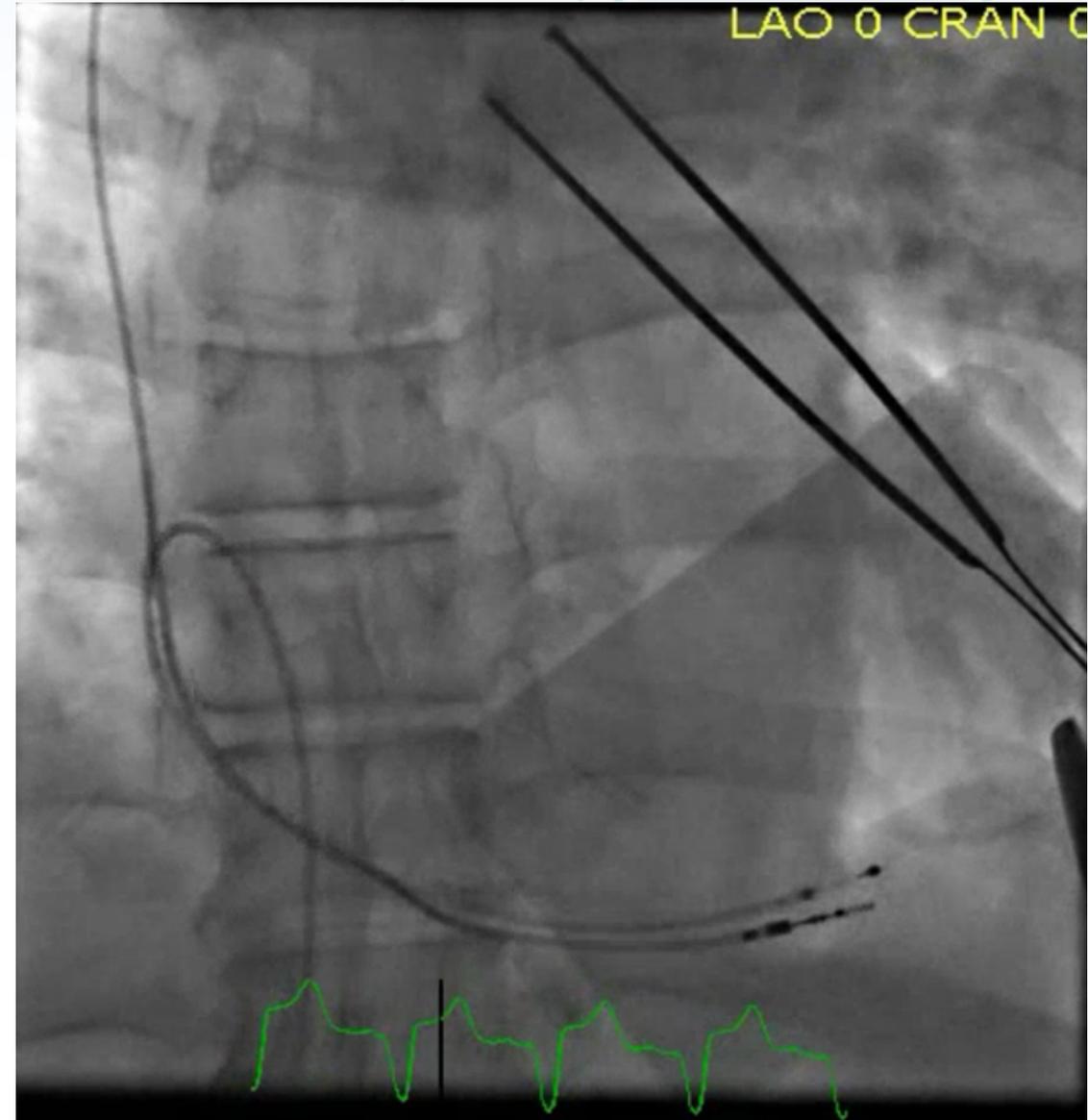
Case Presentation



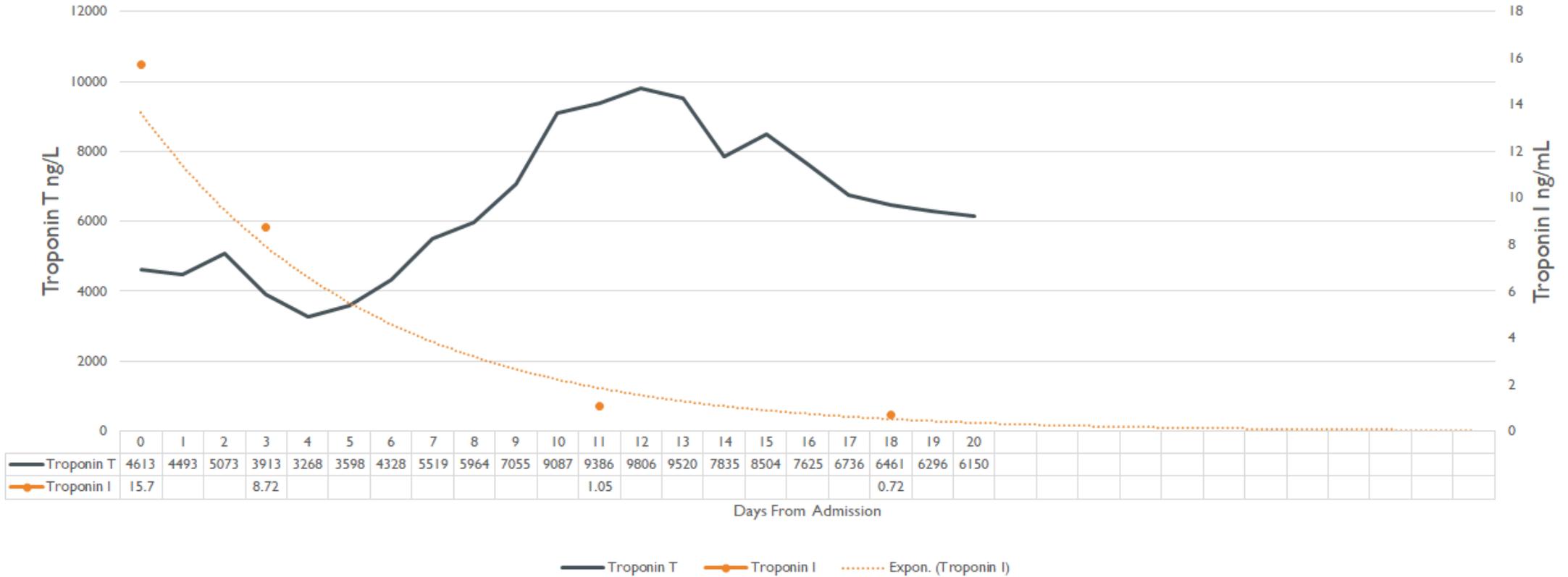
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Internal Fixation Lead

- Allows 4 to 6 weeks of recovery before deciding on permanent pacemaker
- More stable positioning
- Patient can participate in physical therapy
- Time to recover the conduction system



Troponin T versus Troponin I



Incidence of Myocarditis

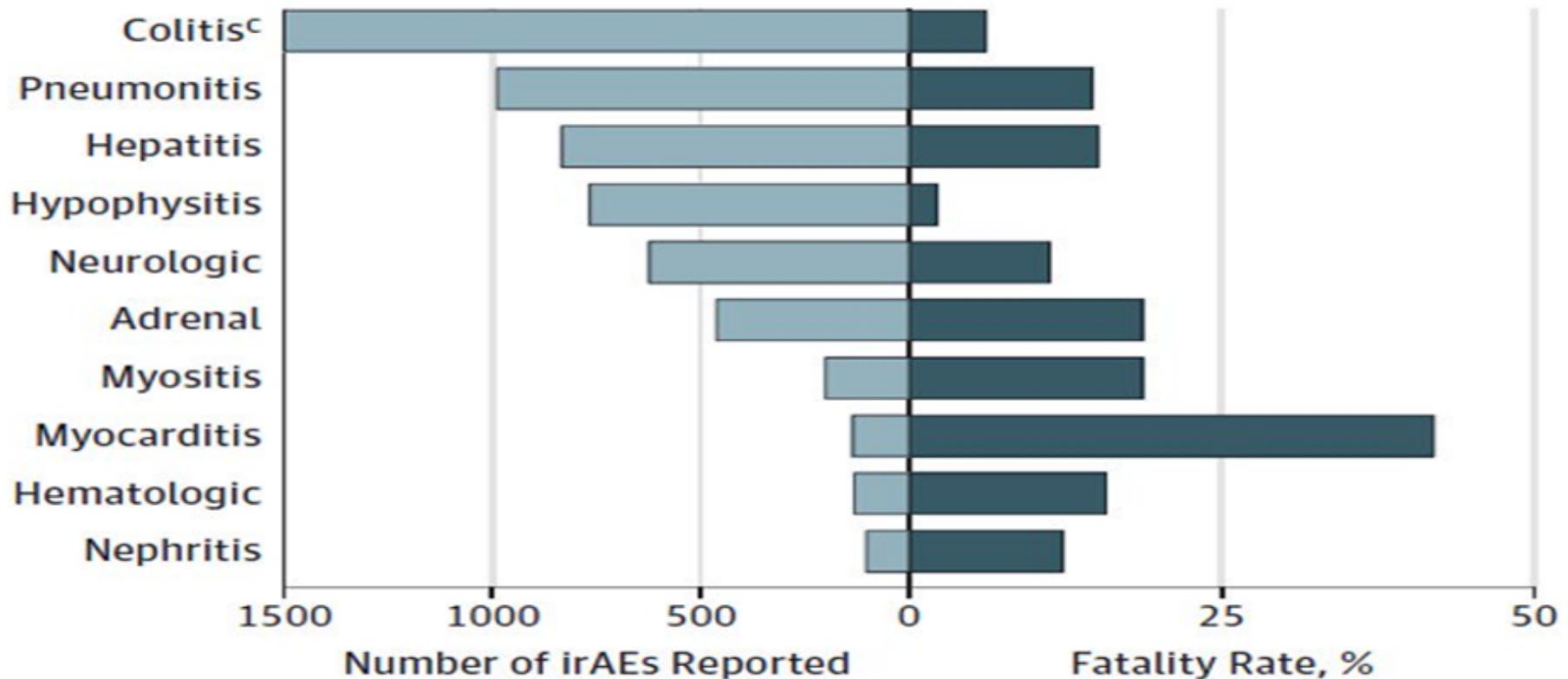
Table 1. Incidence of Myocarditis and Myositis in Patients Receiving Nivolumab or Ipilimumab plus Nivolumab.

Characteristic	Nivolumab (N = 17,620)	Nivolumab plus Ipilimumab (N = 2974)
	<i>no. (%)</i>	
Myocarditis		
Any*	10 (0.06)	8 (0.27)
Fatal events	1 (<0.01)	5 (0.17)
Myositis		
Any	27 (0.15)	7 (0.24)
Fatal events	2 (0.01)	1 (0.03)

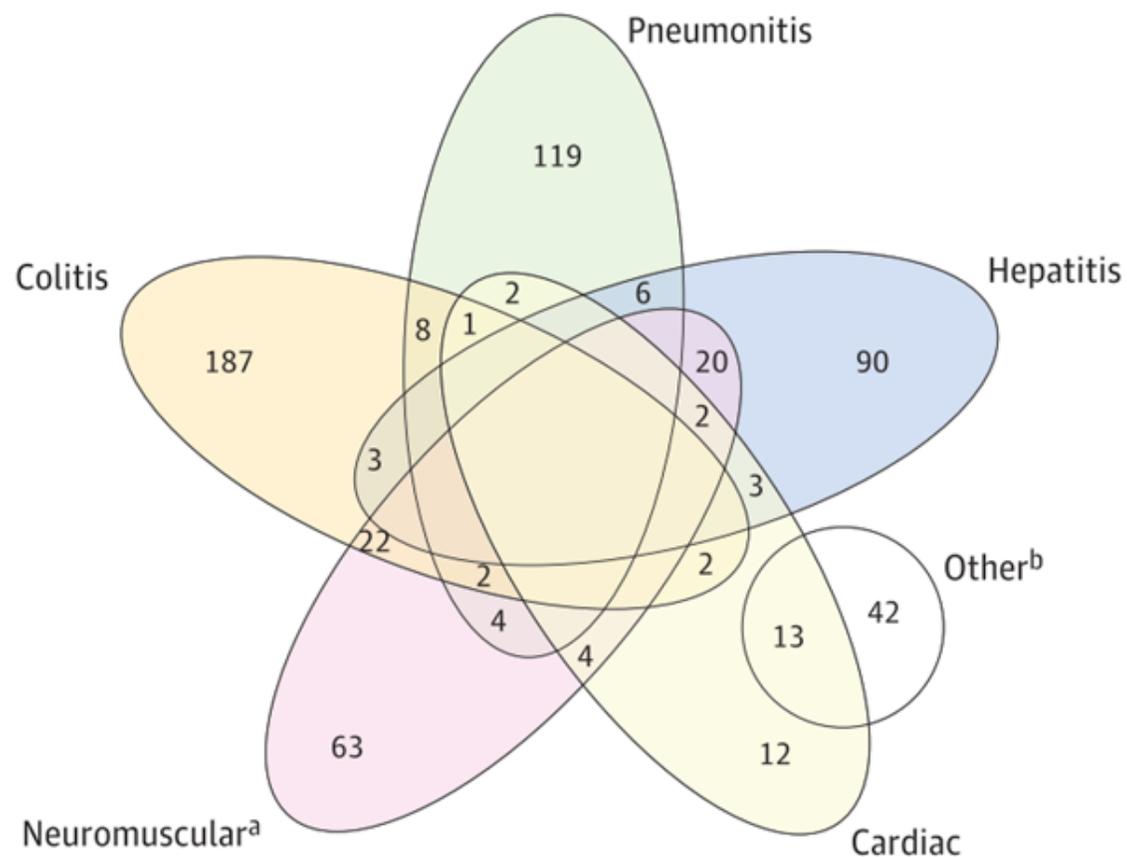
* The number of patients with myocarditis includes six patients with concurrent myocarditis and myositis.

Mortality of Myocarditis

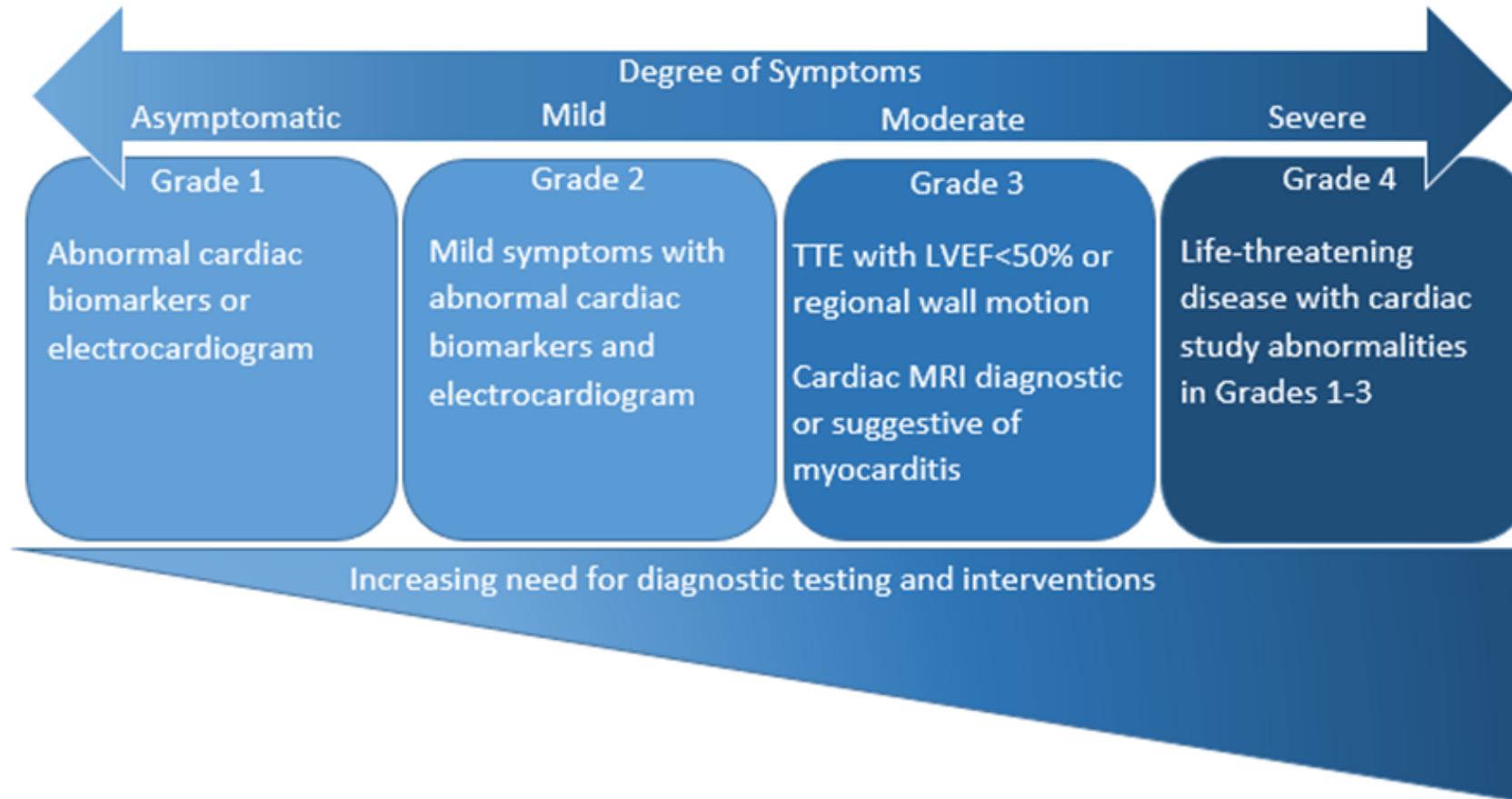
C Cases and fatality rates



Concomitant IRAE



Spectrum of Disease



Cardiac Biomarkers

- Troponin I is preferred over Troponin T, CK, CKMB¹
- NTproBNP and BNP are nonspecific markers- especially in cancer patients
- Discharge troponin T above 1.5 ng/mL was associated with worse prognosis and 4-fold increased risk of major adverse cardiovascular events (MACE)²
- MACE- cardiovascular death, cardiogenic shock, cardiac arrest, or complete heart block²

EKG/TELEMETRY

- Prolonged PR interval, AV block, ventricular arrhythmias, frequent PVCs, ST depressions, diffuse T wave inversions
- Telemetry monitoring should be performed on admission- monitor for PVC burden, arrhythmias, PR prolongation
- Baseline EKG is not predictive of future events but helpful for comparison if changes occur

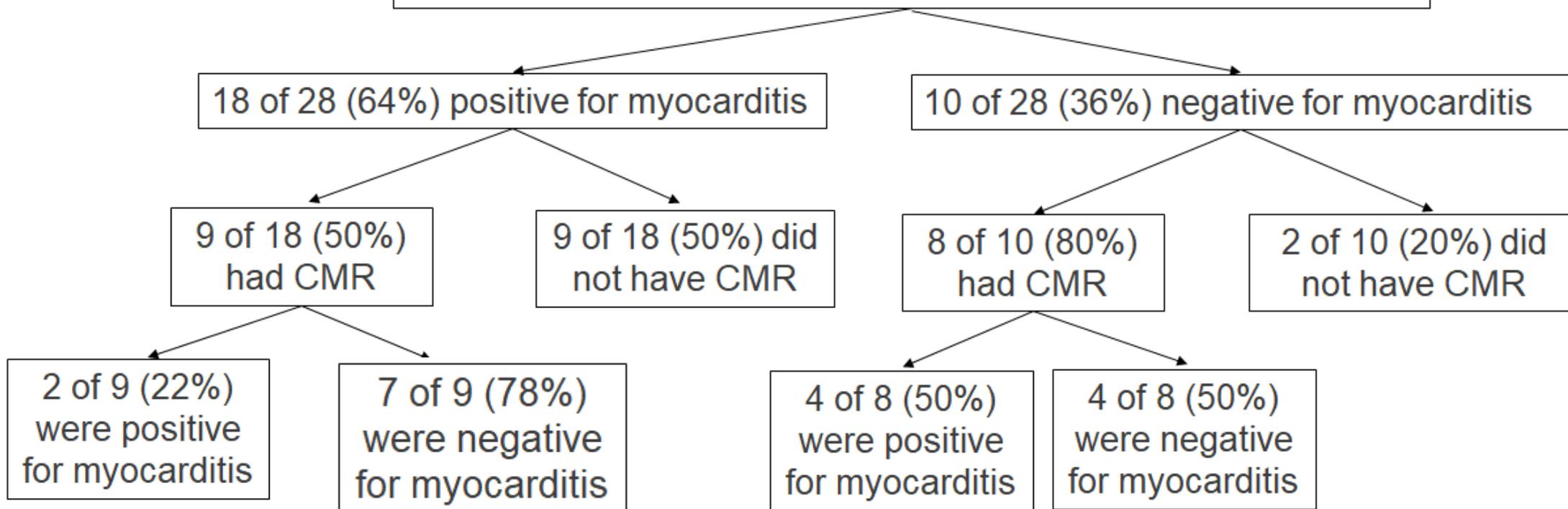
Echocardiography

- LV ejection fraction, wall motion abnormalities, pericardial effusion
- Baseline echocardiogram not predictive of events but helpful in comparison
- 51% of ICI Myocarditis have normal LVEF and 38% of these develop MACE

Mahmood SS et al. Myocarditis in Patients Treated With Immune Checkpoint Inhibitors. *Journal of the American College of Cardiology* 2018;71(16):1755-64

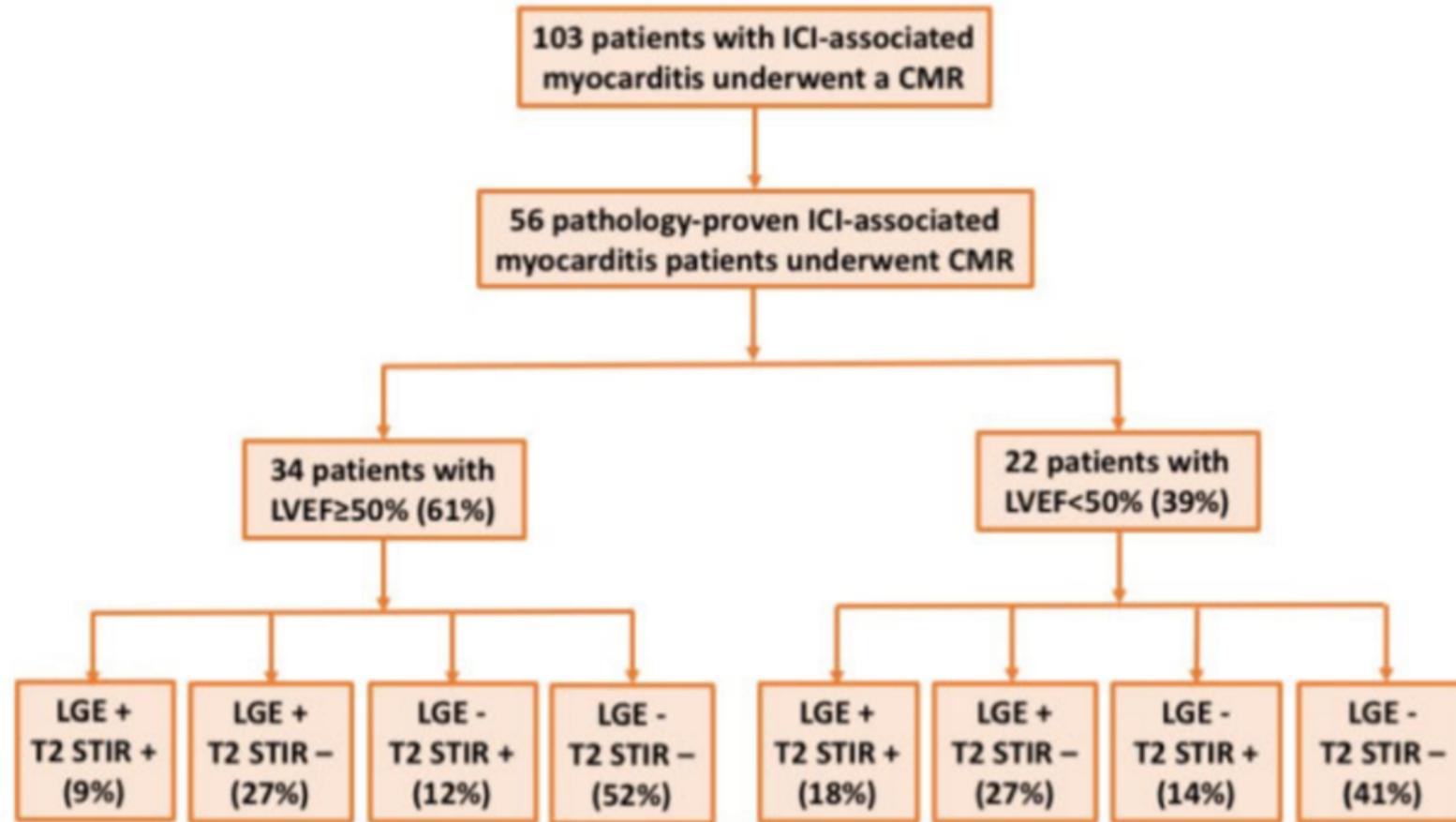
Cardiac MRI

28 Patients with EMB for suspected ICI associated myocarditis



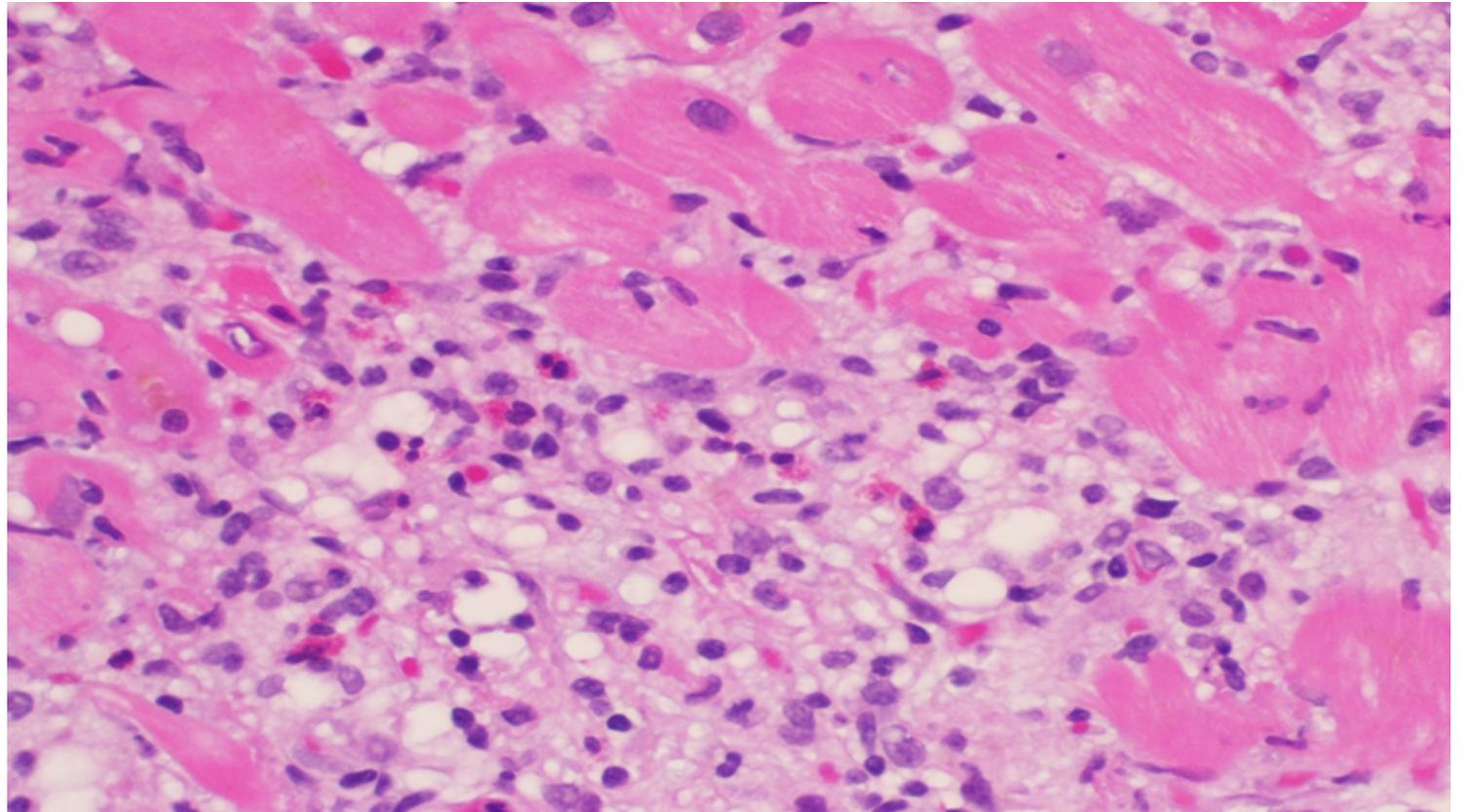
	EMB Positive	EMB Negative	Total
CMR Positive	2 (22%)	4 (50%)	6
CMR Negative	7 (78%)	4 (50%)	11
Total	9	8	17

Cardiac MRI

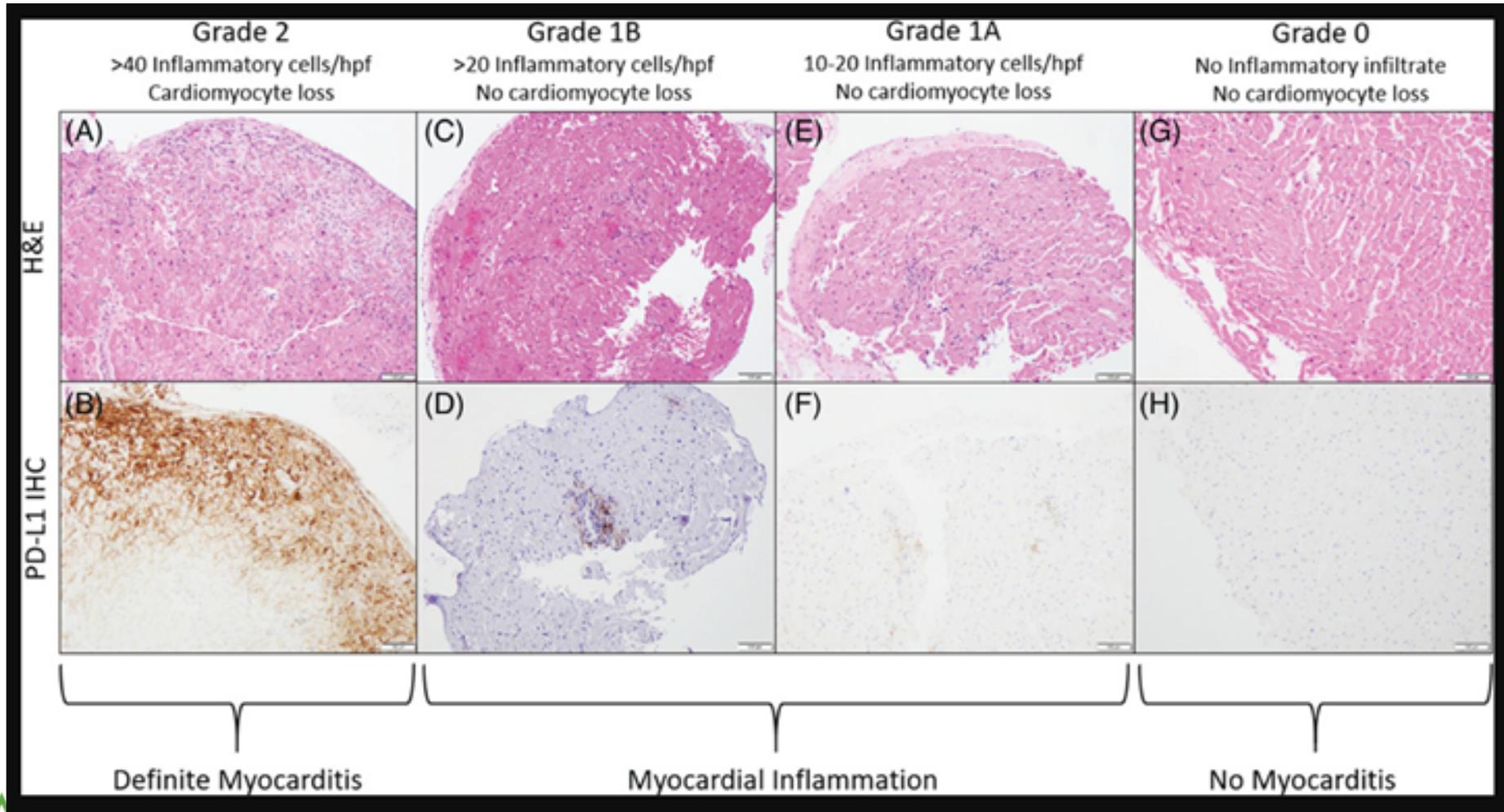


Endomyocardial Biopsy

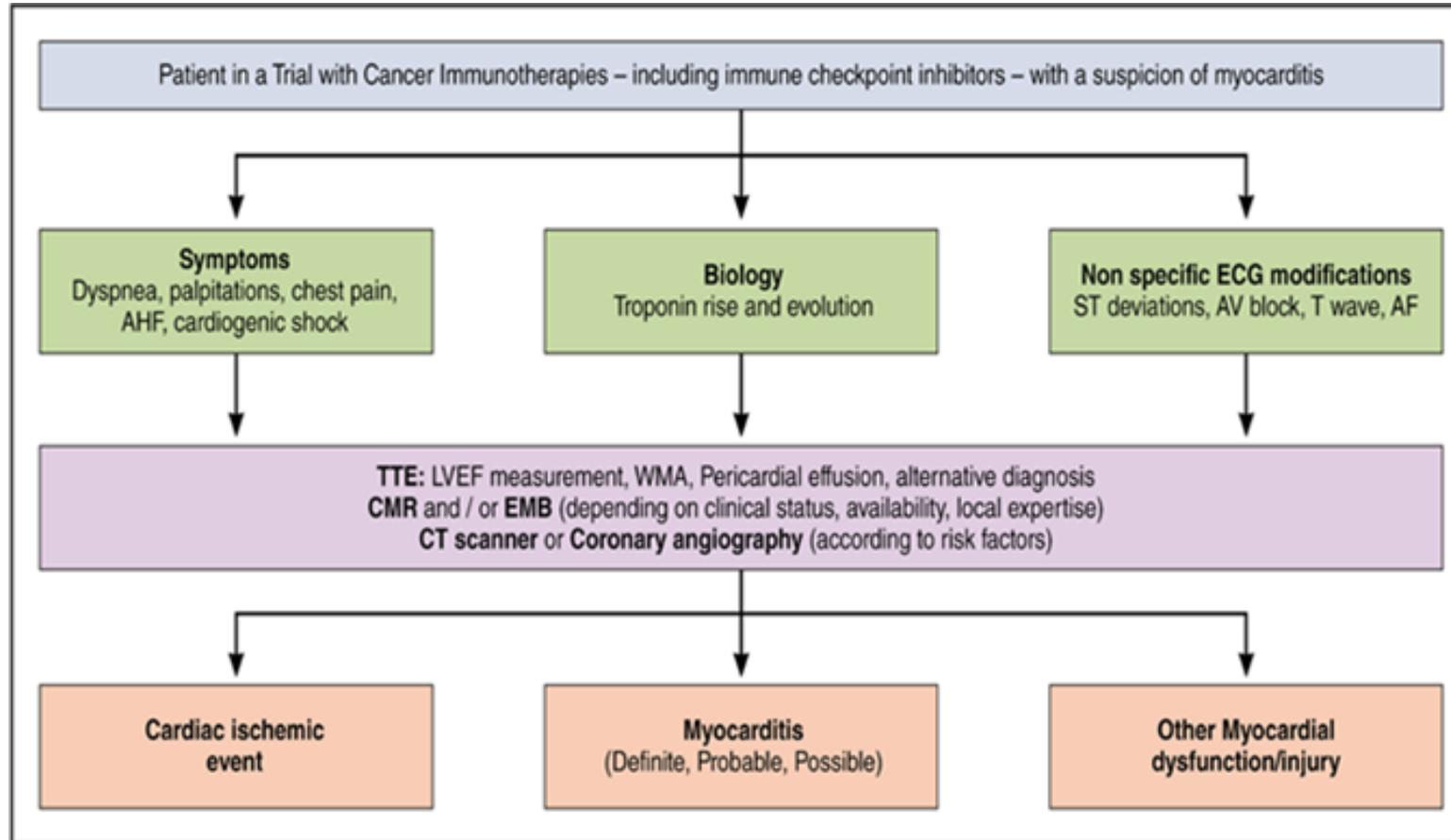
- Tissue diagnosis is the gold standard for diagnosing myocarditis
- Uses Dallas Criteria for histologic diagnosis
 - Myocyte Necrosis
 - Inflammatory Infiltrate



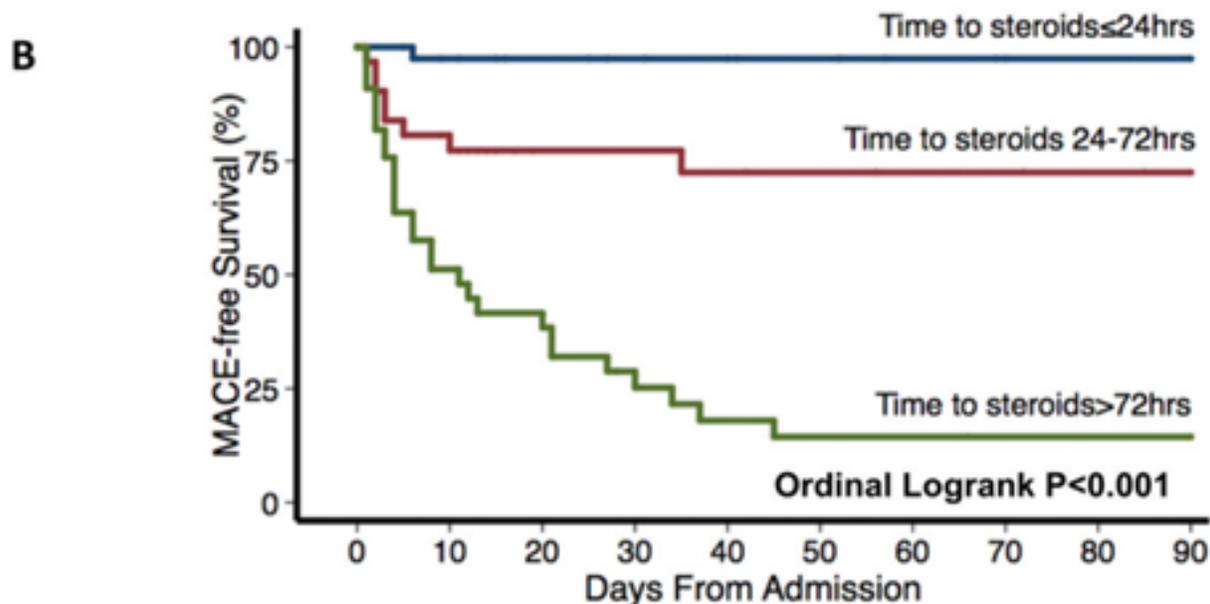
Endomyocardial Biopsy



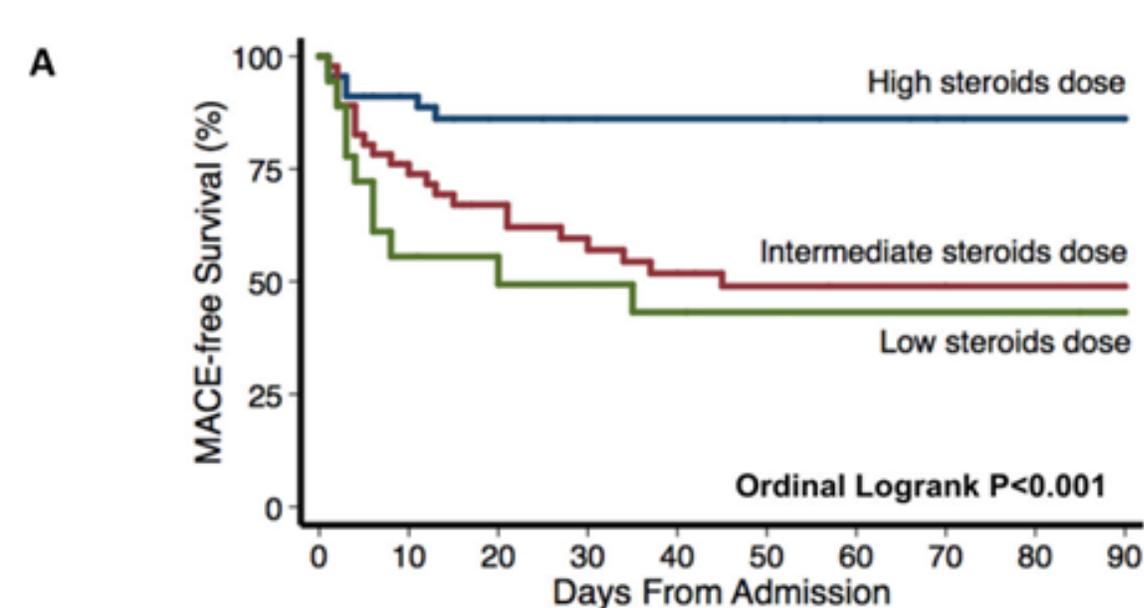
Diagnosis of ICI myocarditis



Treatment of ICI myocarditis



Number at risk	0	10	20	30	40	50	60	70	80	90
Time to steroids \leq 24hrs	40	37	34	32	31	29	27	26	25	25
Time to steroids 24-72hrs	31	24	16	16	15	14	13	13	12	11
Time to steroids >72hrs	33	16	13	8	5	4	4	3	3	3



Number at risk	0	10	20	30	40	50	60	70	80	90
High steroids dose	45	38	30	28	27	27	25	23	22	22
Intermediate steroids dose	46	34	27	23	20	17	16	16	15	15
Low steroids dose	18	10	9	8	7	6	6	6	6	5

Higher initial dose (ie, iv methylprednisolone 1000 mg/d) and earlier initiation of corticosteroids were associated with improved cardiac outcomes with ICI-associated myocarditis.

Treatment of ICI myocarditis

