

PROBLEM

Immune checkpoint inhibitors (ICIs) are associated with cardiotoxicity.

- ✗ Cardiotoxicity with ICIs range from myocarditis and heart failure to potentially serious arrhythmias, pericarditis and vasculitis.
- ✗ Current guideline recommendations lack key prognostic factors, strategies for prevention and a data-driven suggestion for frequency of monitoring.
- ✗ The mechanisms of ICI-related cardiovascular events are not well-known.

SOLUTION

- ✓ With either suspicion or confirmation of ICI-associated cardiotoxicity, discontinuation of the offending agent and initiation of steroids should be initiated promptly.
- ✓ Other conditions including ischemia must be ruled out.
- ✓ Corticosteroids should be continued until resolution of symptoms and normalization of troponin, left ventricular systolic function and conduction abnormalities.
- ✓ Consider abatacept for the treatment of severe ICI myocarditis.

GRADING OF SEVERITY

G1

Mildly abnormal screening tests, no symptoms

G2

Abnormal screening tests with mild symptoms

G3 – Severe

Moderately abnormal screening tests (arrhythmia, cardiac biomarker > upper limit of normal, significant echocardiogram findings), symptoms with mild activity

G4 – Life-Threatening

Moderate to severe decompensation, hemodynamic instability, cardiac biomarker >3 upper limit of normal, requiring intravenous medications or interventions

TREATMENT TABLE

Institute monitoring and management strategies outlined in the treatment table

Immune Checkpoint Inhibitors	<ul style="list-style-type: none"> - Atezolizumab - Avelumab - Cemiplimab - Durvalumab - Ipilimumab - Nivolumab - Pembrolizumab 		
Cardiotoxic Effects (Although these effects are rare, they are associated with high mortality when they do occur)	<ul style="list-style-type: none"> - Myocarditis - Arrhythmias - Cardiomyopathy - Pericarditis - Pericardial effusion - Vasculitis - Takotsubo cardiomyopathy 		
Monitoring Strategies	<ul style="list-style-type: none"> - Cardiac biomarkers - Electrocardiography - Chest X-ray - Endomyocardial biopsy (gold standard) 		
Management Strategies	<p>G1 toxicity</p> <ul style="list-style-type: none"> - Hold ICI - Monitor and trend electrocardiogram and cardiac biomarkers - Rule out other potential causes - Resume ICI under close monitoring if no worsening 	<p>G2-G3 toxicity</p> <ul style="list-style-type: none"> - Permanently discontinue ICI - Mild symptoms: Oral prednisone 1-2 mg/kg/day - Severe symptoms: Methylprednisolone intravenously 1 g/day for 3-5 days - Continue steroid until cardiac function returns to baseline, then taper 4-6 weeks 	<p>G4 toxicity</p> <ul style="list-style-type: none"> - Permanently discontinue ICI - Methylprednisolone intravenously 1 g/day for 3-5 days - Consider initiating abatacept or other immunosuppressive therapies (antithymocyte globulin, infliximab, or mycophenolate mofetil) - Continue steroid until cardiac function returns to baseline, then taper 4-6 weeks - Initiate advanced heart failure management, including hemodynamic support with ventricular assist devices, as indicated

BEST PRACTICES



- ✓ A close collaboration between oncology and cardiology is essential in the management of ICI myocarditis.
- ✓ The diagnosis of ICI-related myocarditis is challenging and relies on clinical judgement and the interpretation of imaging and changes in biomarkers.
- ✓ Discontinuation of therapy and early initiation of high-dose corticosteroids with or without abatacept are the mainstay of management.

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