

**Supplementary-Table-1. Diagnostic certainty criteria for ICI-myocarditis** (adapted from Bonaca et al.)(1,2)

<b>Hierarchical criteria's accounting for different levels of evidence for ICI-myocarditis</b>
For all, other diagnosis/explanations must be excluded (particularly cardiotoxicity of another liable drug used in combination). Overlap between ICI-myocarditis and acute coronary syndrome or venous thromboembolism has been described previously.(3)
<p><b>Definite myocarditis</b> (any one of the below situations is sufficient)</p> <ul style="list-style-type: none"> <li>- Definite cardiac pathology</li> <li>- Definite CMR + syndrome + (biomarker or ECG or WMA)</li> <li>- WMA + syndrome + biomarker + ECG + negative angiography</li> <li>- Definite muscular pathology + (suggestive/definite CMR or WMA or ECG or suggestive cardiac pathology) + biomarker</li> <li>- Suggestive (muscular or cardiac) pathologies + (suggestive/definite CMR or WMA or ECG) + biomarker + syndrome</li> </ul>
<p><b>Probable myocarditis</b> (any one of below situations is sufficient)</p> <ul style="list-style-type: none"> <li>- Definite CMR + (biomarker or ECG or WMA) and no syndrome</li> <li>- Suggestive CMR + biomarker + (syndrome or ECG or WMA)</li> <li>- WMA + syndrome + biomarker + ECG and no available angiography</li> <li>- Suggestive muscular pathology + (suggestive CMR or WMA or ECG) + (biomarker or syndrome)</li> <li>- Suggestive cardiac pathology + (biomarker or syndrome or ECG)</li> <li>- Syndrome + biomarker + ECG + negative angiography + no WMA + normal CMR + normal cardiac pathology</li> </ul>
<p><b>Possible myocarditis</b> (any one of the below situations)</p> <ul style="list-style-type: none"> <li>- Suggestive CMR + biomarker with no (syndrome or ECG or WMA)</li> <li>- Suggestive/aspecific lesions on muscular pathology + biomarker</li> <li>- Suggestive cardiac pathology</li> <li>- Biomarker + (syndrome or ECG) and no alternative diagnosis*</li> </ul>

**Abbreviations:** Biomarker(4): identification of unknown increase of troponin assay above its 99<sup>th</sup> percentile upper reference limit with troponin-T Elecsys (Roche Diagnostics) used in our center; CMR:(5) cardiac magnetic resonance imaging (analysis based on T1 & T2 properties of cardiac tissue); ECG:(6,7) electrocardiogram (12-leads 10 seconds) identifying an unknown abnormality (atrio-ventricular or sinus blocks, bundle branch blocks, ST-T wave changes, micro-voltage, ventricular or supra-ventricular arrhythmias, pathological Q-waves); Syndrome:(4,8) appearance on ICI of any of the following abnormalities (dyspnea, chest pain, diplopia, ptosis, myalgia, muscular weakness, dysphonia, dysphagia, abdominal paradox, syncope, faintness, palpitations, ventricular hyperexcitability on electrocardiographic holter/telemetry (>5% of non-sinus ventricular rhythms), and respiratory muscle involvement probable or definite (**Supplementary-Table-3**); WMA: identification of unknown wall motion abnormality or left ventricular ejection fraction<50% by cardiac imaging.

\* Acute coronary syndrome and ICI-myocarditis may co-occur at presentation.(3) ICI-myocarditis should be reassessed after revascularization particularly if this has not led to resolution of alteration in

biomarkers, ECG or syndrome or if syndrome is including peripheral muscle involvement not explained by cardiac ischemia (diplopia, ptosis, myalgia, muscle weakness, dysphagia, dysphonia).

**Addendum for detailed criteria required depending on modality used for diagnosis of ICI-myocarditis :**

- **Cardiac pathology** (endomyocardial or autopsy samples)(9,10) :
  - **Definite** : Abnormal lympho-histiocytic inflammatory cells infiltrate (CD3<sup>+</sup> cells  $\geq 7/\text{mm}^2$  or CD68<sup>+</sup> cells  $\geq 4/\text{mm}^2$ ) AND cardiomyocytes necrosis.
  - **Suggestive** (borderline): Abnormal lympho-histiocytic inflammatory cells infiltrate (CD3<sup>+</sup> cells  $\geq 7/\text{mm}^2$  or CD68<sup>+</sup> cells  $\geq 4/\text{mm}^2$ ) WITHOUT cardiomyocytes necrosis.
- **Cardiac magnetic resonance imaging** (analysis based on T1 & T2 properties of cardiac tissue, using a SIEMENS Magnetom Area 1.5 Tesla in our center) (5) :
  - **Definite** : Tissue imaging identifying unknown abnormalities in cardiac segments in both T1 (native T1  $\geq 1100\text{msec} \pm$  extracellular volume  $\geq 28\% \pm$  presence of late gadolinium enhancement) AND T2 (T2 $\geq 50\text{msec}$ ) derived maps and sequences.
  - **Suggestive** (borderline): Tissue imaging identifying unknown abnormalities in cardiac segments in either T1 OR T2 derived maps and sequences.
- **Peripheral muscle pathology** (skeletal muscles or autopsy samples) (11):
  - **Definite** : Abnormal endomysial lympho-histiocytic inflammatory cells infiltrate AND abnormal class 1 human leukocyte antigen overexpression on myocytes AND myocytes necrosis.
  - **Suggestive** (borderline): Abnormal endomysial lympho-histiocytic inflammatory cells infiltrate AND abnormal class 1 human leukocyte antigen overexpression on myocytes WITHOUT myocytes necrosis.
  - **Non-specific lesions**: Abnormal class 1 human leukocyte antigen overexpression on myocytes WITHOUT abnormal endomysial lympho-histiocytic inflammatory cells infiltrate WITHOUT myocytes necrosis.

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