

Supplement S1- Certainty Adjudication Criteria as per criteria from Bonaca et al<sup>3</sup>.

1. Definite myocarditis: the presence of at least one of the following:
  - a. Pathology consistent with myocarditis.
  - b. Diagnostic CMR, the clinical syndrome of myocarditis, and positive biomarker or ECG.
  - c. Echocardiography with wall motion abnormality, the clinical syndrome of myocarditis, positive biomarker, positive ECG, and negative angiography for CAD.
2. Probable myocarditis:
  - a. Diagnostic CMR without clinical syndrome of myocarditis, positive ECG, or positive biomarker, OR
  - b. Suggestive CMR with one of the following:
    - i. Clinical syndrome of myocarditis.
    - ii. Positive ECG.
    - iii. Positive biomarker, OR
  - c. Echocardiography with wall motion abnormality and the clinical syndrome of myocarditis with either positive ECG or biomarker, OR
  - d. Clinical syndrome of myocarditis with positron emission tomography scan evidence and no alternative diagnosis.
3. Possible myocarditis:
  - a. Suggestive CMR without clinical syndrome of myocarditis, positive ECG, or positive biomarker, OR
  - b. Echocardiography with wall motion abnormality and the clinical syndrome of myocarditis or positive ECG, OR
  - c. Elevated biomarker with the clinical syndrome of myocarditis or positive ECG and no alternative diagnosis.

Supplement S2- TNF- $\alpha$  and IL-6 levels compared to histologic grade of myocarditis

	No biopsy	Grade 0 <sup>†</sup>	Grade 1A <sup>†</sup>	Grade 1B <sup>†</sup>	Grade 2 <sup>†</sup>	p-value*
TNF- $\alpha$ >22pg/mL, % (Positive/total)	64 (23/36)	100 (2/2)	67 (4/6)	75 (3/4)	71 (12/17)	0.825
TNF- $\alpha$ level if positive, median [IQR] (number of observations)	36 [28,54] (23)	77.5 [38,117] (2)	92 [33,182] (4)	75 [34, 176] (3)	35 [31.5,53] (12)	0.306
IL-6 >5 pg/mL percentage (Positive/total)	72 (26/36)	50 (1/2)	83 (5/6)	50 (2/4)	82 (14/17)	0.429
IL-6 level if positive Median [IQR] (number of observations)	41.5 [20,97] (26)	39 [39,39] (1)	21 [20,23] (5)	10 [8,12] (2)	30 [16,116] (14)	0.194

TNF- $\alpha$ : Tumor Necrosis Factor  $\alpha$ , IL-6: Interleukin-6, IQR: Interquartile Range

\* Calculated with  $\chi^2$  test or Kruskal Wallis

<sup>†</sup> Grading as per histologic criteria previously published<sup>5</sup>

**Supplement S3. Outcomes in Patients with Peak TNF- $\alpha$ >22 pg/mL stratified by sex.**

<b>Outcomes</b>	<b>Females Peak TNF-<math>\alpha</math> &gt; 22 (pg/mL) (n= 12 /18)</b>	<b>Males Peak TNF-<math>\alpha</math> &gt; 22 (pg/mL) (n= 33 /47)</b>	<b>P-value</b>
<b>90-day mortality, n (%)</b>	3/12 (25%)	11/33 (33.3%)	0.59
<b>MACE, n (%)</b>	<b>0</b>	6/33 (18.2%)	0.11
	-	3 (9.4%)	
<b>Heart failure</b>	-	1 (3.1%)	
<b>Pulmonary embolism</b>	-	2 (6.3%)	
<b>Sudden cardiac death</b>	-	0	
<b>Arterial thrombosis</b>	-	3 (9.4%)	
<b>Arrhythmia</b>			

**Supplement S4. Outcomes in Patients with Peak IL-6 > 5 pg/mL stratified by sex.**

<b>Outcomes</b>	<b>Females Peak IL-6 &gt;5 (pg/mL) (n=14/18)</b>	<b>Males Peak IL-6 &gt;5 (pg/mL) (n=31/47)</b>	<b>P-value</b>
<b>90-day mortality, n (%)</b>	3/15 (20%)	10/33 (30.3%)	0.46
<b>MACE, n (%)</b>	<b>0</b>	4/31 (12.9%)	0.29
	-	2 (6.5%)	
<b>Heart failure</b>	-	0	
<b>Pulmonary embolism</b>	-	2 (6.5%)	
<b>Sudden cardiac death</b>	-	0	
<b>Arterial thrombosis</b>	-	3 (9.7%)	
<b>Arrhythmia</b>			