

## **Supplementary Appendix**

Shorter versus Longer Corticosteroid Duration and Recurrent Immune Checkpoint Inhibitor-Associated AKI

[Table of Contents](#)**ICPi-AKI Consortium Investigators****Supplemental Tables**

Table S1. Criteria for ICPi-AKI

Table S2. Kidney Disease: Improving Global Outcomes (KDIGO) Criteria for Acute Kidney Injury

Table S3. Characteristics of Patients with and without Recurrent ICPi-AKI or Death

**Supplemental Figure**

Figure S1. Distribution of Corticosteroid Treatment Duration in Patients with ICPi-AKI

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**Table S1: Criteria for ICPI-AKI**

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**AKI that was directly attributed to the ICPI by the treating provider AND either of the following criteria:**

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**Criteria 1:** Increase in SCr  $\geq$  100% from baseline OR treatment with KRT

**Criteria 2:** Increase in SCr  $\geq$ 50% from baseline AND at least one of the following:

- 1) ATIN on biopsy
  - 2) ICPI held for at least one cycle due to concern for ICPI-AKI
  - 3) Treatment with corticosteroids due to concern for ICPI-AKI
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Abbreviations: AKI, acute kidney injury; ATIN, acute tubulointerstitial nephritis; ICPI, immune checkpoint inhibitor; KRT, kidney replacement therapy; SCr, serum creatinine.

**Table S2: Kidney Disease: Improving Global Outcomes (KDIGO) Criteria for Acute Kidney Injury**

<b>Stage of AKI</b>	<b>Serum Creatinine</b>
Stage 1	1.5-1.9x baseline
Stage 2	2-2.9x baseline
Stage 3	≥3x baseline OR receipt of KRT

Abbreviations: KRT, kidney replacement therapy. Data on urine output were not available and were therefore not considered as part of AKI staging. Based on the KDIGO criteria.<sup>1</sup>

**Table S3. Characteristics of Patients with and without Recurrent ICPI-AKI or Death**

Variable	Recurrent ICPI-AKI or Death (n=17)	No Recurrent ICPI-AKI or Death (n=148)	P Value
Age at ICPI initiation, yrs, median (IQR)	75 (66-81)	69 (60-75)	0.08
Male, n (%)	9 (52.9)	96 (64.9)	0.43
Race, n (%)			0.41
White	14 (82.4)	128 (86.5)	
Black	0 (0)	7 (4.7)	
Other/Unknown	3 (17.7)	13 (8.8)	
Comorbidities, n (%)			
Hypertension	11 (64.7)	98 (66.2)	0.99
Diabetes	3 (17.7)	29 (19.7)	0.99
CHF	1 (5.9)	6 (4.1)	0.54
COPD	2 (11.8)	15 (10.1)	0.69
Cirrhosis	0 (0)	1 (0.7)	0.99
Body mass index, median (IQR)	29 (24-29)	27 (24-31)	0.90
Baseline eGFR, <sup>1</sup> ml/min per 1.73 m <sup>2</sup>			
Median (IQR)	65 (52-77)	73 (60-87)	0.11
eGFR Categories, n (%)			0.31
≥90	2 (11.8)	30 (20.3)	
60-89	10 (58.8)	80 (54.1)	
45-59	1 (5.9)	20 (13.5)	
<45	4 (23.5)	18 (12.2)	
Extrarenal irAE, <sup>2</sup> n (%)	10 (58.8)	73 (49.3)	0.61
Malignancy, n (%)			0.42
Lung	5 (29.4)	35 (23.7)	
Melanoma	4 (23.5)	41 (27.7)	
Genitourinary	7 (41.2)	42 (28.4)	
Other	1 (5.9)	30 (20.3)	
PPI, <sup>3</sup> n (%)	9 (52.9)	86 (58.1)	0.80
Combo anti-CTLA-4 + anti-PD-1/ PD-L1	4 (23.5)	38 (25.7)	0.99
ICPI-AKI stage, <sup>4</sup> n (%)			0.41
Stage 1	4 (23.5)	15 (10.1)	
Stage 2	4 (23.5)	53 (35.8)	
Stage 3	9 (52.9)	80 (54.1)	
KRT, n (%)	2 (11.8)	7 (4.7)	0.23
Rechallenged after ICPI-AKI, n (%)	1 (5.9)	27 (18.2)	0.31

Data are shown as median (IQR) and n (%). Abbreviations: CHF, congestive heart failure; Combo, combination therapy; COPD, chronic obstructive pulmonary disease; CS, corticosteroids; CTLA-4, cytotoxic T lymphocyte-associated antigen 4; eGFR, estimated glomerular filtration rate; ICPI, immune checkpoint inhibitor; IQR, interquartile range; irAE, immune-related adverse event; KRT, kidney replacement therapy; PD-1, programmed cell death 1; PD-L1, programmed death-ligand 1; PPI, proton pump inhibitor; SCr, serum creatinine.

Categorical data were compared using Chi-squared or Fisher's exact test, as appropriate. Continuous data were compared using Student's t-test or Wilcoxon's rank sum test for normally distributed and skewed data, respectively.

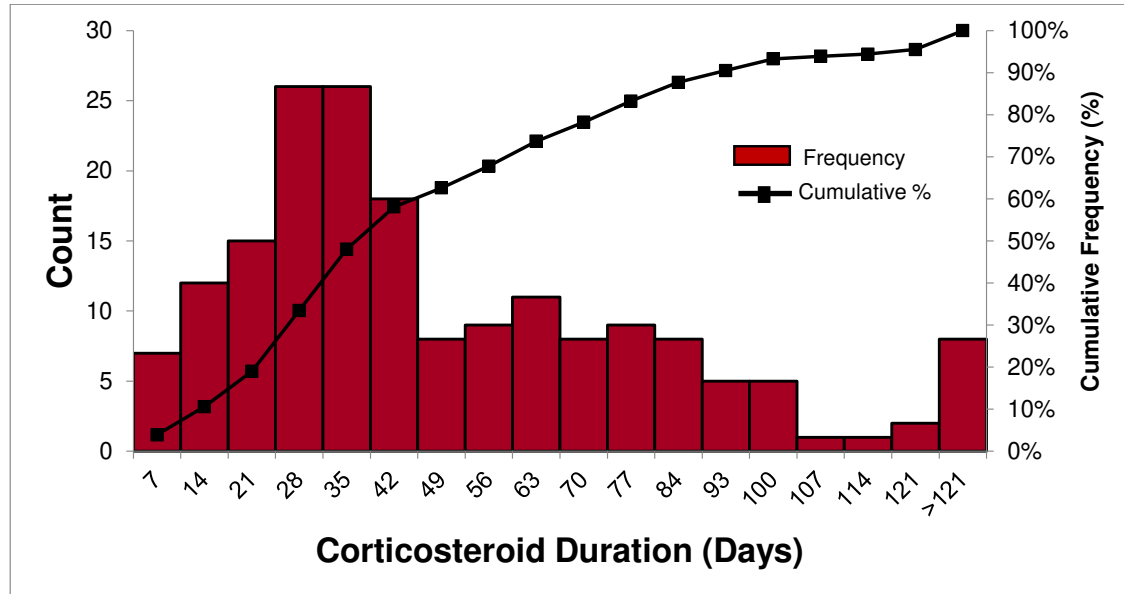
<sup>1</sup>Baseline eGFR was defined based on the SCr value closest and prior to ICPI initiation, and was calculated based on Chronic Kidney Disease-Epidemiology Collaboration equation.<sup>2</sup>

<sup>2</sup>Extrarenal irAEs were assessed prior to (>14 days) or concomitant (within 14 days before or after) with initial ICPI-AKI diagnosis.

<sup>3</sup>PPIs were assessed in the 14 days preceding diagnosis of initial ICPI-AKI episode.

<sup>4</sup>AKI stage at initial episode of ICPI-AKI.

**Figure S1. Distribution of Corticosteroid Treatment Duration in Patients with ICPI-AKI.** Corticosteroid duration was defined as the number of days until they were tapered to a dose of prednisone  $\leq 10$ mg per day (or equivalent). This graph shows that 88% of patients treated with corticosteroids were tapered within 84 days.





## References

1. Kellum JA, Lameire N, Aspelin P, et al. Kidney disease: Improving global outcomes (KDIGO) acute kidney injury work group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl.* 2012.
2. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med.* 2009;150(9):604-12.