Supplemental Appendix

Acute Kidney Injury in Patients Treated with Immune Checkpoint Inhibitors

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Table S1: Collaborating Institutions

Collaborating Institution	Location	No. ICPi-AKI cases (n=429)
United States		
Brigham and Women's Hospital/Dana-Farber Cancer Institute	Boston, MA	20
Duke University	Durham, NC	14
Massachusetts General Hospital	Boston, MA	42
Mayo Clinic	Rochester, MN	24
MD Anderson Cancer Center	Houston, TX	22
Memorial Sloane Kettering Cancer Center	New York, NY	18
Mt. Sinai	New York, NY	5
Northwell Health System	Long Island, NY	15
Northwestern	Chicago, IL	13
Ohio State University	Columbus, Ohio	36
Stanford Healthcare	Palo Alto, CA	22
University Hospitals Cleveland Medical Center	Cleveland, OH	14
University of Alabama Birmingham	Birmingham, AL	6
University of California, Los Angeles	Los Angeles, CA	6
University of California, San Francisco	San Francisco, CA	11
University of Florida, Gainesville	Gainesville, FL	7
University of Miami	Miami, FL	7
University of Pennsylvania	Philadelphia, PA	5
University of Virginia	Charlottesville, VA	7
University of Washington	Seattle, WA	12
International		
Charite Hospital	Berlin, Germany	11
Chi-Mei Medical Center	Tainan, Taiwan	10
Geneva University Hospital	Geneva, Switzerland	7
Guy's and St. Thomas NHS Hospital	London, England	28
Heidelberg University	Heidelberg, Germany	2
Pitie-Salpetriere Hospital	Paris, France	7
Sheba Medical Center	Ramat Gan, Israel	8
University of Toronto	Toronto, Canada	6
Universitair Ziekenhuis Leuven	Leuven, Belgium	14
Vall d'Hebron University Hospital	Barcelona, Spain	30

Abbreviations: ICPI-AKI, immune checkpoint-inhibitor associated acute kidney injury

Table S2: Criteria for ICPi-AKI

AKI that was directly attributed to the ICPi by the treating provider AND either of the following criteria:
Criteria 1: Increase in SCr ≥ 100% from baseline OR treatment with RRT
Criteria 2: Increase in SCr ≥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

Abbreviations: AKI, acute kidney injury; ATIN, acute tubulointerstitial nephritis; ICPi, immune checkpoint inhibitor; RRT, renal replacement therapy; SCr, serum creatinine.

Table S3: Kidney Disease: Improving Global Outcomes (KDIGO) Criteria for Acute Kidney Injury

Stage of AKI	Serum Creatinine
Stage 1	1.5-1.9x baseline
Stage 2	2-2.9x baseline
Stage 3	≥3x baseline OR initiation of RRT

Abbreviations: RRT, renal replacement therapy. Data on urine output were not available and were therefore not considered as part of AKI staging. Based on the KDIGO criteria.[1]

Table S4: Characteristics of Biopsied versus Non-Biopsied Patients with ICPi-AKI

Variable	Biopsied (n=151)	Non-biopsied (*n*=278)	P Value
Age at ICPi initiation, yrs, median (IQR)	65 (58-73)	69 (60-75)	0.05
Male, n (%)	85 (56.3)	181 (65.1)	0.08
Race, n (%)			0.08
White	132 (87.4)	219 (78.8)	
Black	9 (6.0)	18 (6.5)	
Asian	5 (3.3)	16 (5.8)	
Other/Unknown	5 (3.3)	25 (9.0)	
Comorbidities, n (%)			
Hypertension	77 (60.0)	174 (62.6)	0.02
Diabetes	28 (18.5)	49 (17.6)	0.90
CHF	6 (4.0)	11 (4.0)	0.99
COPD	16 (10.6)	29 (10.4)	0.99
Cirrhosis	2 (1.3)	9 (3.2)	0.34
Body mass index, median (IQR)	25.6 (21.9-29.4)	26.4 (23.2-30.6)	0.08
Baseline SCr (mg/dL)	0.9 (0.76-1.16)	1.0 (0.8-1.26)	0.04
Baseline eGFR,[1] ml/min per 1.73 m^2			
Median (IQR)	76.5 (59.7-92.1)	71.5 (55.7-89.6)	0.06
eGFR Categories, n (%)			0.15
≥90	47 (31.1)	64 (23.0)	
60-89	65 (43.1)	127 (45.7)	
45-59	27 (17.9)	45 (16.2)	
30-44	10 (6.6)	33 (11.9)	
<30	2 (1.3)	9 (3.2)	0.27
Autoimmune Disease, n (%)	20 (13.2)	27 (9.7)	0.26
Extrarenal irAE,[2] n (%)	56 (37.1)	145 (52.2)	0.003
Malignancy, n (%)			0.21
Melanoma	36 (23.8)	68 (24.5)	
Lung	49 (32.5)	77 (27.7)	
Genitourinary	27 (17.9)	73 (26.3)	
Other	39 (25.8)	60 (21.6)	
PPI,[3] n (%)	82 (39.4)	69 (31.2)	0.09
Concomitant nephrotoxic chemotherapy,[4] n (%)			
Cisplatin	4 (2.7)	3 (1.1)	0.25
VEGF/TKI	3 (2.0)	20 (65.0)	0.02
ICPi, [5] n (%)			
Anti-CTLA-4	34 (22.5)	69 (24.8)	0.64
Anti-PD-1	120 (79.5)	227 (81.7)	0.58
Anti-PD-L1	14 (9.3)	28 (10.1)	0.87
Combo anti-CTLA-4 + anti-PD-1/ PD-L1	34 (22.5)	65 (23.4)	0.90
Initial ICPi-AKI episode by stage,[5] n (%)			<0.001
Stage 1	18 (11.9)	59 (21.2)	
Stage 2	40 (26.5)	104 (37.4)	
Stage 3	93 (61.6)	115 (41.4)	
Nephrologist involved, n (%)	147 (97.4)	214 (77.0)	<0.001

Data are shown as median (IQR) and n (%). Abbreviations: CHF, congestive heart failure; Combo, combination therapy; COPD, chronic obstructive pulmonary disease; 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; PD-1, programmed cell death 1; PD-L1, programmed death-ligand 1; PPI, proton pump inhibitor; SCr, serum creatinine; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor.

[1]Baseline eGFR calculated based on Chronic Kidney Disease-Epidemiology Collaboration equation.[2]
[2]Extrarenal irAEs were assessed prior to (>14 days) or concomitant (within 14 days before or after) with ICPi-AKI diagnosis
[3]PPIs were assessed in the 14 days preceding ICPi-AKI.
[4]Concomitant chemotherapies were assessed in the 30 days preceding ICPi-AKI.
[5]AKI stages are defined by Kidney Disease: Improving Global Outcomes criteria.[1]

Data on body mass index are missing in 1 patient. All other data are complete.

Table S5: Clinical Features of Patients Receiving Non-Corticosteroid Immunosuppression (n=22)

Age/ Sex	Cancer Type	ICPi Regimen	Biopsy Findings	Alternative Immuno-suppression	Renal Recovery[1]	Re-challenge with ICPi	Recurrent ICPi-AKI after Rechallenge	Survival Status at Last Follow-up	Days from ICPi-AKI to Last Follow-up or Death
72M	Melanoma	Ipi/Nivo		Infliximab	Yes	No	--	Alive	152
73M	Colon	PD-L1		Tocilizumab	Yes	No	--	Alive	524
69M	Melanoma	Ipi/Nivo		MMF	Yes	Yes	Yes	Alive	347
50F	Melanoma	CTLA-4/PD-1		MMF	Yes	No	--	Alive	584
72M	Melanoma	Ipi/Nivo		Infliximab	Yes	Yes	Yes	Deceased	200
33F	Melanoma	Ipi		Infliximab	Yes	No	--	Alive	1191
56F	Lung Adeno	Pembro	ATIN	MMF	No	No	--	Alive	119
66M	HCC	Atezo		MMF	Yes	No	--	Deceased	53
46M	Lung Adeno	Pembro	ATIN	Infliximab	No	No	--	Alive	283
60M	Lung Adeno	Pembro	ATIN	MMF	No	No	--	Alive	688
76M	Lung Adeno	Pembro		MMF	No	No	--	Deceased	141
71F	Gastric Adeno	Pembro	Membranous with lupus-like features	IVIG	No	Yes	Yes	Deceased	38
51M	HCC	Nivo	ATIN, chronic TMA, IC-mediated GN	Infliximab	No	Yes	Yes	Alive	1014
60M	RCC	Ipi/Nivo		MMF	No	No	--	Deceased	17
68F	Lung SCC	Atezo		MMF	No	No	--	Deceased	7
66M	RCC	Ipi/Nivo		MMF	Yes	No	--	Alive	132
68M	Melanoma	Ipi/Nivo	ATIN	MMF	Yes	No	--	Deceased	69
63M	Sarcoma	Ipi/Nivo	ATIN, IgA Nephropathy	MMF	No	No	--	Deceased	108
57F	Melanoma	Ipi/Nivo	Pauci-immune GN	PLEX, Rituximab	No	No	--	Alive	297
52F	Lung Adeno	Durva	Pauci-immune GN	Rituximab	No	No	--	Alive	150
81M	Melanoma	Nivo	AA Amyloidosis	Colchicine	No	No	--	Deceased	130
42M	Rectal	Pembro	AA Amyloidosis	Tocilizumab	No	No	--	Alive	555

Abbreviations: Adeno, adenocarcinoma; Atezo, atezolizumab; ATIN, acute tubulointerstitial nephritis; Durva, durvalumab; F, female; GBM, glioblastoma multiforme; GN, glomerulonephritis; HCC, hepatocellular carcinoma; IC, immune complex; ICPi-AKI, immune checkpoint inhibitor-associated acute kidney injury; Ipi, Ipilimumab; IVIG, intravenous immunoglobulin; M, male; MMF, mycophenolate mofetil; Nivo, Nivolumab; Pembro, Pembrolizumab; PLEX, plasmapheresis; RCC, renal cell carcinoma; RCT, randomized clinical trial; SCC, small cell cancer; TMA, thrombotic microangiopathy.

[1]Renal recovery is defined as return of SCr ≤50% of baseline within 90 days of ICPi-AKI.

Table S6: Characteristics of ICPi-AKI Patients with and without Renal Recovery

Characteristic	All patients (*n*=429)	Renal Recovery		P Value
		Yes (*n*=276)	No (*n*=153)	
Age (yrs), median (IQR)	68 (59-75)	69 (60-75)	65 (58-74)	0.14
Sex, n (%)				
Male	266/429 (62.0)	185/266 (69.6)	81/266 (30.5)	0.005
Female	163/429 (38.0)	91/163 (55.8)	72/163 (44.2)	
Race, n (%)				0.04
White	351/429 (81.8)	234/351 (66.7)	117/351 (33.3)	
Non-White	78/429 (18.2)	42/78 (53.9)	36/78 (46.2)	
Hypertension, n (%)				0.36
Yes	251/429 (58.5)	166/251 (66.1)	85/251 (33.9)	
No	178/429 (41.5)	110/178 (61.8)	68/178 (38.2)	
Diabetes, n (%)				0.43
Yes	77/429 (17.9)	53/77 (68.8)	24/77 (31.2)	
No	352/429 (82.1)	223/352 (63.4)	129/352 (36.7)	
Baseline eGFR[1] (ml/min/1.73m^2)				
Median (IQR)	73 (57-90)	68 (53-85)	86 (65-98)	<0.001
eGFR categories				<0.001
≥90	111/429 (25.9)	49/111 (44.1)	62/111 (55.9)	
60-89	192/429 (44.8)	128/192 (66.7)	64/192 (33.3)	
45-59	72/429 (16.8)	56/72 (76.4)	17/72 (23.6)	
<45	54/429 (12.6)	44/54 (81.5)	10/54 (18.5)	
Malignancy, n (%)				<0.001
Lung	126/429 (29.4)	62/126 (49.2)	64/126 (50.8)	
Other	303/429 (70.6)	214/303 (70.6)	89/303 (29.4)	
PPI,[2] n (%)				0.23
Yes	208/429 (48.5)	140/208 (67.3)	68/208 (32.7)	
No	221/429 (51.5)	136/221 (61.5)	85/221 (38.5)	
NSAIDs,[2] n (%)				0.37
Yes	81/429 (18.9)	56/81 (69.1)	25/81 (30.9)	
No	348/429 (81.1)	220/348 (63.2)	128/348 (36.8)	
Antibiotics,[2] n (%)				0.49
Yes	40/429 (9.3)	28/40 (70.0)	12/40 (30.0)	
No	389/429 (90.7)	248/389 (63.8)	141/389 (36.3)	
Receipt of PPI, NSAIDs, or Antibiotics, n (%)				0.05
Yes	266/429 (62.0)	181/266 (68.1)	85/266 (32.0)	
No	163/429 (38.0)	95/163 (58.3)	68/163 (41.7)	
Receipt of concomitant nephrotoxic chemotherapies,[3] n (%)				0.34
Yes	71/429 (16.6)	42/71 (59.2)	29/71 (40.8)	
No	358/429 (83.4)	234/358 (65.4)	124/358 (34.6)	
Combination ICPi therapy,[4] n (%)				0.03
Yes	99/429 (23.1)	73/99 (73.7)	26/99 (26.3)	
No	330/429 (76.9)	203/330 (61.5)	127/330 (38.5)	
Extrarenal irAE,[5] n (%)				0.09
Yes	201/429 (46.9)	138/201 (68.7)	63/201 (31.3)	
No	228/429 (53.2)	138/228 (60.5)	90/228 (39.5)	
Concomitant extra-renal irAE, n (%)				0.03
Yes	114/429 (26.6)	83/114 (72.8)	31/114 (27.2)	
No	315/429 (73.4)	193/215 (61.3)	122/315 (38.7)	
Days from ICPi initiation to AKI, n (%)				0.22
<30	55/429 (12.8)	36/55 (65.5)	19/55 (34.6)	
30-59	56/429 (13.1)	39/56 (69.6)	17/56 (30.4)	
60-89	64/429 (14.9)	47/64 (73.4)	17/64 (26.6)	
≥90	254/429 (59.2)	154/254 (60.6)	100/254 (39.4)	
ICPi-AKI stage,[6] n (%)				<0.001
Stage 1	77/429 (17.9)	70/77 (90.1)	7/77 (9.1)	
Stage 2	144/429 (33.6)	102/144 (70.8)	42/144 (29.2)	
Stage 3	208/429 (48.5)	104/208 (50.0)	104/208 (50.0)	
Blood on urinalysis,[7] n (%)				<0.001
<2+	257/317 (81.1)	175/257 (68.1)	82/257 (31.9)	
≥2+	60/317 (18.9)	27/60 (45.0)	33/60 (55.0)	
Leukocyte esterase on urinalysis,[7] n (%)				<0.001
<2+	238/317 (75.1)	165/238 (69.3)	73/238 (30.7)	
≥2+	79/317 (24.9)	37/79 (46.8)	42/79 (53.2)	
Urine protein:creatinine, g/g, n (%)				0.01
<1	162/206 (78.6)	108/162 (66.7)	54/162 (33.3)	
≥1	44/206 (21.4)	19/44 (43.2)	25/55 (56.8)	

Eosinophilia, cells per µl, n (%)				0.60
<500	387/426 (90.8)	248/387 (64.1)	139/387 (35.9)	
≥500	39/426 (9.2)	27/39 (69.2)	12/39 (30.8)	
Nephrologist involved in treatment of AKI, n (%)				0.89
Yes	361/429 (84.1)	233/361 (64.5)	128/361 (35.5)	
No	68/429 (15.9)	43/68 (63.2)	25/48 (36.8)	
Treatment with CS, n (%)				0.09
Yes	350/429 (81.6)	232/350 (66.3)	118/230 (3.37)	
No	79/429 (18.4)	44/79 (55.7)	35/79 (44.3)	
Treatment with CS within 3d of AKI, n (%)				0.01
Yes	160/347 (46.1)	117/160 (73.1)	43/160 (26.9)	
No	187/347 (53.9)	112/187 (60.0)	75/187 (40.1)	
SCr at CS initiation (mg/dL), median (IQR)	2.5 (2.0-3.7)	2.4 (2.0-3.6)	2.0 (1.5-2.6)	0.90
Received IV pulse CS, n (%)				0.01
Yes	100/350 (28.6)	56/100 (56.0)	44/100 (44.0)	
No	250/350 (71.4)	176/250 (70.4)	74/250 (29.6)	
Initial daily oral CS dose (prednisone equivalent units, mg), median (IQR)	60 (50-80)	60 (60-80)	60 (40-65)	0.12
Nadir SCr after treatment[8] (mg/dL), median (IQR)	1.3 (1.1-1.7)	1.2 (1.0-1.5)	1.6 (1.3-2.1)	<0.001

Abbreviations: AKI, acute kidney injury; BRAF, v-raf murine sarcoma viral oncogene homolog B1; CTLA-4, cytotoxic T lymphocyte–associated antigen 4; combo, combination therapy; CS, corticosteroid; eGFR, estimated glomerular filtration rate; irAEs, immune-related adverse events; ICPi, immune checkpoint inhibitor; IV, intravenous; NSAID, non-steroidal anti-inflammatory drug; PD-1, programmed cell death 1; PD-L1, programmed death-ligand 1; PPI, proton pump inhibitor; RRT, renal replacement therapy; SCr, serum creatinine.

[1]Baseline eGFR calculated based on Chronic Kidney Disease-Epidemiology Collaboration equation.[2]
[2]PPIs, NSAIDs, and antibiotics were assessed in the 14 days preceding AKI.
[3]Refers to treatment with nephrotoxic chemotherapies in the 30 days preceding AKI, including cisplatin, carboplatin, tyrosine kinase and/or vascular endothelial growth factor inhibitors, pemetrexed, BRAF inhibitors, and paclitaxel
[4]Denotes whether the patient ever received combination therapy prior to AKI.
[5]Extrarenal irAEs were assessed prior to (>14 days) or concomitant (within 14 days before or after) with ICPi-AKI.
[6]AKI stages are defined by Kidney Disease: Improving Global Outcomes criteria.[1]
[7]From initial dipstick at the time of AKI diagnosis.
[8]Within 3 months of AKI diagnosis.

112 patients (26.1%) were missing data on blood and leukocyte esterase on urine dipstick, 223 (52.0%) were missing data on urine protein:Cr ratio, 3 (0.7%) were missing data on eosinophils, and 3 (0.7%) were missing data on the timing of corticosteroid treatment. All other data are complete.

Table S7: Characteristics of Patients Rechallenged Versus Not Rechallenged after ICPi-AKI

Variable	All (*n*=429)	Rechallenged (n=121)	Not Rechallenged (*n*=308)	P Value
Age at ICPi initiation, yrs, median (IQR)	68 (59-75)	66 (60-74)	68 (59-75)	0.62
Male, n (%)	266 (62.0)	81 (66.9)	185 (60.1)	0.22
Race, n (%)				0.21
White	351 (81.8)	104 (86.0)	247 (80.2)	
Nonwhite	78 (18.2)	17 (14.1)	61 (19.8)	
Malignancy, n (%)				0.06
Lung	126 (29.4)	27 (22.3)	99 (32.1)	
Melanoma	104 (24.2)	39 (32.2)	65 (21.1)	
Genitourinary	100 (23.3)	28 (23.1)	72 (23.4)	
Other	99 (23.1)	27 (22.3)	72 (23.4)	
Baseline eGFR,[1] ml/min per 1.73 m^2, median (IQR)	73.3 (57.1-90.4)	73.3 (60.7-88.1)	73.6 (55.4-91.5)	0.97
Autoimmune disease, n (%)	47 (11.0)	13 (10.7)	34 (11.0)	0.99
Extrarenal irAE,[2] n (%)	201 (46.9)	58 (47.9)	143 (46.4)	0.83
Initial ICPi-AKI episode by stage,[3] n (%)				0.002
AKI stage 1	77 (18.0)	27 (22.3)	50 (16.2)	
AKI stage 2	144 (33.6)	52 (43.0)	92 (30.0)	
AKI stage 3	208 (48.5)	42 (34.7)	166 (53.9)	
RRT, n (%)	33 (7.7)	3 (2.5)	30 (9.7)	0.001
Rechallenged with same initial class of ICPi, n (%)	---	98 (81.0)	---	
Rechallenged with a different class of ICPi, n (%)	---	23 (19.0)	---	
Treated with corticosteroids, n (%)	350 (81.6)	96 (79.3)	254 (82.5)	0.50
Biopsied, n (%)	151 (35.2)	34 (28.1)	117 (38.0)	0.06
ATIN on Biopsy, n (%)	125 (82.8)	26 (76.5)	99 (84.6)	0.30
Nadir SCr,[4] mg/dl, median (IQR)	1.3 (1.1-1.7)	1.2 (1.0-1.5)	1.4 (1.1-1.8)	0.001
Renal recovery,[5] n (%)	276 (64.3)	93 (76.8)	183 (59.4)	<0.001

Abbreviations: AKI, acute kidney injury; ATIN, acute tubulointerstitial nephritis; ICPi, immune checkpoint inhibitor; RRT, renal replacement therapy; SCr, serum creatinine.

[1]Baseline eGFR calculated based on Chronic Kidney Disease-Epidemiology Collaboration equation.[2]
[2]Extrarenal irAEs were assessed prior to (>14 days) or concomitant (within 14 days before or after) with ICPi-AKI.
[3]AKI stages are defined by Kidney Disease: Improving Global Outcomes criteria.[1]
[4]Lowest SCr in the 90 days following ICPi-AKI onset.
[5]Defined as a return of SCr to ≤50% of the baseline SCr within 90 days of ICPi-AKI.

Table S8: Characteristics of Patients with and without Recurrent ICPi-AKI after Rechallenge

Variable	All Rechallenged (*n*=121)	Recurrent ICPi-AKI (*n*=20)	No Recurrent ICPi-AKI (*n*=101)	P Value
Days, initial ICPi-AKI to rechallenge, median (IQR)	56 (33-121)	58 (37-105)	56 (33-122)	0.86
Renal Recovery from initial ICPi-AKI,[1] n (%)	93 (76.9)	15 (75.0)	78 (77.2)	0.78
SCr at rechallenge (mg/dL), median (IQR)	1.3 (1.1-1.5)	1.3 (1.1-1.6)	1.3 (1.1-1.5)	0.46
On CS at rechallenge, n (%)	59 (48.8)	11 (55.0)	48 (47.5)	0.63
Prednisone dose (mg/day), median (IQR)	10 (20-53)	10 (8-30)	10 (8-20)	0.76
Rechallenge Regimen, n (%)				0.99
CTLA-4	17 (14.0)	3 (14.3)	14 (13.9)	
PD-1	89 (73.6)	15 (71.4)	74 (73.3)	
PD-L1	10 (8.3)	1 (4.8)	9 (8.9)	
Rechallenged with same initial class of ICPi, n (%)	98 (81.0)	14 (70.0)	84 (83.2)	0.34
Rechallenged with a different class of ICPi, n (%)	23 (19.0)	6 (30.0)	17 (16.8)	
Age at ICPi initiation (yrs), median (IQR)	67 (61-73)	67 (62-72)	66 (60-74)	0.92
Female, n (%)	81 (66.9)	14 (70.0)	67 (66.3)	0.99
Autoimmune Disease, n (%)	13 (10.7)	1 (5.0)	23 (11.9)	0.69
Extrarenal irAE,[2] n (%)	58 (47.9)	11 (55.0)	47 (46.5)	0.63
Stages of initial ICPi-AKI,[3] n (%)				0.67
Stage 1 AKI	27 (22.3)	6 (30.0)	21 (20.8)	
Stage 2 AKI	52 (43.0)	8 (40.0)	44 (43.6)	
Stage 3 AKI	42 (34.7)	6 (30.0)	36 (35.6)	
Biopsied, n (%)	34 (28.1)	7 (35.0)	27 (26.7)	0.59
ATIN on biopsy, n (%)	26 (76.5)	3 (42.9)	23 (85.2)	0.04
Died, n (%)	44 (36.4)	12 (60.0)	32 (31.7)	0.02
Days from rechallenge to recurrent ICPi-AKI, median (IQR)	---	72.5 (20.5-120.5)	---	---
SCr at recurrent ICPi-AKI (mg/dL), median (IQR)	---	1.0 (0.9-1.1)	---	---
Stages of recurrent ICPi-AKI, n (%)				
Stage 1 AKI	---	4 (20)	---	---
Stage 2 AKI	---	8 (40)	---	---
Stage 3 AKI[4]	---	8 (40)	---	---
ICPi held at time of AKI, n (%)	---	20 (100)	---	---
ICPi-AKI treated with CS, n (%)	---	14 (70)	---	---
Days from ICPi-AKI to CS, median (IQR)	---	5 (3-13)	---	---
Received IV pulse CS, n (%)	---	1 (7.1)	---	---
Initial daily oral CS dose (mg of prednisone)	---	40 (40-60)	---	---
RRT at the time of CS, n (%)	---	0 (0)	---	---
Received non-CS immuno-suppressant,[5] n (%)	---	2 (10)	---	---
Renal Recovery,[6] n (%)	---	10 (50)	---	---
Days to Renal Recovery, median (IQR)	---	34 (27-38)	---	---
Nadir SCr (mg/dL),[7] median (IQR)	---	1.4 (1.1-1.7)	---	---

Data are shown as median (IQR) and n (%).

Abbreviations: AKI, acute kidney injury; ATIN, acute tubulointerstitial nephritis; CTLA-4, cytotoxic T lymphocyte–associated antigen 4; CS, corticosteroid; ICPi, immune checkpoint inhibitor; IV, intravenous; irAE, immune-related adverse event; PD-1, programmed cell death 1; PD-L1, programmed death-ligand 1; RRT, renal replacement therapy; SCr, serum creatinine.

[1]Defined as a return of SCr to ≤50% of the baseline SCr
[2]Extrarenal irAEs were assessed prior to (>14 days) or concomitant (within 14 days before or after) with ICPi-AKI.
[3]AKI stages are defined by Kidney Disease: Improving Global Outcomes criteria.[1]
[4]2 patients had AKI requiring RRT and were not liberated.
[5]One patient received Anakinra, and another received infliximab.
[6]Defined as a return of SCr to ≤50% of the baseline SCr within 90 days of ICPi-AKI.
[7]Lowest SCr in the 90 days following ICPi-AKI onset.

Figure S1: Participating Sites in the ICPi-AKI Consortium

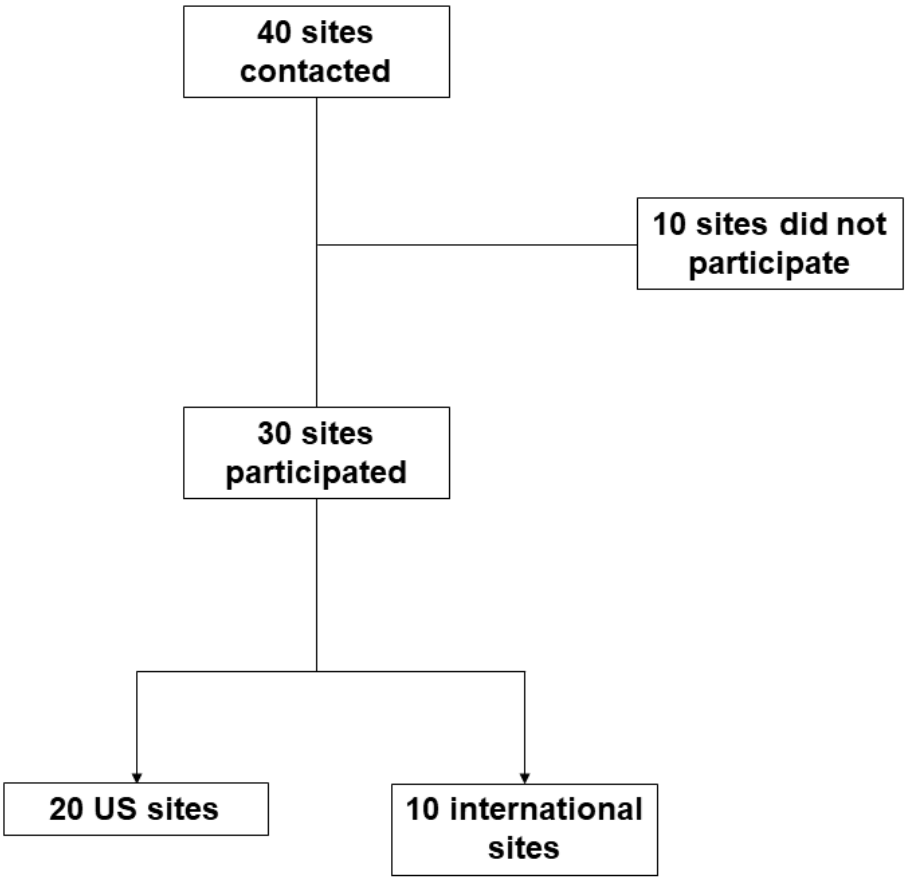


Figure S2: ICPi Initiation by Year among Patients with and without ICPi-AKI

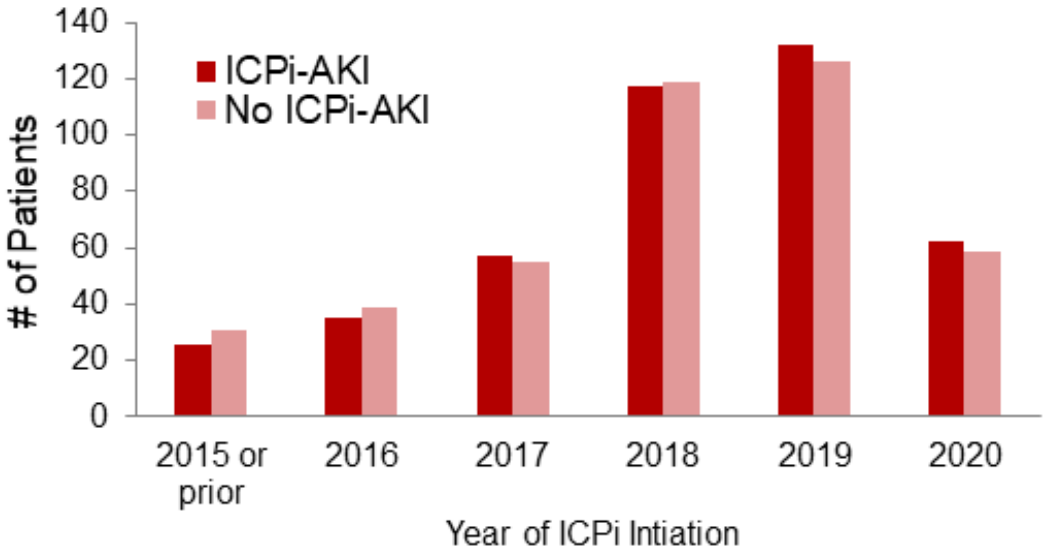
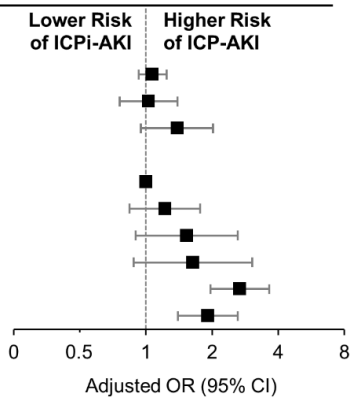


Figure S3: Risk Factors for Stage 2 ICPi-AKI or Higher

Variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age (per 10 years)	1.13 (1.00-1.27)	1.07 (0.93-1.24)
Male sex	1.02 (0.77-1.36)	1.03 (0.76-1.39)
Combination ICPi therapy	1.48 (1.04-2.10)	1.39 (0.95-2.02)
Baseline eGFR (ml/min/1.73m^2)		
≥90 (REF)	1	1
60-89	1.38 (1.00-1.90)	1.22 (0.84-1.76)
45-59	1.82 (1.13-2.92)	1.53 (0.90-2.62)
<45	1.94 (1.11-3.39)	1.64 (0.88-3.05)
PPI use*	2.84 (2.11-3.83)	2.68 (1.97-3.64)
Prior or concomitant extrarenal irAEs**	2.07 (1.54-2.79)	1.91 (1.40-2.62)



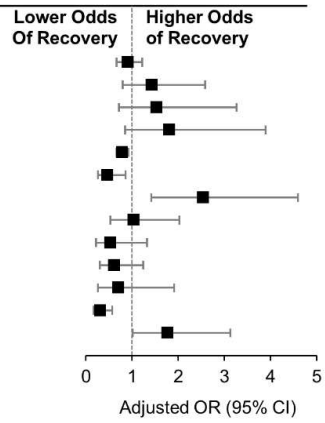
n=781 (352 patients with stage 2 or 3 ICPi-AKI; 429 patients without ICPi-AKI). All model covariates are shown in the figure.

*Denotes PPI use within 14 days preceding ICPi-AKI among those with ICPi-AKI, and PPI use at the time of ICPi initiation among patients without ICPi-AKI.
**Extrarenal irAEs were assessed prior to (>14 days) or concomitant (within 14 days before or after) with ICPi-AKI diagnosis among patients with ICPi-AKI, and at any time after ICPi initiation among patients without ICPi-AKI.

Abbreviations: eGFR, estimated glomerular filtration rate; ICPi, immune checkpoint inhibitor; irAEs, immune-related adverse events; PPI, proton pump inhibitor.

Figure S4: Predictors of Renal Recovery among Patients Treated with Corticosteroids

Variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age (per 10 years)	1.09 (0.90-1.34)	0.90 (0.66-1.22)
Male sex	2.01 (1.26-3.20)	1.43 (0.80-2.58)
White	1.86 (1.01-3.43)	1.53 (0.71-3.26)
Combination Therapy	2.81 (1.50-5.26)	1.81 (0.85-3.89)
eGFR (per 10 points)	0.74 (0.65-0.83)	0.78 (0.66-0.92)
Lung cancer	0.31 (0.19-0.50)	0.47 (0.26-0.86)
Concomitant ATIN-causing medication*	1.74 (1.09-2.80)	2.54 (1.41-4.59)
Concomitant extrarenal irAEs**	1.56 (0.90-2.71)	1.03 (0.53-2.02)
≥2+ Blood on urinalysis	0.50 (0.25-0.98)	0.53 (0.22-1.32)
≥2+ Leukocyte esterase on urinalysis	0.38 (0.21-0.69)	0.61 (0.30-1.24)
≥1 g/g Urine protein:Cr ratio	0.44 (0.21-0.94)	0.70 (0.26-1.91)
Stage 3 AKI	0.26 (0.16-0.42)	0.31 (0.17-0.58)
Corticosteroids within 3 days of ICPi-AKI	2.24 (1.38-3.64)	2.09 (1.16-3.79)

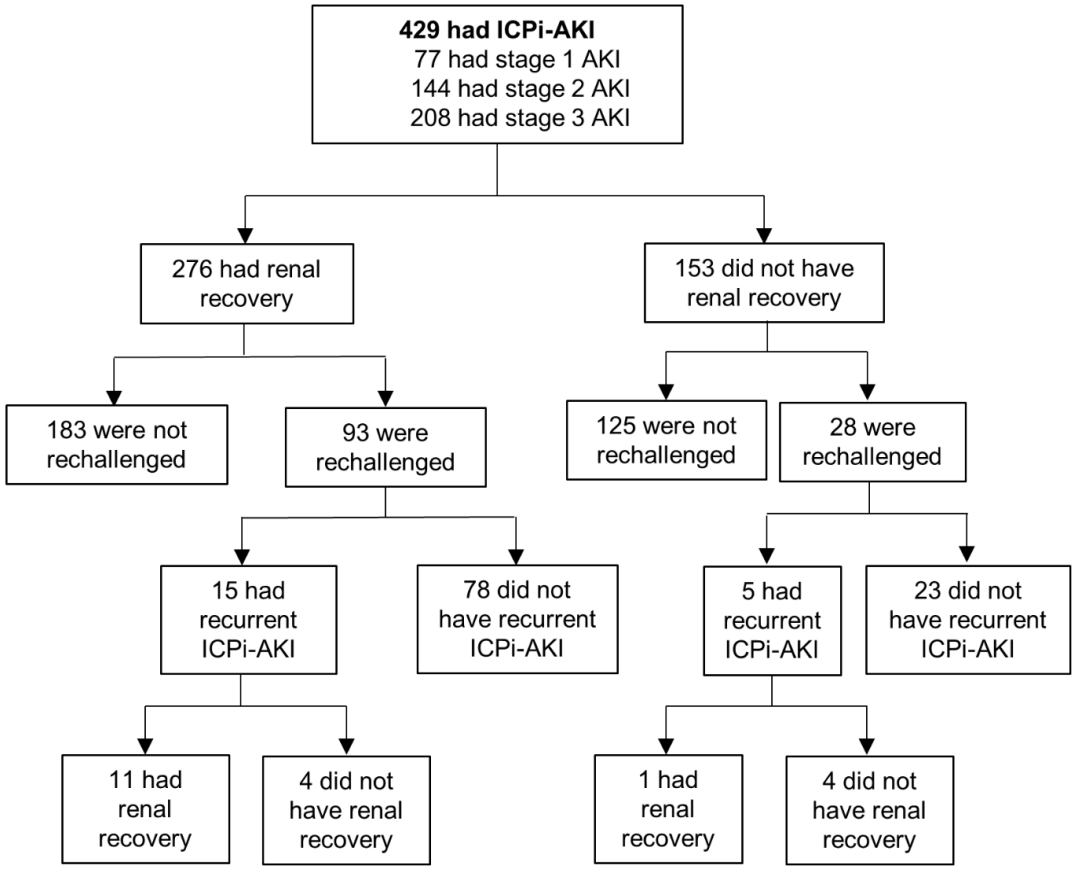


n=334 (including 227 patients with renal recovery). Renal recovery was defined as a return of serum creatinine to ≤50% of the baseline value within 90 days of ICPi-AKI. Patients who were died within 14 days of ICPi-AKI (n=16) were excluded. All model covariates are shown in the figure.

*Denotes receipt of NSAIDs, PPIs, antibiotics in the 14 days preceding ICPi-AKI.
**Extrarenal irAEs were assessed as occurring concomitantly (within 14 days before or after) with ICPi-AKI.

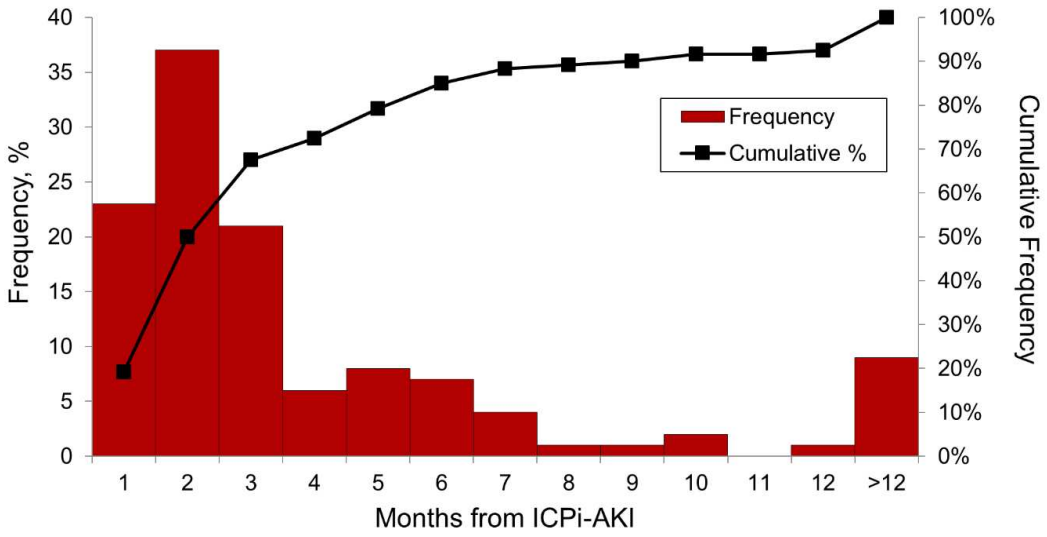
Abbreviations: AKI, acute kidney injury; ATIN, acute tubulointerstitial nephritis; Cr, creatinine; eGFR, estimated glomerular filtration rate; ICPi, immune checkpoint inhibitor; irAE, immune-related adverse events; NSAIDs, non-steroidal anti-inflammatory drugs; PPI, proton pump inhibitor.

Figure S5: Flowchart of Patients with ICPi-AKI



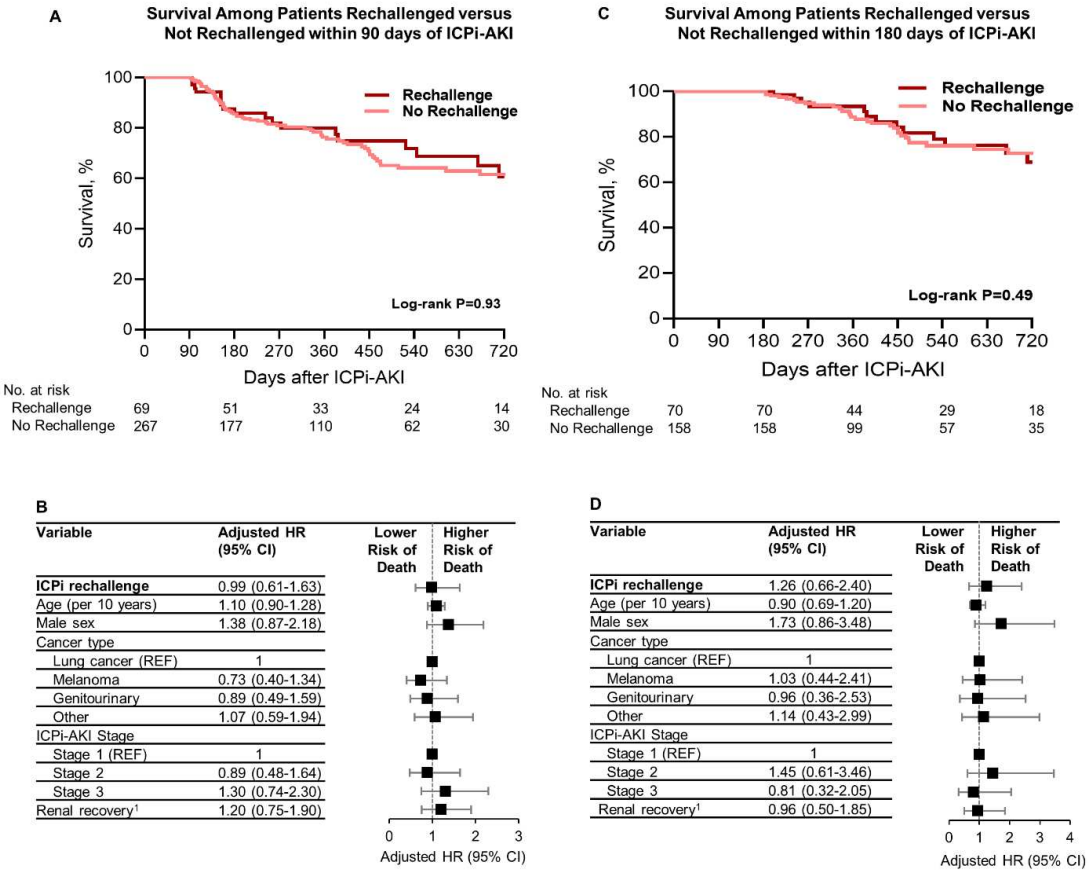
Stages of AKI are defined according to Kidney Disease: Improving Global Outcomes criteria.[1] Renal recovery is defined as a return of serum creatinine to ≤50% of the baseline value within 90 days of ICPi-AKI.

Figure S6: Months from ICPi-AKI to Rechallenge



121 patients were rechallenged at a median of 1.8 months (IQR, 1.1-4.0) following ICPi-AKI

Figure S7: Survival Among Patients Rechallenged versus Not Rechallenged



B

Variable	Adjusted HR (95% CI)
ICPi rechallenge	0.99 (0.61-1.63)
Age (per 10 years)	1.10 (0.90-1.28)
Male sex	1.38 (0.87-2.18)
Cancer type	
Lung cancer (REF)	1
Melanoma	0.73 (0.40-1.34)
Genitourinary	0.89 (0.49-1.59)
Other	1.07 (0.59-1.94)
ICPi-AKI Stage	
Stage 1 (REF)	1
Stage 2	0.89 (0.48-1.64)
Stage 3	1.30 (0.74-2.30)
Renal recovery[1]	1.20 (0.75-1.90)

D

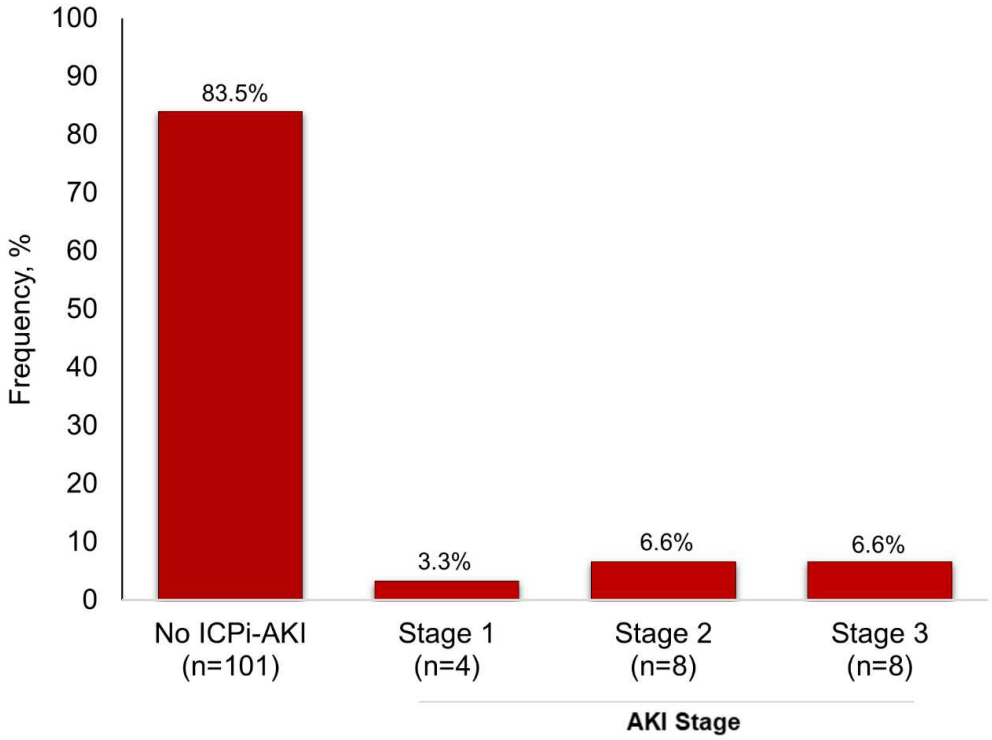
Variable	Adjusted HR (95% CI)
ICPi rechallenge	1.26 (0.66-2.40)
Age (per 10 years)	0.90 (0.69-1.20)
Male sex	1.73 (0.86-3.48)
Cancer type	
Lung cancer (REF)	1
Melanoma	1.03 (0.44-2.41)
Genitourinary	0.96 (0.36-2.53)
Other	1.14 (0.43-2.99)
ICPi-AKI Stage	
Stage 1 (REF)	1
Stage 2	1.45 (0.61-3.46)
Stage 3	0.81 (0.32-2.05)
Renal recovery[1]	0.96 (0.50-1.85)

Kaplan-Meier curves and multivariable Cox regression models were used to estimate the effect of ICPi rechallenge versus no ICPi rechallenge on overall survival. To eliminate the potential for immortal time bias, we limited this analysis to patients who survived at least 90 days after the initial ICPi-AKI event, and we compared the survival of patients rechallenged in the first 90 days to those not rechallenged in the first 90 days (panels A and B). We repeated this analysis in patients who survived at least 180 days following the initial ICPi-AKI event, thereby comparing the survival of patients rechallenged in the first 180 days to those not rechallenged in the first 180 days (panels C and D).

[1]Renal recovery is defined as a return of serum creatinine to ≤50% of the baseline value within 90 days of ICPi-AKI. All model covariates are shown in the figure.

Abbreviations: HR, hazard ratio.

Figure S8: Frequency and Severity of Recurrent ICPi-AKI after Rechallenge (n=121)



Acknowledgements
Of the 429 patients in this study, 24 (5.6%) were reported in a study of biomarkers and clinical features of ICPi-AKI;[3] 10 (2.3%) were reported in a study of AKI among patients receiving ICPis;[4] 1 (0.2%) was reported in a study of ICPi-AKI after PD-L1 inhibitors;[5] 21 (4.9%) were included in a study of patients describing rapid corticosteroid taper versus standard of care for ICPi-AKI;[6] 2 (0.5%) were reported in a study of AA amyloidosis attributed to ICPis;[7] 30 (7.0%) were reported in 3 publications describing patients with ICPi-AKI admitted to a hospital in Spain;[8–10] 3 (0.7%) were included in a study of ICPi-AKI patients with lesions other than acute tubulointerstitial nephritis on biopsy;[11] 7 (1.6%) with ICPi-AKI and 9 (2.1%) control patients without ICPi-AKI were included in 2 publications, neither of which assessed renal toxicities from ICPis;[12,13] and 2 (0.5%) were included in a study of ICPi-AKI in Canada.[14] The 138 patients with ICPi-AKI described in our prior multicenter study[15] were not included in the current study.

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Confirmation of eligibility

Study ID	_____
Did the patient have a ≥100% increase (i.e., doubling) of serum creatinine (SCr) relative to baseline, or the need for renal replacement therapy? Note: Baseline SCr refers to the nearest value prior to initiation of immune checkpoint inhibitor (ICPi) therapy	◯ Yes ◯ No
Was the AKI attributed to the ICPi by the treating provider? *The patient must have received ICPi within 180 days of the AKI	◯ Yes ◯ No
STOP, THIS PATIENT IS NOT ELIGIBLE	
THIS PATIENT IS ELIGIBLE, please proceed with data entry	
Did the patient have a ≥50% increase in SCr from baseline? Note: Baseline SCr refers to the nearest value prior to initiation of immune checkpoint inhibitor (ICPi) therapy	◯ Yes ◯ No
Was the AKI attributed the ICPi by the treating provider?	◯ Yes ◯ No
Does the patient fulfill one or more of the following criteria? 1) Tubulointerstitial nephritis on biopsy 2) ICPi was held for at least one cycle due to concern for ICPi-AKI 3) The patient was treated with steroids due to concern for ICPi-AKI	◯ Yes ◯ No
Which of the following criteria did the patient meet (check one or more)	☐ Tubulointerstitial nephritis on biopsy ☐ ICPi was held for at least one cycle due to concern for ICPi-AKI ☐ The patient was treated with steroids due to concern for ICPi-AKI
STOP, THIS PATIENT IS NOT ELIGIBLE	
Did this patient have a history of a renal transplant?	◯ Yes ◯ No
STOP, THIS PATIENT IS NOT ELIGIBLE	
THIS PATIENT IS ELIGIBLE, please proceed with data entry	

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Demographics

Unless otherwise indicated, the timing of the data below refers to initiation of immune checkpoint inhibitor (ICPi) therapy	
Age (years) at time of AKI	_____
Gender	◯ Male ◯ Female
Race	◯ White ◯ Black ◯ Asian ◯ Unknown
Select assessment(s) of proteinuria performed within 6 months prior to initiation of ICPi therapy (if any were performed more than once, use the most recent value)	☐ None ☐ Spot urine protein to creatinine ratio ☐ Spot urine albumin to creatinine ratio ☐ 24 hr urine collection ☐ Urinalysis
Enter the most recent spot urine protein:Cr ratio (g/g) prior to ICPi therapy For example, enter "3" if the patient had 3 g protein per g of creatinine	_____
Enter the most recent albumin:Cr ratio (mg/g) prior to ICPi therapy For example, enter "30" if the patient had 30 mg albumin per gram of creatinine	_____
Enter the most recent 24 hr urine collection for protein (g/day) prior to ICPi therapy	_____
Enter the results of the most recent urine protein quantification by urinalysis prior to ICPi therapy	◯ neg/trace ◯ 1+ ◯ 2+ ◯ 3+ ◯ 4+
Weight (kg) Pay careful attention to the units and enter the weight in kg, not lbs	_____
Height (cm) Pay careful attention to the units and enter the height in cm, not inches	_____

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Baseline serum creatinine (SCr) . Please enter in mg/dl Note: Baseline SCr refers to the nearest value prior to initiation of ICPi therapy	_____ (*Serum creatinine should be in mg/dl)
Was a CBC with differential performed within three months prior to initiation of ICPi therapy?	◯ Yes ◯ No
What was the total white blood cell (WBC) count?	_____ (If more than one CBC with diff was performed within 3 months prior to ICPi initiation, use the closest one)
What was the neutrophil percentage? (enter as a number between 0 to 100, and without a "%" sign)	_____ (If more than one CBC with diff was performed within 3 months prior to ICPi initiation, use the closest one)
What was the lymphocyte percentage? (enter as a number between 0 to 100, and without a "%" sign)	_____ (If more than one CBC with diff was performed within 3 months prior to ICPi initiation, use the closest one)
What was the eosinophil percentage? (enter as a number between 0 to 100, and without a "%" sign)	_____ (If more than one CBC with diff was performed within 3 months prior to ICPi initiation, use the closest one)
What was the platelet count? (enter as a two- or three-digit number)	_____ (If more than one CBC with diff was performed within 3 months prior to ICPi initiation, use the closest one)
Malignancy treated with ICPi	◯ Melanoma ◯ Lung adenocarcinoma ◯ Lung squamous cell ◯ Lung small cell ◯ Head and neck cancer ◯ Renal Cell ◯ Bladder/Urothelial ◯ Pancreatic ◯ Hodgkin Lymphoma ◯ Non-Hodgkin Lymphoma ◯ Other
Specify other malignancy	_____

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Past medical history (check all that apply)	☐ Hypertension ☐ Diabetes mellitus ☐ Chronic kidney disease (eGFR < 60 ml/min/1.73m2 for > 3 months) ☐ Congestive heart failure ☐ COPD ☐ Chronic liver disease ☐ None of above
Enter other relevant past medical history (e.g., history of solid organ transplantation)	_____
What is the presumed cause of CKD?	◯ Hypertension ◯ Diabetes ◯ Other ◯ Unknown
Enter cause of CKD	_____
History of autoimmune disease (check all that apply) **Note, we are specifically looking for autoimmune disease that was present PRIOR to initiation of ICPi therapy, not an immune-related adverse event that happened AFTER starting the ICPi	☐ None ☐ Type 1 diabetes mellitus ☐ Asthma ☐ Psoriasis ☐ Grave's Disease ☐ Hashimoto's thyroiditis ☐ Systemic lupus ☐ Rheumatoid arthritis ☐ ANCA vasculitis ☐ Inflammatory bowel disease (UC or Crohn's) ☐ Celiac disease ☐ Primary biliary cirrhosis/sclerosing cholangitis ☐ Autoimmune hepatitis ☐ Other
Other autoimmune disease	_____
Comments	_____

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ICPi Treatment

All questions in this section refer to ICPi therapy administered PRIOR to the initial episode of AKI	
Date of initiation of ICPi therapy	_____
Did the patient ever receive simultaneous (i.e., at the same point in time) combination therapy with a CTLA-4 inhibitor AND a PD-1/PD-L1 inhibitor prior to AKI?	◯ Yes ◯ No
Check the CTLA-4 inhibitor the patient received simultaneously with a PD-1/PD-L1 inhibitor.	◯ ipilimumab (CTLA-4) ◯ tremelimumab (CTLA-4) ◯ other
Other CTLA-4 inhibitor	_____
Check the PD-1/PD-L1 inhibitor the patient received simultaneously with a CTLA-4 inhibitor.	◯ nivolumab (PD-1) ◯ pembrolizumab (PD-1) ◯ atezolizumab (PD-L1) ◯ avelumab (PD-L1) ◯ durvalumab (PD-L1) ◯ other
Other PD-1/PD-L1 inhibitor	_____
Check all ICPis ever received prior to first episode of AKI	☐ ipilimumab (CTLA-4) ☐ tremelimumab (CTLA-4) ☐ nivolumab (PD-1) ☐ pembrolizumab (PD-1) ☐ atezolizumab (PD-L1) ☐ avelumab (PD-L1) ☐ durvalumab (PD-L1) ☐ other
Other ICPi	_____
Check all ICPis received within 8 weeks prior to the first episode of AKI. If ICPi therapy had already been completed/discontinued >8 weeks prior to AKI, provide the last ICPi regimen given prior to AKI	☐ ipilimumab (CTLA-4) ☐ tremelimumab (CTLA-4) ☐ nivolumab (PD-1) ☐ pembrolizumab (PD-1) ☐ atezolizumab (PD-L1) ☐ avelumab (PD-L1) ☐ durvalumab (PD-L1) ☐ other
Other ICPi	_____
Date of last ICPi dose prior to initial episode of AKI	_____

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AKI clinical features

Was the patient hospitalized as a result of their ICPi-AKI?	◯ Yes ◯ No
Was a nephrologist involved in the management of the ICPi-AKI?	◯ Yes ◯ No
Did the patient have any EXTRA-renal immune-related adverse events in which the onset was prior to AKI? (defined as an onset occurring >14 days before AKI was first detected)	◯ Yes ◯ No
Select all extra-renal adverse events prior to AKI	☐ Rash ☐ Colitis ☐ Hepatitis ☐ Pneumonitis ☐ Thyroid disease ☐ Hypophysitis ☐ Primary Adrenal Insufficiency ☐ Type 1 DM ☐ Myocarditis ☐ Other (free text)
Provide other immune related adverse event prior to AKI	_____
Did the patient have any EXTRA-renal immune-related adverse events in which the onset was concurrent with the AKI? (defined as an onset occurring within 14 days prior to or after AKI was first detected)	◯ Yes ◯ No
Select all extra-renal immune related adverse events occurring concomitantly with AKI	☐ Rash ☐ Colitis ☐ Hepatitis ☐ Pneumonitis ☐ Thyroid disease ☐ Hypophysitis ☐ Primary Adrenal Insufficiency ☐ Type 1 DM ☐ Myocarditis ☐ Other (free text)
Provide other immune related adverse events occurring concomitantly with AKI	_____
Did the patient take any of the following within 14 days preceding detection of AKI?	☐ Antibiotics ☐ NSAIDs ☐ Proton pump inhibitors
Which antibiotic did patient receive?	_____
Did the patient receive cisplatin within a month prior to AKI diagnosis?	◯ Yes ◯ No

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Why was the AKI attributed to the ICPi instead of the cisplatin?	_____
Did the patient receive a tyrosine kinase inhibitor (TKI) and/or a vascular endothelial growth factor (VEGF) inhibitor within a month prior to AKI diagnosis?	◯ Yes ◯ No (ex: aflibercept, axitinib, bevacizumab, cabozantinib, dasatinib, erlotinib, gefitinib, imatinib, levantinib, nilotinib, pazopanib, ponatinib, ramucirumab, ranibizumab, regorafenib, sorafenib, sunitinib)
Which tyrosine kinase and/or VEGF inhibitor did the patient receive?	☐ aflibercept (Zaltrap) ☐ axitinib (Inlyta) ☐ bevacizumab (Avastin) ☐ cabozantinib (Cabometyx) ☐ dasatinib (Sprycel) ☐ erlotinib (Tarceva) ☐ gefitinib (Iressa) ☐ imatinib (Gleevec) ☐ levantinib (Lenvima) ☐ nilotinib (Tasigna) ☐ pazopanib (Votrient) ☐ ponatinib (Iclusig) ☐ ramucirumab (Cyramza) ☐ ranibizumab (Lucentis) ☐ regorafenib (Stivarga) ☐ sorafenib (Nexavar) ☐ sunitinib (Sutent) ☐ other
Which other TKI/VEGF inhibitor did the patient receieve?	_____
Why was the AKI attributed to the ICPi instead of the TKI/VEGF inhibitor?	_____
Did the patient receive another potentially nephrotoxic chemotherapy agent within a month prior to AKI diagnosis?	◯ Yes ◯ No
Which potentially nephrotoxic chemotherapy agent did the patient receive?	_____ (ex: gemcitabine, carboplatin)
Why was the AKI attributed to the ICPi instead of the chemotherapy agent?	_____
Was the patient already receiving glucocorticoids for an alternative condition when AKI was first detected?	◯ Yes ◯ No
Enter the daily dose of glucocorticoids (in prednisone equivalents) the patient was already receiving when AKI was first detected A steroid conversion calculator can be found here: https://www.mdcalc.com/steroid-conversion-calculator	_____

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Enter the reason the patient was already receiving glucocorticoids when AKI was first detected (e.g., to treat an extra-renal immune related adverse event)	_____
You indicated that this patient had a ≥50% (i.e., ≥1.5-fold) increase in SCr relative to baseline. Enter the date the patient first had a ≥50% increase in SCr.	_____
You indicated that this patient had a ≥100% increase (i.e., doubling) in SCr relative to baseline. Enter the date the patient first had a ≥100% increase in SCr.	_____
SCr (mg/dl) at time point when patient first fulfilled criteria for AKI	_____ (Please ensure serum creatinine is in mg/dl)
Peak SCr (mg/dl) during AKI episode (limit to within 4 weeks of AKI diagnosis)	_____ (Please ensure serum creatinine is in mg/dl)
Quantification of proteinuria during AKI (check all that apply)	☐ none ☐ spot urine protein:Cr ratio ☐ spot urine albumin:Cr ratio (microalbumin) ☐ 24 hour urine collection for protein (*Please indicate any quantification within 7 days AFTER AKI onset)
Spot urine protein:Cr ratio (g/g) at AKI diagnosis For example, enter "3" if the patient had 3 g protein per gram of creatinine	_____ (*Please indicate value within 7 days AFTER AKI onset)
Spot urine albumin:Cr ratio (mg/g) at AKI diagnosis For example, enter "30" if the patient had 30 mg albuminuria per gram of creatinine	_____ (*Please indicate value within 7 days AFTER AKI onset)
24 hr urine collection for protein (g/day) at AKI diagnosis	_____ (*Please indicate value within 7 days AFTER AKI onset)
Urinalysis (urine dipstick) performed?	◯ Yes ◯ No
Initial dipstick protein at AKI diagnosis	◯ neg/trace ◯ 1+ ◯ 2+ ◯ 3+ ◯ 4+

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Initial dipstick leukocyte esterase at AKI diagnosis	◯ neg/trace ◯ 1+ ◯ 2+ ◯ 3+
Initial dipstick blood at AKI diagnosis	◯ neg/trace ◯ 1+ ◯ 2+ ◯ 3+ ◯ N/A (taken from foley catheter)
Review of urine sediment with microscopy performed? (either sent to the clinical lab or reviewed manually by a nephrologist)	◯ Yes ◯ No
List all urine microscopy findings at AKI diagnosis	_____ (*Please include findings like 10-20 WBCs per hpf, RBCs, casts, renal tubular epithelial cells, etc.)
Was a CBC with differential performed within one week before or after AKI diagnosis?	◯ Yes ◯ No
What was the total white blood cell (WBC) count?	_____ (if more than one CBC with diff was performed within 1 week before or after AKI diagnosis, please list the closest value)
What was the neutrophil percentage? (enter as a number between 0 to 100, and without a "%" sign)	_____ (if more than one CBC with diff was performed within 1 week before or after AKI diagnosis, please list the closest value)
What was the lymphocyte percentage? (enter as a number between 0 to 100, and without a "%" sign)	_____ (if more than one CBC with diff was performed within 1 week before or after AKI diagnosis, please list the closest value)
What was the eosinophil percentage? (enter as a number between 0 to 100, and without a "%" sign)	_____ (If more than one CBC with diff was performed within 1 week before or after AKI diagnosis, use the closest one)
What was the platelet count?	_____ (if more than one CBC with diff was performed within 1 week before or after AKI diagnosis, please list the closest value)
Renal ultrasound performed within 14 days of AKI diagnosis?	◯ Yes ◯ No
Right kidney size (cm)	_____

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Left Kidney size (cm)	_____
Was a renal biopsy performed?	◯ Yes ◯ No
Paste the entire biopsy report, including light microscopy, immunofluorescence, and electron microscopy (remove patient name and MRN)	_____
Was tubulointerstitial nephritis the primary lesion on biopsy?	◯ Yes ◯ No
Did another lesion co-occur with tubulointerstitial nephritis on biopsy?	◯ Yes ◯ No
What was the lesion on biopsy?	◯ IgA nephropathy ◯ Pauci-immune glomerulonephritis ◯ Minimal change disease ◯ Membranous nephropathy ◯ Thrombotic microangiopathy ◯ Paraprotein-associated disease ◯ Acute tubular necrosis/injury (ATN/ATI) ◯ Other
Please describe the other lesion on biopsy	_____
Antinuclear antibody (ANA)	◯ Not performed ◯ Negative ◯ Positive (*Only refers to testing performed within 2 weeks before or after AKI onset)
Anti-dsDNA	◯ Not performed ◯ Negative ◯ Positive (*Only refers to testing performed within 2 weeks before or after AKI onset)
C3 level	◯ Not performed ◯ Normal/High ◯ Low (*Only refers to testing performed within 2 weeks before or after AKI onset)
C4 level	◯ Not performed ◯ Normal/High ◯ Low (*Only refers to testing performed within 2 weeks before or after AKI onset)
ANCA	◯ Not performed ◯ Negative ◯ Positive (*Only refers to testing performed within 2 weeks before or after AKI onset)

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Did the patient receive PET imaging within 2 weeks before or after AKI diagnosis?	◯ Yes ◯ No
Please list any imaging results relevant to the kidneys	_____
Comments	_____

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AKI Managment

Questions in this section refer to the initial episode of ICPi-associated AKI	
How was ICPi therapy managed at the time of AKI?	◯ Held ◯ Same regimen continued without interruption ◯ Planned ICPi therapy already completed at time of AKI
Was the AKI treated with glucocorticoids?	◯ Yes ◯ No
Why was glucocorticoid therapy withheld?	_____
Date of initiation of glucocorticoid therapy	_____
Was the patient on dialysis at the time of glucocorticoid initiation?	◯ Yes ◯ No
Enter the SCr (mg/dl) at the time of glucocorticoid initiation	_____ (Please ensure units for SCr are mg/dl)
Did patient receive intravenous pulse glucocorticoids?	◯ Yes ◯ No
Enter number of glucocorticoid pulses received	_____
Enter the cumulative dose of pulse steroids in gram equivalents of methylprednisolone (Solumedrol). For example, if the patient received Solumedrol 500mg IV daily x 3 days, enter "1.5" Steroid conversion calculator can be found here: https://www.mdcalc.com/steroid-conversion-calculator	_____
Enter the initial oral prednisone dose (or in prednisone equivalent units, in mg) at the time of AKI Steroid conversion calculator can be found here: https://www.mdcalc.com/steroid-conversion-calculator	_____
Enter the date upon which prednisone was tapered to a dose ≤10 mg per day	_____
Was the patient treated with an immunosuppressive agent other than/in addition to glucocorticoids?	◯ Yes ◯ No

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Enter the name of the alternative agent, route of administration, the dose, and the timing in relation to steroids (e.g., SCr remained elevated for 7 days following initiation of prednisone, and therefore cellcept 1g BID PO was added on day 8, and was continued for 30 days)	
Comments	

Treatment Outcomes

Did the patient achieve complete renal recovery? This is defined as a return of SCr to within 25% of the baseline SCr (the nearest value prior to ICPi initiation). Please limit response to the time period within 3 months following AKI diagnosis.	◯ Yes ◯ No
Enter the date when complete renal recovery was first achieved	_____
Did the patient require renal replacement therapy?	◯ Yes ◯ No
Select the date dialysis was initiated	_____
Was dialysis able to be discontinued? (Note: Select "No" if patient discontinued dialysis for palliative reasons and did not have renal recovery)	◯ Yes ◯ No
Select the date dialysis was discontinued	_____
Enter the nadir SCr (mg/dl) (i.e., the lowest value achieved) following liberation from dialysis. Limit time period to the 3 months following AKI episode. (Note: do not use any values from within 7 days of dialysis)	_____
Enter the nadir SCr (mg/dl) (i.e., the lowest value achieved) within 3 months following AKI onset.	_____
Select the date of the nadir SCr	_____
Enter SCr (mg/dl) at 7 days (+/- 3 days) after the date of AKI onset	_____ (*If no test was performed, enter N/A)
Enter SCr (mg/dl) at 14 days (+/- 3 days) after the date of AKI onset	_____ (*If no test was performed, enter N/A)
Enter SCr (mg/dl) at 21 days (+/- 3 days) from the date of the initial AKI episode	_____ (*If no test was performed, enter N/A)
Enter SCr (mg/dl) at 28 days (+/- 3 days) after the date of AKI onset	_____ (*If no test was performed, enter N/A)
Enter SCr (mg/dl) at 35 days (+/- 3 days) after the date of AKI onset	_____ (*If no test was performed, enter N/A)

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Enter SCr (mg/dl) at 42 days (+/- 3 days) after the date of AKI onset	_____ (*If no test was performed, enter N/A)
Was the patient re-challenged with an ICPi after AKI	◯ Yes ◯ No
Why was the patient not re-challenged?	☐ Death or transition to hospice ☐ Occurrence of another more severe immune-related adverse event ☐ Directly because of ICPi-AKI ☐ Progression of disease on the ICPi ☐ The patient was in remission ☐ Other
Please enter another reason why the patient was not re-challenged with ICPi	_____
Enter date of re-challenge	_____
Enter SCr (mg/dl) at time of re-challenge Note: If the patient was on dialysis at the time of re-challenge, enter "30"	_____
Enter prednisone dose (if any) in mg, in prednisone equivalent units, at time of re-challenge. Note: Enter "0" if patient not on prednisone at time of re-challenge	_____
Select all ICPis received during re-challenge	☐ ipilimumab(CTLA-4) ☐ tremelimumab(CTLA-4) ☐ nivolumab(PD-1) ☐ pembrolizumab(PD-1) ☐ atezolizumab(PD-L1) ☐ avelumab(PD-L1) ☐ durvalumab(PD-L1) ☐ other
Enter other ICPi	_____
Was the patient on a potential tubulointerstitial nephritis-causing medication at the time of ICPi re-challenge (e.g., PPI, NSAIDs, antibiotics)?	◯ Yes ◯ No
If the patient was on one of these medications at the time of re-challenge, which one(s) were they on?	☐ PPIs ☐ NSAIDs ☐ Antibiotics
Did ICPi-AKI recur with rechallenge? Note: ICPi-AKI defined as ≥50% increase in SCr from baseline and attributed to the ICPi. The baseline SCr here is the SCr at the time of ICPi re-challenge.	◯ Yes ◯ No

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How long were they continued on immunotherapy, in # of cycles, from the date of re-challenge? Definition of a cycle: a period of treatment followed by a period of rest (no treatment) that is repeated on a regular schedule. For example, treatment given once followed by three weeks of rest is one treatment cycle	_____
Select date patient first fulfilled criteria for ICPi-AKI after re-challenge	_____
Enter SCr (mg/dl) at time of diagnosis of ICPi-AKI after re-challenge	_____
Enter peak SCr (mg/dl) following ICPi-AKI after re-challenge	_____
How was ICPi therapy managed at the time of ICPi-AKI after re-challenge?	◯ Held ◯ Same regimen continued without interruption ◯ Planned ICPi therapy already completed at time of AKI
Was ICPi-AKI after re-challenge treated with glucocorticoids?	◯ Yes ◯ No
Why was glucocorticoid therapy withheld?	_____
Date of initiation of glucocorticoid therapy for ICPi-AKI after re-challenge	_____
Did patient receive intravenous pulse glucocorticoids for ICPi-AKI after re-challenge?	◯ Yes ◯ No
Enter number of glucocorticoid pulses received	_____
Enter the cumulative dose of pulse steroids in gram equivalents of methylprednisolone (Solumedrol). For example, if the patient received Solumedrol 500mg IV daily x 3 days, enter "1.5" Steroid conversion calculator can be found here: https://www.mdcalc.com/steroid-conversion-calculator	_____
Enter the initial oral steroid dose (or in prednisone equivalent units, in mg) at the time of ICPi-AKI Steroid conversion calculator can be found here: https://www.mdcalc.com/steroid-conversion-calculator	_____
Enter the date upon which prednisone was tapered to a dose ≤10 mg per day	_____

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Was the patient on dialysis at the time of glucocorticoid initiation?	◯ Yes ◯ No
Was the patient treated with an immunosuppressive agent other than/in addition to glucocorticoids?	◯ Yes ◯ No
Enter the name of the alternative agent, route of administration, the dose, and the timing in relation to steroids (e.g., SCr remained elevated for 7 days following initiation of prednisone, and therefore cellcept 1g BID PO was added on day 8, and was continued for 30 days)	_____
Did the patient achieve complete renal recovery from ICPi-AKI after re-challenge? This is defined as a return of SCr to within 25% of the baseline SCr (the nearest value prior to ICPi initiation). Please limit response to the time period within 3 months following AKI diagnosis.	◯ Yes ◯ No
Enter the date when complete renal recovery was achieved after re-challenge.	_____
Did patient require dialysis for ICPi-AKI after re-challenge?	◯ Yes ◯ No
Enter the date dialysis was initiated	_____
Was dialysis able to be discontinued? (Note: Select "No" if patient discontinued dialysis for palliative reasons and did not have renal recovery)	◯ Yes ◯ No
Select the date dialysis was discontinued	_____
Enter the nadir SCr (mg/dl) (i.e., the lowest value achieved) following liberation from dialysis. Limit time period to the 3 months following re-challenge ICPi-AKI episode. (Note: do not use any values from within 7 days of dialysis)	_____
Enter the nadir SCr (mg/dl) (i.e., the lowest value achieved) within 3 months following re-challenge ICPi-AKI onset.	_____
Select the date of nadir SCr	_____
Enter the date of last patient follow-up	_____
Survival status at last follow-up	◯ Alive ◯ Deceased

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Enter the most recent SCr (mg/dl) value Note: Enter 30 if patient on dialysis	_____
Date of most recent SCr value (mg/dl)	_____
Were the dates provided actual dates or were they dummy coded?	◯ Actual dates ◯ Dummy-coded
Comments	_____