Supplemental Data

Supplemental Table 1. Table of baseline characteristics with patients dichotomized by CCL14 concentrations above and at or below 1.3 ng/mL.

	All patients	\leq 1.3 ng/mL	> 1.3 ng/mL	p value
Patients	335	124	211	
Male	209 (62.4%)	81 (65.3%)	128 (60.7%)	0.416
Age ¹ (years)	64 (55 - 73)	63 (55 - 71)	64 (55 - 73)	0.473
BMI^{1} (kg/m ²)	29 (25 - 35)	30 (26 - 36)	28 (25 - 35)	0.131
Race				
Black or African American	35 (10.4%)	17 (13.7%)	18 (8.5%)	
Other/Unknown	17 (5.1%)	2 (1.6%)	15 (7.1%)	0.030
White or Caucasian	283 (84.5%)	105 (84.7%)	178 (84.4%)	
Chronic comorbidities				
СКД	59 (17.6%)	17 (13.7%)	42 (20.0%)	0.181
Diabetes	110 (32.8%)	42 (34.1%)	68 (32.5%)	0.810
CHF	73 (21.8%)	32 (26.4%)	41 (19.4%)	0.168
CAD	118 (35.2%)	56 (45.5%)	62 (29.8%)	0.004
Hypertension	228 (68.1%)	88 (71.5%)	140 (66.4%)	0.333
COPD	54 (16.1%)	16 (13.0%)	38 (18.1%)	0.281
Cancer	85 (25.4%)	23 (18.5%)	62 (29.5%)	0.028
Reason for ICU admission				
Respiratory	96 (28.7%)	24 (19.4%)	72 (34.1%)	0.004
Surgery	105 (31.3%)	41 (33.1%)	64 (30.3%)	0.627
Cardiovascular	149 (44.5%)	54 (43.5%)	95 (45.0%)	0.821
Sepsis	75 (22.4%)	19 (15.3%)	56 (26.5%)	0.021
Neurological	17 (5.1%)	8 (6.5%)	9 (4.3%)	0.442
Trauma	7 (2.1%)	3 (2.4%)	4 (1.9%)	0.713
Other	109 (32.5%)	39 (31.5%)	70 (33.2%)	0.809
Vasopressors ²	213 (63.6%)	81 (65.3%)	132 (62.6%)	0.640
Diuretics ²	181 (54.0%)	76 (61.3%)	105 (49.8%)	0.042
Fluid balance over the 72 hours prior	3271 (1285 -	2267 (365 -	4244 (1851 -	~0.001
to enrollment ^{1,3} (mL)	6422)	4219)	7430)	<0.001
Days from ICU admission to	11(07-22)	14(08-28)	11(07-19)	0.037
enrollment ¹	1.1 (0.7 - 2.2)	1.4 (0.0 - 2.0)	1.1 (0.7 - 1.9)	0.057
Mechanical ventilation	187 (55.8%)	65 (52.4%)	122 (57.8%)	0.363
Baseline serum creatinine ¹ (mg/dL)	1.0 (0.8 - 1.2)	1.0 (0.7 - 1.2)	1.0 (0.8 - 1.3)	0.036
Enrollment serum creatinine ¹ (mg/dL)	2.4 (1.7 - 3.3)	1.7 (1.3 - 2.5)	2.8 (2.1 - 3.6)	<0.001
Enrollment KDIGO Stage				
No AKI	18 (5.4%)	16 (12.9%)	2 (0.9%)	
Stage 1	37 (11.0%)	23 (18.5%)	14 (6.6%)	<0.001
Stage 2	169 (50.4%)	67 (54.0%)	102(48.3%)	
Stage 3	111 (33.1%)	18 (14.5%)	93 (44.1%)	
Enrollment non-renal APACHE III score ¹	54 (43 - 71)	48 (37 - 64)	57 (45 - 74)	<0.001

¹ Median (interquartile range)

² Vasopressors and diuretics are defined as any use from 3 days before through Day 1 (day of study enrollment).

³ Fluid balance is cumulative from the day prior to through the day of enrollment.

Supplemental Table 2A - Comparison of the AUCs for Pre-Enrollment Urine Output (UO) with Urine CCL14 Concentration for the development of Persistent Severe AKI

Predictor*	ROC AUC	P-value for AUC Difference
uCCL14 concentration	0.82 (0.77 - 0.87)	< 0.0001
Mean pre-enrollment weight-adjusted hourly UO**	0.63 (0.57 - 0.70)***	

* Two patients in the analysis cohort did not have pre-enrollment UO data and were excluded from analysis (N=333)

** pre-enrollment includes a maximum of 24 hours of UO data

*** to facilitate comparison, AUC is reported as 1 – (actual AUC) since a lower mean UO is associated with the presence of PS-AKI

Supplemental Table 2B – Urine output and Urine CCL14 Concentration in a Logistic Regression Model for the Development of Persistent Severe AKI

Variable	Odds Ratio	P-value
Mean pre-enrollment weight-adjusted hourly UO	0.76 (0.57 - 1.00)	0.053
Urine CCL14 > 1.3 and ≤ 13	5.91 (2.91 - 13.07)	<0.001
Urine CCL14 > 13	23.70 (9.98 - 61.16)	<0.001

			,					
Cutoff	0/2	0/2			Negative	Positive	Negative	Positive
(ng/mI)	70 below	20 above	Sensitivity	Specificity	Predictive	Predictive	Likelihood	Likelihood
(lig/lilL)	below	above			Value	Value	Ratio	Ratio
0.2	26	06.4	99%	5%	92%	34%	0.19	1.04
0.2	3.0	96.4	95% - 100%	2% - 9%	62% - 100%	29% - 39%	0.02 - 1.42	1.01 - 1.08
0.2	6.2	02.7	99%	9%	95%	35%	0.10	1.09
0.3	6.3	93.7	95% - 100%	6% - 13%	76% - 100%	29% - 40%	0.01 - 0.75	1.04 - 1.14
			99%	15%	97%	36%	0.06	1.16
0.4	10.1	89.9	95% - 100%	10% - 20%	85% - 100%	31% - 42%	0.01 - 0.45	1.10 - 1.23
			98%	19%	96%	37%	0.10	1.21
0.5	13.4	86.6	94% - 100%	14% - 25%	85% - 99%	32% - 43%	0.02 - 0.39	1 13 - 1 30
			05%	25%	92%	38%	0.02 0.05	1 27
0.6	18.2	81.8	90% - 99%	19% - 31%	82% - 97%	33% - 44%	0.08 - 0.44	1.27
			9/1%	28%	90%	30%	0.00 0.44	1 31
0.7	21.2	78.8	870% 070%	23% 35%	81% 96%	330/ 150/	0.11 0.47	1 10 1 44
			03%	33%	90%	40%	0.22	1.1) - 1.44
0.8	24.8	75.2	9570 8604 0704	270/ 400/	9070 8204 0604	4070	0.22	1.39
			020/	27% - 40%	010/	34% - 47%	0.11 - 0.44	1.23 - 1.33
0.9	27.5	72.5	95%	3/%	91%	42%	0.19	1.48
			80% - 97%	51% - 44%	84% - 90%	30% - 48%	0.10 - 0.39	1.52 - 1.00
1	31.0	69.0	92%	42%	91%	44%	0.19	1.59
-			85% - 96%	36% - 49%	84% - 96%	37% - 50%	0.10 - 0.37	1.40 - 1.80
1.1	33.7	66.3	91%	46%	91%	45%	0.20	1.68
			84% - 96%	39% - 53%	84% - 96%	38% - 52%	0.11 - 0.36	1.47 - 1.92
1.2	35.8	64.2	91%	49%	92%	47%	0.19	1.78
	00.0	0.1.2	84% - 96%	42% - 56%	85% - 96%	40% - 53%	0.10 - 0.34	1.55 - 2.05
1.3	37.0	63.0	91%	51%	92%	47%	0.18	1.84
110	07.0	0010	84% - 96%	44% - 57%	86% - 96%	40% - 54%	0.10 - 0.33	1.59 - 2.13
14	40.3	597	88%	54%	90%	49%	0.22	1.93
	.0.5	0,11	81% - 94%	47% - 61%	84% - 95%	41% - 56%	0.13 - 0.37	1.65 - 2.26
1.5	41.2	58.8	88%	56%	91%	49%	0.21	1.98
1.5	41.2	50.0	81% - 94%	49% - 62%	84% - 95%	42% - 56%	0.13 - 0.36	1.69 - 2.33
1.6	127	573	87%	57%	90%	50%	0.22	2.05
1.0	42.7	57.5	80% - 93%	51% - 64%	84% - 95%	43% - 57%	0.13 - 0.37	1.73 - 2.42
17	12.6	56 /	86%	58%	90%	50%	0.23	2.07
1.7	43.0	50.4	79% - 92%	51% - 65%	84% - 94%	43% - 58%	0.14 - 0.38	1.74 - 2.45
1.9	46.0	54.0	85%	61%	90%	52%	0.24	2.21
1.0	40.0	54.0	77% - 91%	55% - 68%	84% - 94%	44% - 59%	0.15 - 0.38	1.84 - 2.65
1.0	17.5	52.5	85%	63%	89%	53%	0.24	2.29
1.9	47.5	52.5	76% - 91%	56% - 69%	83% - 94%	45% - 60%	0.16 - 0.38	1.90 - 2.77
2	10 1	516	84%	64%	89%	53%	0.26	2.32
2	40.4	51.0	75% - 90%	57% - 70%	83% - 93%	45% - 61%	0.17 - 0.39	1.92 - 2.82
2.1	40.4	51.0	84%	64%	89%	53%	0.26	2.32
2.1	40.4	51.0	75% - 90%	57% - 70%	83% - 93%	45% - 61%	0.17 - 0.39	1.92 - 2.82
2.2	40 C	50.4	83%	65%	89%	54%	0.26	2.39
2.2	49.6	50.4	74% - 89%	59% - 72%	83% - 93%	46% - 62%	0.17 - 0.40	1.96 - 2.91
2.2	50.1	40.0	83%	66%	89%	54%	0.26	2.45
2.5	50.1	49.9	74% - 89%	60% - 72%	83% - 93%	47% - 62%	0.17 - 0.40	2.0 - 3.0
2.4	50.7	40.2	83%	67%	89%	55%	0.26	2.52
2.4	50.7	49.5	74% - 89%	61% - 73%	83% - 93%	47% - 63%	0.17 - 0.39	2.05 - 3.09
2.5	52.2	47.0	81%	68%	88%	56%	0.28	2.56
2.5	52.2	47.8	72% - 88%	62% - 74%	82% - 92%	48% - 63%	0.19 - 0.41	2.07 - 3.17
2.6	50.7	160	80%	70%	88%	57%	0.28	2.69
2.6	53.7	46.3	71% - 87%	64% - 76%	82% - 92%	49% - 65%	0.19 - 0.42	2.15 - 3.35
			80%	72%	88%	58%	0.28	2.81
2.7	54.6	45.4	71% - 87%	65% - 77%	82% - 92%	50% - 66%	0.19 - 0.41	2.24 - 3.53
2.0		4.1	80%	73%	88%	59%	0.27	2.95
2.8	55.5	44.5	71% - 87%	67% - 79%	83% - 92%	51% - 67%	0.19 - 0.40	2.34 - 3.73
			80%	74%	88%	60%	0.27	3.05
2.9	56.1	43.9	71% - 87%	68% - 79%	83% - 93%	51% - 68%	0.19 - 0.40	2.40 - 3.87
			80%	75%	88%	61%	0.27	3.16
3	56.7	43.3	71% - 87%	68% - 80%	83% - 93%	52% - 69%	0.18 - 0.39	2.48 - 4.03
		1	77%	78%	88%	63%	0.20	3 48
3.5	59.7	40.3	68% - 85%	72% - 83%	82% - 92%	54% - 71%	0.29	2 67 - 4 53
	1		75%	80%	87%	65%	0.21 - 0.42	3 77
4	61.8	38.2	66% - 83%	74% - 85%	82% - 91%	56% - 73%	0 22 - 0 43	2.85 - 5.0
1	1	1	0070 - 0070	1 - 70 - 0,0 70	02/0 - 71/0	5070 - 7570	0.22 - 0.43	2.05 - 5.0

Supplemental Table 3. Operating characteristics for CCL14 concentration cutoffs from 0.2 to 30 ng/mL for the primary endpoint, persistent severe AKI.

Cutoff	0%	0%			Negative	Positive	Negative	Positive
(ng/mL)	below	above	Sensitivity	Specificity	Predictive	Predictive	Likelihood	Likelihood
(001011	400.0	710/	020/	Value	Value	Ratio	Ratio
4.5	64.5	35.5	/1%	82%	85%	00% 56% 74%	0.36	3.89
		22.4	68%	84%	84%	68%	0.38	4.26
5	66.9	33.1	59% - 77%	79% - 89%	79% - 89%	58% - 76%	0.29 - 0.50	3.08 - 5.90
5 5	69.3	30.7	65%	86%	83%	69%	0.41	4.54
5.5	07.5	50.7	55% - 73%	81% - 90%	78% - 88%	59% - 78%	0.32 - 0.53	3.20 - 6.44
6	70.7	29.3	61% 51% - 70%	86% 81% - 90%	82% 76% - 87%	68% 58% - 77%	0.45	4.42
		2 0 1	58%	86%	81%	67%	0.49	4.22
6.5	71.6	28.4	48% - 68%	81% - 90%	75% - 86%	57% - 77%	0.39 - 0.61	2.94 - 6.07
7	73.4	26.6	55%	87%	80%	67%	0.52	4.23
			45% - 64%	82% - 91%	74% - 85%	57% - 77%	0.42 - 0.64	2.89 - 6.19
7.5	75.8	24.2	49% 39% - 59%	83% - 92%	72% - 83%	55% - 77%	0.38	2.74 - 6.11
0	77.0	22.0	46%	88%	77%	66%	0.61	4.01
8	77.0	23.0	37% - 56%	84% - 92%	72% - 82%	55% - 77%	0.51 - 0.73	2.65 - 6.07
8.5	77.9	22.1	46%	90%	77%	69%	0.60	4.54
			37% - 56%	85% - 93%	72% - 82%	57% - 79%	0.50 - 0.71	2.93 - 7.02
9	78.5	21.5	45% 35% - 54%	90% 85% - 93%	71% - 82%	56% - 79%	0.52 - 0.73	2.81 - 6.76
0.5	70.0	21.2	45%	90%	77%	69%	0.61	4.56
9.5	/8.8	21.2	35% - 54%	86% - 94%	71% - 82%	57% - 79%	0.52 - 0.73	2.91 - 7.13
10	78.8	21.2	45%	90%	77%	69%	0.61	4.56
			35% - 54%	86% - 94%	76%	57% - 79% 71%	0.52 - 0.73	2.91 - 7.13
11	81.2	18.8	32% - 51%	88% - 95%	71% - 81%	59% - 82%	0.55 - 0.75	3.11 - 8.40
12	92.1	17.0	38%	92%	75%	70%	0.67	4.77
12	62.1	17.9	29% - 48%	88% - 95%	70% - 80%	57% - 81%	0.58 - 0.78	2.89 - 7.89
13	83.9	16.1	35%	93%	75%	72%	0.69	5.32
			33%	<u>89% - 90%</u> 95%	74%	75%	0.00 - 0.80	6.14
14	85.7	14.3	24% - 42%	91% - 97%	69% - 79%	60% - 86%	0.62 - 0.81	3.33 - 11.3
15	87.2	12.8	30%	96%	74%	77%	0.73	6.75
	07.12	1210	22% - 39%	92% - 98%	68% - 79%	61% - 88%	0.65 - 0.83	3.45 - 13.2
16	87.8	12.2	28% 20% - 38%	96% 92% - 98%	73% 68% - 78%	70% 60% - 88%	0.75	6.34 3 23 - 12 5
17	07.0	12.2	28%	96%	73%	76%	0.75	6.34
17	87.8	12.2	20% - 38%	92% - 98%	68% - 78%	60% - 88%	0.67 - 0.85	3.23 - 12.5
18	88.4	11.6	27%	96%	73%	77%	0.76	6.82
			19% - 37%	93% - 98%	68% - 78%	61% - 89%	0.67 - 0.85	3.35 - 13.9
19	88.7	11.3	19% - 37%	93% - 98%	68% - 78%	63% - 90%	0.67 - 0.85	3.64 - 16.2
20	80.2	10.7	26%	97%	73%	81%	0.76	8.47
20	09.3	10.7	18% - 36%	94% - 99%	67% - 78%	64% - 92%	0.68 - 0.85	3.83 - 18.7
21	89.6	10.4	25%	97%	73%	80%	0.77	8.18
			25%	94% - 99%	73%	80%	0.09 - 0.80	8 18
22	89.6	10.4	18% - 35%	94% - 99%	67% - 78%	63% - 92%	0.69 - 0.86	3.69 - 18.1
23	90.1	99	24%	97%	72%	79%	0.79	7.60
	50.1).)	16% - 33%	94% - 99%	<u>67% - 77%</u>	61% - 91%	0.71 - 0.88	3.40 - 17.0
24	90.7	9.3	22% 15% - 31%	97%	12% 66% - 77%	//% 59% - 90%	0.81 0.73 - 0.89	7.01 3.12 - 15.8
			21%	97%	71%	77%	0.82	6.72
25	91.0	9.0	14% - 30%	94% - 99%	66% - 76%	58% - 90%	0.74 - 0.90	2.98 - 15.2
26	91.3	8.7	20%	97%	71%	76%	0.83	6.43
			15% - 29%	94% - 99%	66% - 76% 71%	56% - 90% 75%	0.75 - 0.91	2.83 - 14.6
27	91.6	8.4	12% - 28%	91% 94% - 99%	66% - 76%	55% - 89%	0.84	2.69 - 14.0
20	01.6	0 4	19%	97%	71%	75%	0.84	6.14
28	91.6	8.4	12% - 28%	94% - 99%	66% - 76%	55% - 89%	0.76 - 0.92	2.69 - 14.0
29	91.6	8.4	19%	97%	71%	75%	0.84	6.14
			12% - 28%	94% - 99% 100%	00% - /0% 67%	JJ% - 89%	0.76-0.92	2.09 - 14.0
30	100.0	0.0	0% - 0%	100% - 100%	62% - 72%	na	1.0 - 1.0	na

Secondary Endpoint	Median (IQR) in days from enrollment				
KRT	2.8 (1.7 - 7.2)				
Death	15.5 (5.4 - 30.1)				
KRT or death	4.3 (2.0 - 14.0)				

Supplemental Table 4. Time to Secondary Outcomes (KRT and Death)

Supplemental Table 5. NRI and IDI analysis of the addition of urinary CCL14 stratified by two cutoffs at 1.3 and 13 ng/mL to the clinical model in Table 3. Event = persistent severe AKI; non-event = not persistent severe AKI.

	Value	95% CI	P-value
IDI	0.06	0.03 - 0.09	< 0.001
IDI_event	0.04	0.02 - 0.07	0.001
IDI_non_event	0.02	0.01 - 0.04	0.003
cfNRI	0.53	0.30 - 0.77	< 0.001
cfNRI_event	0.39	0.20 - 0.58	< 0.001
cfNRI_non_event	0.14	0.00 - 0.28	0.044
AUC_ref_model	0.86	0.82 - 0.90	< 0.001
AUC_new_model	0.88	0.85 - 0.92	< 0.001
AUC difference	0.03	0.01 - 0.05	0.018

Clinical variables in the reference model are body mass index, non-renal APACHE III score, serum creatinine trajectory, KDIGO stage at enrollment, and diabetes.

Supplemental Table 6. Multivariable logistic regression model using clinical variables for prediction of persistent severe AKI without (Reference Model) and with (New Model) urinary CCL14 as a categorical variable with three levels stratified by two cutoffs at 1.3 and 13 ng/mL. and excluding those found to not have Stage 2 or 3 AKI at enrollment

	Reference N	Iodel	New Model with U	rine CCL14
Variable	Odds Ratio	P-value	Odds Ratio	P-value
Body mass index	0.78 (0.53 - 1.12)	0.194	0.81 (0.54 - 1.17)	0.281
Non-renal APACHE III score	1.47 (1.10 - 2.00)	0.011	1.37 (1.00 - 1.90)	0.052
Serum creatinine trajectory†	1.52 (1.14 - 2.09)	0.006	1.44 (1.06 - 2.01)	0.023
KDIGO stage at enrollment	7.02 (3.92 - 12.96)	< 0.001	5.32 (2.86 - 10.2)	< 0.001
Diabetes	0.58 (0.29 - 1.11)	0.105	0.50 (0.24 - 1.02)	0.058
Urine CCL14 > 1.3 and \leq 13	Not Included	NA	3.77 (1.71 - 8.97)	0.002
Urine CCL14 > 13	Not Included	NA	10.6 (3.96 - 30.8)	< 0.001

[†]Change in serum creatinine concentration over the prior day as determined using two serum creatinine results with mean (±SD) collection times at 19 (±9) h and 7 (±4) h prior to enrollment For the categorical CCL14 variable, CCL14 \leq 1.3 ng/mL was the reference level All numeric variables were standardized by subtracting the mean and dividing by the standard deviation; N = 260 (40% Persistent). The clinical variables in the reference model were selected based on association with persistent severe AKI as described previously.⁹

Supplemental Figure 1 – Risk of persistent severe AKI stratified by CCL14 level below and above 1.3 ng/mL. Within each CCL14 stratum the individual components of the composite endpoint are displayed. The relative risk (95% CI) of persistent severe AKI for those patients with CCL14 level above 1.3 ng/mL to those with CCL14 level below 1.3 ng/mL is 5.9 (3.2 – 11).



Supplemental Figure 2 -Cumulative incidence of KRT, death and KRT or death within 90 days of enrollment in the Ruby study stratified by CCL14 concentrations below and above 1.3 ng/mL. The number of patients with CCL14 concentrations below and above 1.3 ng/mL are 124 and 211, respectively. The log rank test was used to compute the p-value for the differences between the strata.





Supplemental Figure 3 : Comparison of CCL14 concentrations in 4 populations: healthy (378), chronic conditions without acute illness (366), Ruby Intention-to-Diagnose (ITD) Full cohort (335, 225 of whom did not develop persistent severe AKI), and those adjudicated to have Stage 2 or 3 at enrollment (280, 170 of whom did not develop persistent severe AKI). Bottom and top whiskers represent the 10th and 90th percentiles of the CCL14 concentrations in that group, respectively. Bottom and top boxes represent the 1st and 3rd quartiles, respectively. Middle bar is the median. The horizontal dashed lines correspond to the 1.3 and 13 ng/mL cutoffs. P-value computed using the Kruskal-Wallis test < 0.0001.



Operating Characteristics for ITD cohort:	ohort:	ITD	for	Characteristics	Operating
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Endpoint	Cutoff (ng/mL)	% below	% above	Sensitivity	Specificity	Negative Predictive Value	Positive Predictive Value	Negative Likelihood Ratio	Positive Likelihood Ratio
Persistent	1.3	37.0	63.0	91% 84% - 96%	51% 44% - 57%	92% 86% - 96%	47% 40% - 54%	0.18 0.10 - 0.33	1.84 1.59 - 2.13
severe AKI	13	83.9	16.1	35% 27% - 45%	93% 89% - 96%	75% 69% - 80%	72% 58% - 84%	0.69 0.60 - 0.80	5.32 3.07 - 9.22

Operating Characteristics for AKI Stage 2 or 3 cohort:

Endpoint	Cutoff (ng/mL)	% below	% above	Sensitivity	Specificity	Negative Predictive Value	Positive Predictive Value	Negative Likelihood Ratio	Positive Likelihood Ratio
Persistent	1.3	30.4	69.6	91% 84% - 96%	44% 37% - 52%	88% 79% - 94%	51% 44% - 58%	0.21 0.11 - 0.38	1.63 1.41 - 1.88
severe AKI	13	81.8	18.2	35% 27% - 45%	93% 88% - 96%	69% 63% - 75%	76% 63% - 87%	0.69 0.60 - 0.80	5.02 2.75 - 9.16