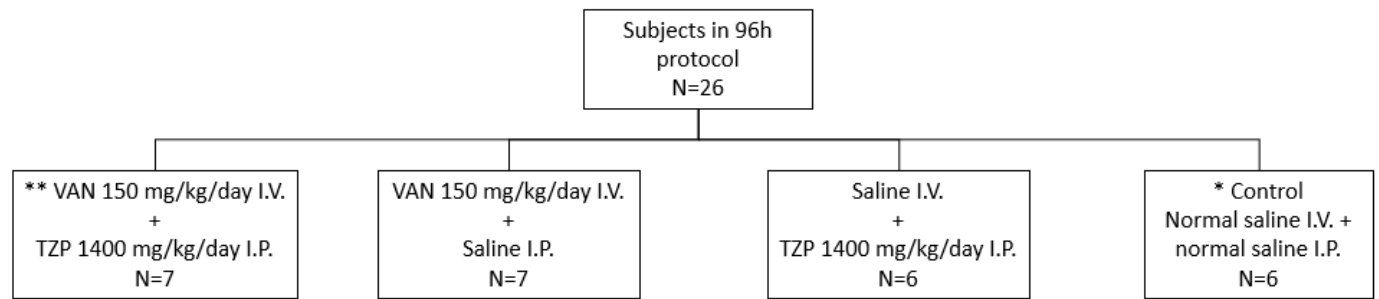


Supplemental figure 1: Study treatment groups assignment

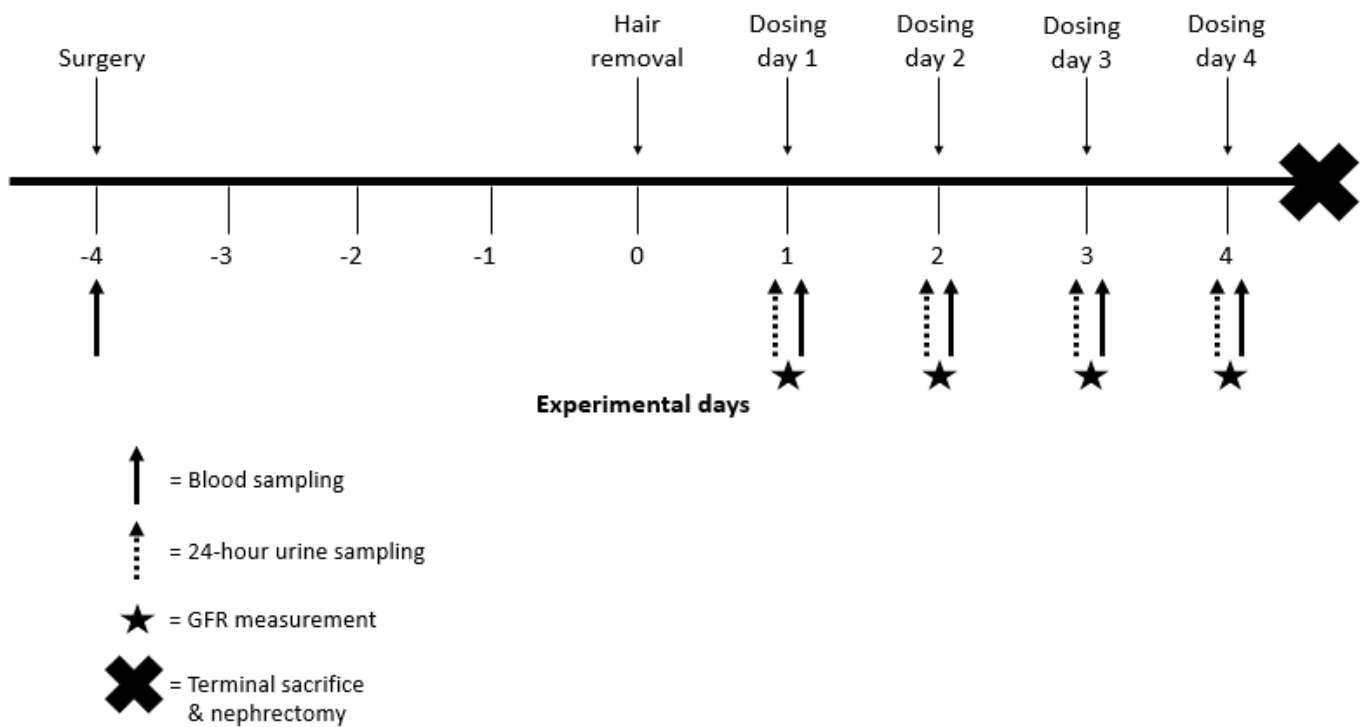


Animal dosing group disposition. Abbreviations: VAN, vancomycin; TZP, piperacillin-tazobactam; I.V., intravenous; I.P., intraperitoneal.

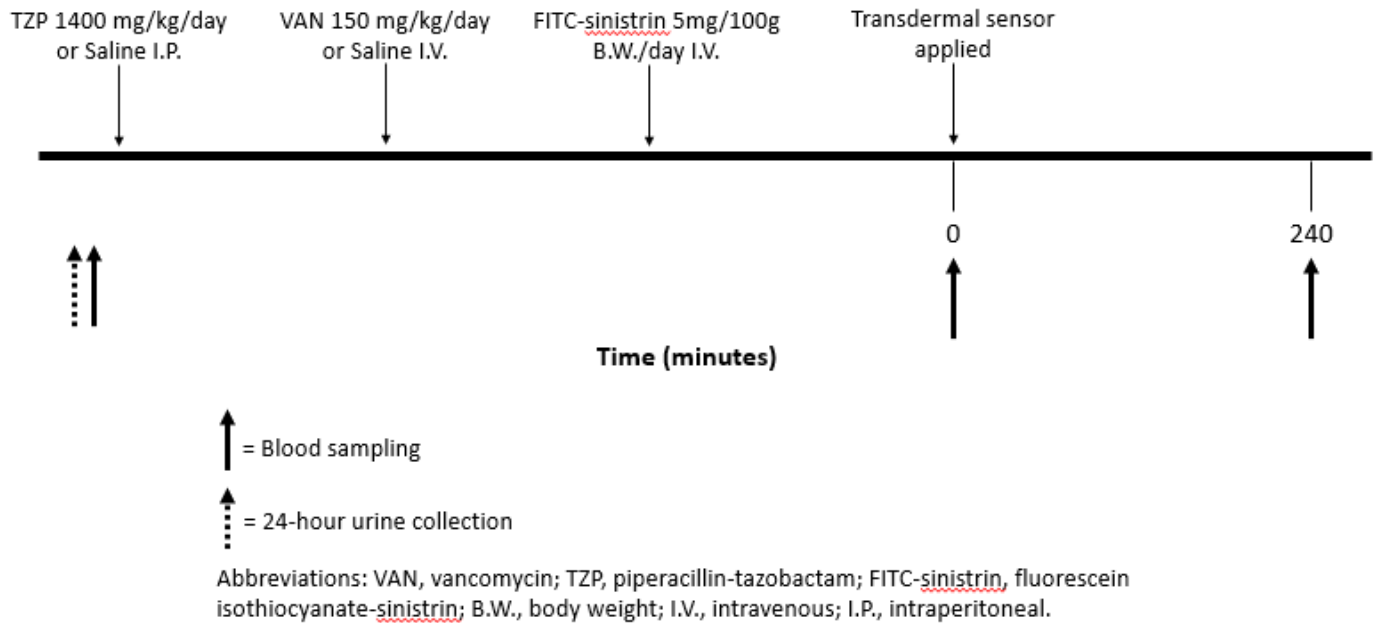
\* One animal contributed partial GFR data

\*\* One animal contributed partial plasma data

Supplemental figure 2: Overall experimental timeline

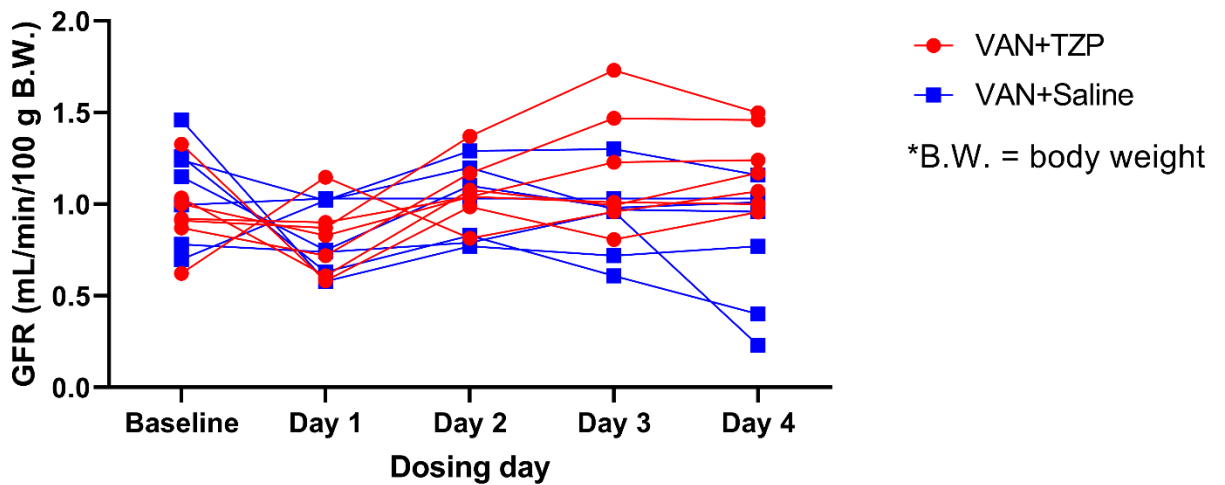


Supplemental figure 3: Daily experimental timeline

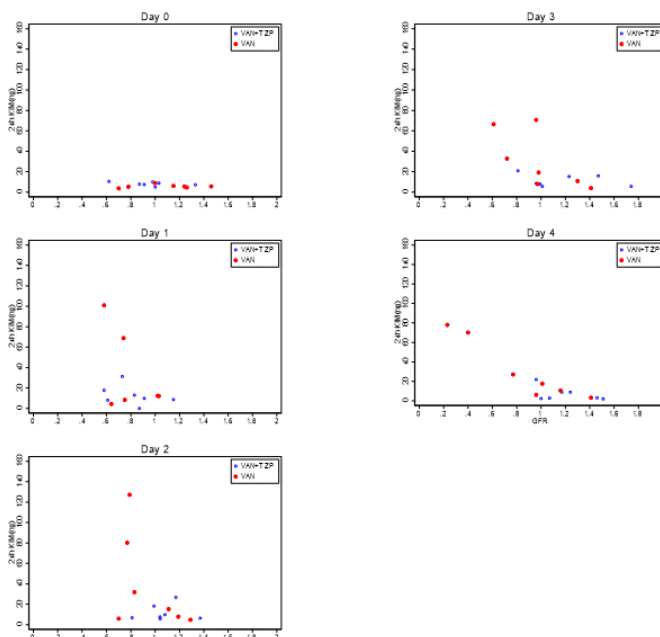


Supplemental figure 4: Direct comparison of individual GFRs in the VAN+TZP and VAN alone groups. Only rats which received VAN had a significant decline in GFR by day 4 (-0.35 mL/min/100 g body weight, 95% CI: -0.63 to -0.07,  $p=0.013$ ).

Supplemental figure 4: GFR comparison between VAN+TZP and VAN+Saline groups



Supplemental figure 5: Spearman correlations between GFR and 24-hour urinary KIM-1 across treatment days for VAN+TZP and VAN alone groups. On day 0 (baseline), all rats in both VAN+TZP and VAN groups had similarly low KIM-1 levels prior to administration of study drug. After drug dosing on day 1 and day 2, we begin to see VAN group rats (red data points) with decreased GFR and higher KIM-1 levels. Following study drug dosing on day 3, urinary KIM-1 for the VAN group was significantly correlated with decreasing GFR (Spearman's rho: -0.45,  $p = 0.022$ ). A similar correlation was observed between GFR and KIM-1 for the VAN group rats on day 4 (Spearman's rho: -0.41,  $p = 0.036$ ).



**Supplementary Table 1: Summary of weight loss, urinary output, and urinary biomarkers**

Characteristic	Treatment group			
	VAN	TZP	VAN+TZP	Saline control
Number of animals	7	6	7	6
Baseline weight (g), mean $\pm$ SD	274.04 $\pm$ 8.46	280.53 $\pm$ 13.29	277.46 $\pm$ 5.19	278.25 $\pm$ 11.04
Weight change (g), mean $\pm$ SD	-1.39 $\pm$ 6.09	-2.27 $\pm$ 6.25	-1.59 $\pm$ 5.44	+5.50 $\pm$ 9.06
Urine output (mL), mean $\pm$ SD				
Baseline	8.73 $\pm$ 3.09	10.95 $\pm$ 4.78	11.43 $\pm$ 3.95	8.1 $\pm$ 1.42
Day 1	15.67 $\pm$ 3.7	12.98 $\pm$ 2.88	17.1 $\pm$ 3.07	11.58 $\pm$ 1.59
Day 2	8.83 $\pm$ 2.63	6.40 $\pm$ 2.54	9.13 $\pm$ 2.6	8.38 $\pm$ 2.18
Day 3	7.64 $\pm$ 3.22	7.73 $\pm$ 3.53	10.34 $\pm$ 3.57	7.15 $\pm$ 1.37
Day 4	13.4 $\pm$ 8.95	4.43 $\pm$ 3.65	11.3 $\pm$ 5.53	4.49 $\pm$ 3.27
KIM-1 (ng), median (IQR)				
Baseline	5.58 (4.59 to 6.09)	6.43 (5.7 to 7.65)	7.91 (7.2 to 9.94)	7.22 (6.73 to 7.92)
Day 1	12.2 (8.37 to 68.8)	8.44 (5.81 to 9.46)	9.88 (8.12 to 17.8)	9.97 (8.74 to 10.44)
Day 2	15.3 (5.91 to 80.2)	5.53 (4.18 to 6.88)	7.59 (6.4 to 18.2)	8.58 (8.4 to 9.70)
Day 3	19.3 (8.0 to 66.6)	6.11 (4.26 to 8.31)	8.5 (5.7 to 15.9)	8.62 (7.69 to 10.1)
Day 4	17.7 (6.21 to 70.2)	1.92 (0.4 to 3.16)	3.2 (2.46 to 9.03)	6.3 (3.2 to 9.98)
Clusterin (ng), median (IQR)				
Baseline	2282 (1466 to 3004)	2734 (2120 to 3080)	3750 (2608 to 5164)	1743 (1074 to 2563)
Day 1	4362 (2021 to 4505)	2314 (1962 to 2829)	3879 (2517 to 8381)	2186 (1281 to 2496)
Day 2	2564 (1431 to 7520)	1168 (787 to 1401)	2522 (1291 to 3150)	1380 (1075 to 2342)
Day 3	2139 (1530 to 5572)	1268 (1139 to 1421)	2534 (1497 to 4592)	1160 (832 to 1456)
Day 4	1199 (833 to 2429)	219 (129 to 1895)	746 (573 to 3269)	616 (401 to 1376)

Osteopontin (ng), median (IQR)				
Baseline	0.31 (0 to 0.68)	0.38 (0.15 to 0.60)	0.38 (0 to 0.837)	0.29 (0.21 to 0.31)
Day 1	0.99 (0.27 to 1.32)	0.86 (0.48 to 1.35)	0.58 (0.45 to 1.68)	0.33 (0.22 to 0.48)
Day 2	1.33 (0.84 to 2.58)	0.77 (0.56 to 1.12)	0.88 (0.65 to 1.40)	0.62 (0.44 to 0.70)
Day 3	2.16 (0.67 to 2.34)	1.01 (0.42 to 1.46)	1.12 (1.09 to 1.68)	0.37 (0.17 to 0.43)
Day 4	0.54 (0.23 to 1.02)	0.23 (0.06 to 0.50)	0.49 (0.36 to 0.81)	0.15 (0.11 to 0.19)
GFR (mL/min/100 g B.W.), mean $\pm$ SD				
Baseline	1.08 $\pm$ 0.27	1.09 $\pm$ 0.38	0.96 $\pm$ 0.21	1.08 $\pm$ 0.53
Day 1	0.79 $\pm$ 0.19	0.98 $\pm$ 0.18	0.81 $\pm$ 0.19	0.97 $\pm$ 0.26
Day 2	0.95 $\pm$ 0.24	1.06 $\pm$ 0.12	1.07 $\pm$ 0.17	1.06 $\pm$ 0.13
Day 3	0.99 $\pm$ 0.29	1.15 $\pm$ 0.14	1.17 $\pm$ 0.33	1.01 $\pm$ 0.22
Day 4	0.85 $\pm$ 0.42	1.11 $\pm$ 0.23	1.20 $\pm$ 0.22	1.24 $\pm$ 0.18