Supplemental Materials

Table S1 Summary of Clinical Study Designs

Study	**Dose regimen**	**Subjects dosed cefiderocol**	**Plasma PK sampling**
Phase 1 single ascending single dose and multiple dose study for healthy subjects in Japan	Part 1: Single cefiderocol 0.1-, 0.25-, 0.5-, 1-, 2-g doses or matching placebo infused over 1 hour Part 2: Multiple cefiderocol 1- or 2-g doses, or matching placebo infused over 1 hour q8hr for 10 days	Part 1: 30 Part 2: 24	Part 1: Predose, 0.5, 1, 1.25, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 10, 12, 16, 24, 36 and 48 hours from the start of the infusion Part 2: Day 1 (morning dose: first dose): predose, 0.5, 1, 1.25, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 10, 12 and 16 hours Days 2, 3, 5, 8 and 9 (each morning dose): predose Day 10 (morning dose: last dose): predose, 0.5, 1, 1.25, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 10, 12, 16, 24, 36 and 48 hours from the start of the infusion
Phase 1 renal impairment study in US	Single cefiderocol 1-g dose infused over 1 hour	38; 8 subjects each: normal renal function, mild and moderate renal impairment; 6 subjects: severe renal impairment; 8 subjects: ESRD requiring hemodialysis	Predose, 0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 12, 16, 24, 36, 48 and 72 hours from the start of the infusion
Phase 2 study for patients with cUTI and AUP	Cefiderocol 2-g doses infused over 1 hour q8hr with adjustments for creatinine clearance and body size	300	Just prior to the infusion of the dose, −0.25 to 0 hours at the end of infusion, and 1 ± 0.5 hours after the end of infusion on Day 3

q8hr = every 8 hours

Table S2 Dose Regimen of Cefiderocol in the Phase 2 cUTI Study

Nominal Dose 6.0 g/day			
	Creatinine Clearance (mL/min)		
Body Weight (kg)	**≥ 71**	**41 – 70**	**21 - 40**
≥70	2.0 g q8hr	1.0 g q6hr	1.0 g q8hr
60	2.0 g q8hr	1.5 g q8hr	1.0 g q8hr
50	1.5 g q6hr	1.5 g q8hr	0.75 g q6hr
40	2.0 g q8hr	1.0 g q6hr	1.0 g q8hr
30	1.5 g q6hr	1.5 g q8hr	1.0 g q8hr

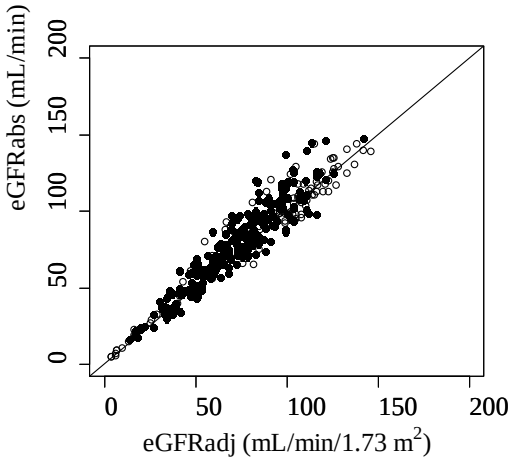
q8hr = every 8 hours, q6hr = every 6 hours

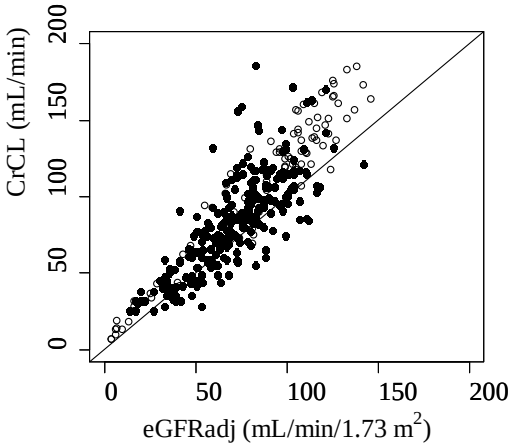
Table S3 MIC Distribution for Each Pathogen

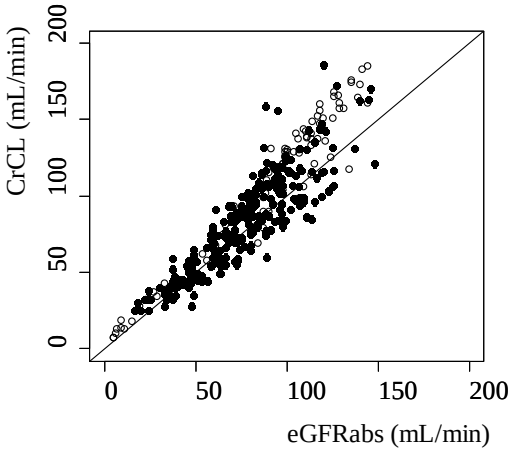
	MIC (µg/mL)											
Pathogen	**<=0.004**	**0.008**	**0.015**	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**
CITROBACTER FREUNDII	0	0	0	0	0	1	0	0	1	0	0	0
CITROBACTER FREUNDII COMPLEX	0	0	0	0	0	0	0	1	0	0	0	0
ENTEROBACTER CLOACAE	0	0	0	0	0	0	1	0	0	0	0	0
ENTEROBACTER CLOACAE COMPLEX	0	0	0	1	1	5	1	0	0	0	0	0
ESCHERICHIA COLI	13	3	8	22	21	20	12	8	6	4	1	0
KLEBSIELLA OXYTOCA	0	1	0	0	0	0	0	0	0	0	0	0
KLEBSIELLA PNEUMONIAE	0	3	4	1	3	2	9	4	4	3	3	1
MORGANELLA MORGANII	0	0	2	0	0	1	0	0	0	0	0	0
PROTEUS MIRABILIS	3	2	1	1	2	3	1	0	0	0	0	0
PSEUDOMONAS AERUGINOSA	0	1	0	3	2	2	2	0	0	0	0	0
SERRATIA MARCESCENS	0	0	1	0	0	0	0	0	0	0	0	0

MIC = minimum inhibitory concentration

Figure S1 Correlations of Renal Function Markers

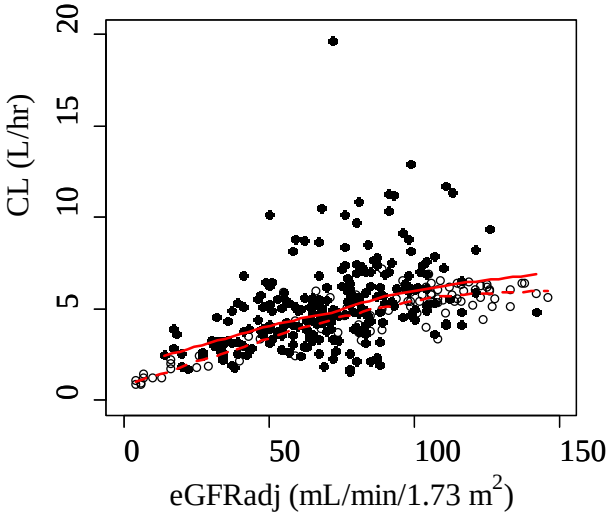


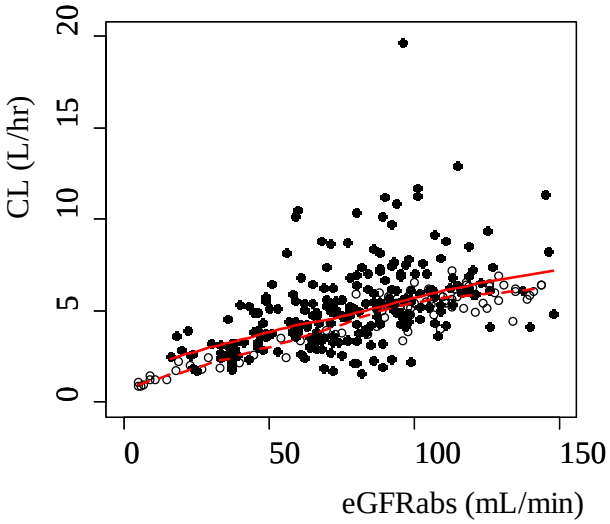




Filled circle: patients with infection. Unfilled circle: subjects without infection. Solid line: y = x.

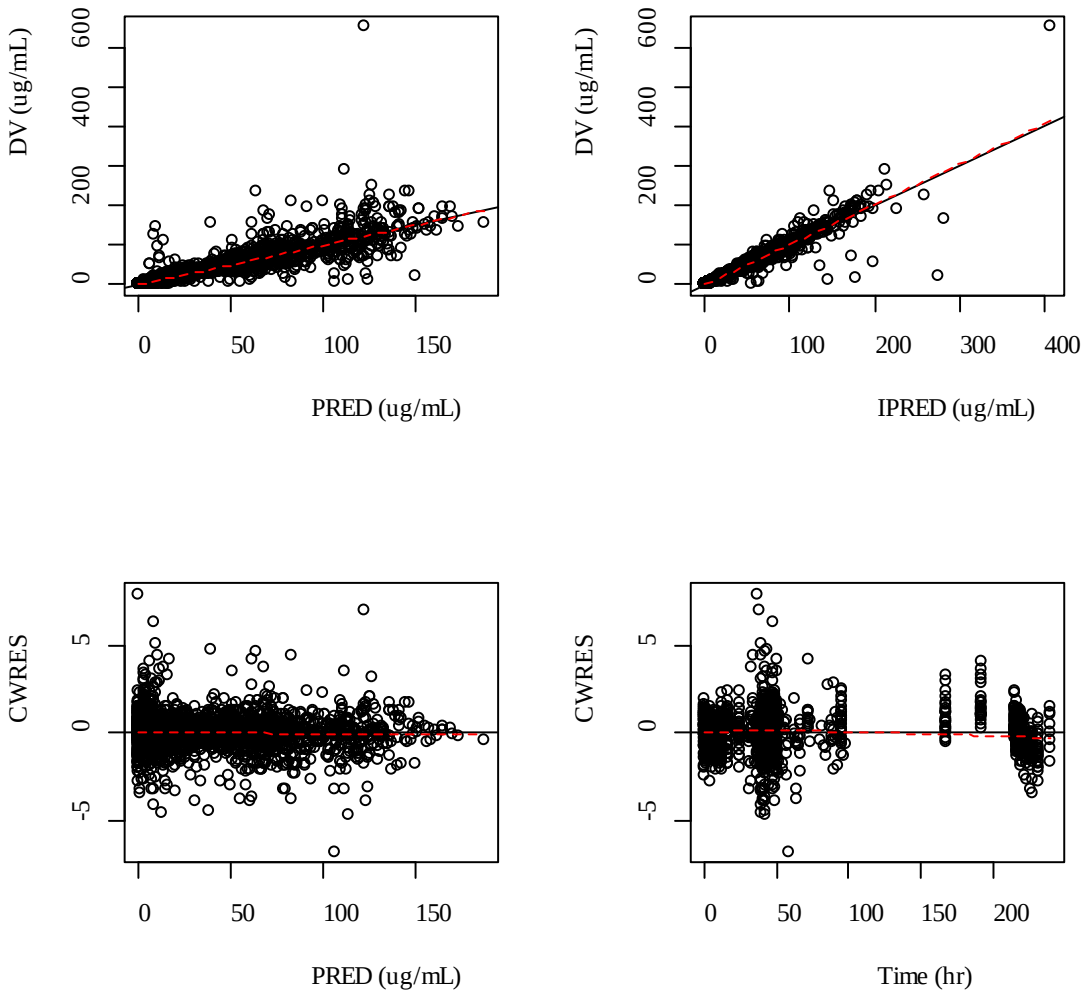
Figure S2　Relationships between CL and eGFRadj and eGFRabs





Filled circle: patients with infection. Unfilled circle: subjects without infection. Line: a LOWESS line (solid: patients with infection, dashed: subjects without infection).

Figure S3 Goodness-of-fit Plots for the Final Model with CrCL



Solid line: y = x in upper figures and y = 0 in lower figures. Dashed line: a LOWESS line.