were performed in duplicate using C/T free concentrations reflective of the peak and trough of a 3g q8h dose (120/25.2 μg/mL,7.5/1.6 μg/mL) and the peak of a 1.5g q8h dose (60/12.6 μg/mL) in humans. The activity of C/T 120, 60, and 7.5 alone and C/T 7.5 in combination with free peak concentrations of FEP, CIP, CST, ATM, MEM, TZP, FOF, or AMK was tested for all isolates. Colony counts were determined at 0, 3, 6, and 24h by serial dilution plating. Synergy was defined at ≥ 2 $\log_{10}$ CFU reduction from the most active agent.

Results. MICs of the 4 MDR *P. Aeruginosa* isolates are in Table 1. As the C/T concentrations increased, bacterial reduction improved, achieving a mean (±SD) $\log_{10}$CFU change from 0 h of 0.03 (±0.67), −1.19 (±1.03), −2.59 (±0.86) with C/T 7.5, 60, 120, respectively. C/T 7.5 was synergistic with CST (PSA C8-21, PSA C45-10) and FOF (PSA C28-5, PSA C14-22) in two of four isolates. No synergy was observed with double β-lactam therapy or CIP. AMK alone achieved maximal bacterial kill; therefore, synergy could not be assessed.

Conclusion. C/T 3g and 1.5g q8h peak concentrations demonstrate killing against the MDR PSA. CST and FOF were synergistic with C/T *in vitro*. Our findings aide in identification of novel treatment options and dosing regimens for the treatment of MDR *P. Aeruginosa*.

Table 1. MICs of C/T and comparators against 4 PSA isolates.

Isolate	C/T	FEP	CAZ	CIP	CST	ATM	TZP	MEM	AMK	FOF
PSA C8-21	4	64	128	8	1	128	256	32	8	>64
PSA C28-5	4	64	128	32	1	64	512	32	8	16
PSA C45-10	8	64	128	2	1	128	512	8	2	>64
PSA C14-22	16	32	128	1	2	128	256	16	8	>64

FEP, cefepime; CAZ, ceftazidime; CIP, ciprofloxacin; CST, colistin; ATM, aztreonam; TZP, piperacillin-tazobactam; MEM, meropenem; AMK, amikacin; FOF, fosfomycin

Disclosures. **D. P. Nicolau**, Merck: Investigator and Speaker's Bureau, Research support.

835. Impact of an Extended Infusion B-lactam Strategy on Outcomes in Critically Ill Patients with Pseudomonas Infections

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Background. *Pseudomonas aeruginosa* (PSA) is frequently associated with nosocomial infections resulting in significant morbidity and mortality. High MICs in MDR strains highlights the need to maximize antibiotic exposure with the goal of improving patient outcomes. For β-lactams, optimal efficacy is achieved when free drug concentrations are above the MIC for ~ 40–60% of the dosing interval. Unfortunately, due to significant pharmacokinetic variability in the critically ill, achieving this target with standard intermittent infusions (II) is challenging, resulting in preference for extended (EI) or continuous infusion strategies. Additional data in patients with PSA infections are needed to understand the association between infusion strategy and clinical outcome.

Methods. A single-center, retrospective chart review. Adult patients with positive respiratory or blood cultures for PSA treated with cefepime or piperacillin/tazobactam managed in an ICU from January 2012 to May 2016 were included. Primary endpoint was clinical cure (CC) at end of therapy (EOT) between patients receiving EI or II. Secondary endpoints included microbiologic eradication (ME), 28-day mortality, length of ICU and hospital stay, and effect of baseline kidney function on clinical cure.

Results. Eighty-three patients were included in the analysis. Patient characteristics were well matched except for a higher frequency of malignancy in the EI arm (P = 0.02). CC was achieved in an overwhelming majority of EI patients compared with II (89.2% vs. 69.6%, P = 0.031). Further, patients with normal renal function (CrCL ≥ 60; P = 0.02) or APACHE II ≥ 17 (P = 0.04) receiving II experienced higher failure rates. In multivariate analysis, use of II associated with 4-fold higher incidence of clinical failure (OR 4.5 [1.3–16.3]). For other secondary endpoints, ME was observed in 73% of EI vs. 65% of II (P = 0.44) and 28-day mortality was observed in 13% of patients in both arms (P = 0.94). No significant differences were observed with other secondary variables.

Conclusion. Use of an EI strategy in critically ill patients with PSA infections improves CC. Further, EI benefitted those patients with normal to augmented renal clearance suggesting that improved exposure may play a role in clinical outcomes.

Disclosures. **K. Klinker**, The Medicines Company: Scientific Advisor, Consulting fee.

836. Influence of Polymyxin B Dose on Development and Recovery of Acute Kidney Injury

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Background. Nephrotoxicity is a common adverse effect of polymyxin B (PMB) with reported acute kidney injury (AKI) rates of 20% to >60%. Data on PMB dosing to optimize efficacy while minimizing toxicity are limited. Previous studies suggest higher doses improve outcomes but are also associated with more AKI. Data are needed to evaluate optimal dosing and contributing factors to minimize AKI and to evaluate renal recovery.

Methods. Retrospective study evaluating PMB in adults at NewYork-Presbyterian Hospital from 2012 to 2016. Patients who received PMB dosed twice daily for ≥2 days were included. Patients on renal replacement therapy within 48 hours prior to PMB or with AKI at time of PMB initiation were excluded. A classification and regression tree (CART) analysis was performed to identify the PMB dose most predictive of AKI which defined the breakpoint for high- vs. low-dose PMB cohorts for all subsequent comparisons. The primary outcome was to determine whether high-dose PMB independently predicted AKI. Secondary outcomes included in-hospital mortality, time to AKI, and recovery of renal function.

Results. 246 patients were included: majority were male (59%) with median age 41 years. Median PMB dose was 2.9 mg/kg/day or 180 mg/day for a median duration of 10 days. AKI occurred in 64% and 38% had recovery of renal function by hospital discharge. The breakpoint for high-dose PMB determined by CART was 160 mg/day, putting 104 in low-dose and 142 in high-dose groups. High-dose PMB was associated with AKI compared with low-dose PMB on univariable (75% vs.. 49%, P < 0.001) and multivariable (OR 3.43; 95% CI 1.68,6.99; P = 0.001) analyses. Concomitant vancomycin (OR 3.34; 95% CI 1.74,6.41;P < 0.001), history of transplant (OR 4.96; 95% CI 2.14,11.48;P < 0.001), and previous PMB exposure (OR 2.37; 95% CI 1.23,4.57; P = 0.01) were also identified as independent predictors of AKI. No significant differences were found for in-hospital mortality (28% vs. 21%, P = 0.326), renal recovery (37% vs. 41%, P = 0.723), time to AKI (median 5 vs. 6 days, P = 0.125) between groups.

Conclusion. High-dose PMB (>160 mg/day) was independently associated with AKI as well as concomitant vancomycin, history of transplant, and previous PMB exposure. High-dose PMB did not have a significant impact on in-hospital mortality, recovery of renal function, or time to development of AKI.

Disclosures. **M. Yin**, Gilead Sciences: Consultant, Consulting fee.

837. Assessing the Risk of Nephrotoxicity Associated With Non-renally Adjusted Intravenous Polymyxin B Compared with Traditional Dosing

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