outcomes. For carbapenems, achieving greater than 40% time above minimum inhibitory concentration (T>MIC) has been shown to be correlated with clinical efficacy. Increasing bacterial resistance and rising MICs makes it more difficult for clinicians to rely on traditional dosing strategies to meet pharmacodynamic goals. Further optimization methods beyond extended infusion may be necessary to achieve certain pharmacodynamics goals.

Methods. We performed a Monte Carlo simulation investigating a novel method of meropenem administration, bolus to prolonged infusion (BPI). Multiple meropenem dosing regimens utilizing BPI were evaluated over 5000 patients utilizing pharmacokinetic profiles from 30 total patients. Patients were studied in 3 separate groups: <120 kg, ≥120 kg/non-critically ill and ≥120 kg/critically-ill. Bolus doses varied from 250–1000 mg and were paired with infusion doses varying from 500–1500 mg. Bolus plus infusion time totaled 3 hours and each dose was modeled with an 8-hour interval for both first dose and at steady state; BPI dosing was utilized for each dose. The primary outcome was probability of target attainment (PTA) of 40% time above minimum inhibitory concentration (T>MIC). Secondary outcomes included PTA 54% T>MIC and PTA 100% T>MIC.

Results. All doses studied achieved > 90% PTA of 40% T>MIC for MICs of ≤8 μg/mL at both first dose and steady state in the <120 kg and ≥120 kg/non-critically ill patient groups. In the ≥120 kg/critically ill patient group, all doses achieved > 90% PTA of 40% T>MIC for MICs of ≤4 μg/mL.

Conclusion. BPI achieves high probability of target attainment at nonresistant MICs for *Pseudomonas aeruginosa* and enteric Gram-negative organisms across the 3 patient groups studied.

Disclosures. **All authors:** No reported disclosures.

1548. Characterizing Cefepime Neurotoxicity: Experience from a Tertiary Care Center Performing β-lactam Therapeutic Drug Monitoring

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Background. Based on prior studies, elderly patients and those with renal dysfunction are prone to cefepime (CFP) toxicity. The toxicokinetics and toxicodynamics for CFP are not well established. Lamoth et al. reported a 50% probability of CFP neurotoxicity at a serum trough concentration of ≥22 mg/L, whereas Huwyler et al. observed CFP neurotoxicity when concentrations exceeded 35 mg/L. The objectives of this study were to quantify the incidence of CFP neurotoxicity and to assess the association between CFP concentrations and neurotoxicity.

Methods. We conducted a retrospective review between March 2016 and May 2018, of adult patients with serum CFP trough concentrations ≥25 mg/L. To be considered a CFP neurotoxicity case, patients were required to fulfill at least two of the NCI criteria for neurological toxicity such as, presence of new-onset confusion, delirium, or drowsiness. Following this, cases were classified as (1) high likelihood of toxicity (HLT) if they either had a neurology consult or EEG findings consistent with CFP toxicity and if their symptoms improved after discontinuation of CFP, (2) possible toxicity (PT) if neurology consult or EEG was absent or if we were unable to assess improvement after CFP was discontinued, or (3) nontoxicity (NT). Cases were independently reviewed by an ID pharmacist and physician. Additional data such as comorbidities, renal function, and use of anti-epileptics were collected.

Results. One hundred and forty-two patients were included in the analysis. Neurotoxicity (HLT+PT) related to CFP occurred in 18/142 (13%) patients; 67% (12/18) were considered HLT. The median age in the HLT cohort was 68 years (interquartile range [IQR], 57–74), with toxicity occurring a median of 6 days (IQR, 5–8) after starting CFP. At the time of neurotoxicity, HLT patients had diminished renal function with a median SCr of 1.6 mg/dL (IQR, 1.2–2.4) and a corresponding CrCl of 35.8 mL/minute (IQR, 19.2–50.9). The median CFP trough concentration in the HLT patients was 62 mg/L (IQR, 50–73) vs. 70mg/L (IQR, 41–115) in the PT and 42 mg/L (IQR, 31–61) in the NT groups.

Conclusion. Our data emphasize the need for careful dosing in older patients with renal insufficiency. Interestingly, our study reveals higher cefepime troughs (~3-fold higher) associated with neurotoxicity than previously reported.

Disclosures. **All authors:** No reported disclosures.

1549. Impact of New Fluoroquinolone Breakpoints on *Enterobacteriaceae* Susceptibility Rates and Clinical Outcomes

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Background. In January 2019, the Clinical and Laboratory Standards Institute (CLSI) lowered the Fluoroquinolone (FQ) susceptibility breakpoints for Enterobacteriaceae. The new breakpoints were updated primarily based on FQ pharmacodynamics, and only limited clinical data. We sought to evaluate clinical outcomes among patients who received an FQ for infection with Enterobacteriaceae with MIC values that would now be considered resistant, using the new interpretive criteria. We also assessed the potential impact of the new breakpoints on overall blood and urine Enterobacteriaceae susceptibility rates at our medical center.

Methods. All positive blood and urine cultures with Enterobacteriaceae between September 1, 2018 and February 28, 2019 were included. Enterobacteriaceae isolates with ciprofloxacin MICs of 0.5 and 1 μg/mL (based on new breakpoints, now considered non-susceptible) were identified. We assessed the length of stay (LOS), mortality, and 30-day readmissions among patients who received an FQ for treatment. The impact of the new breakpoints on overall Enterobacteriaceae susceptibilities from urine and blood isolates was also determined.

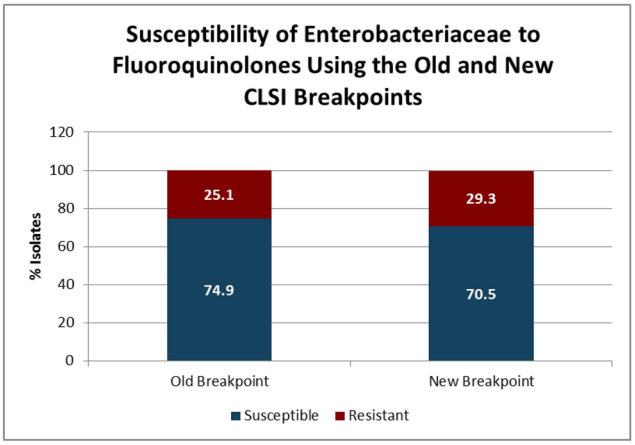
Results. A total of 1,761 cultures (191 blood, 1,570 urine) grew Enterobacteriaceae. One-hundred and twenty-five (7%) cultures grew isolates with a ciprofloxacin MIC of 0.5 or 1 μg/mL. Eighteen patients with Enterobacteriaceae isolated (4 blood, 14 urine) received an FQ. Among these patients, the median LOS was 4 days; one patient was readmitted within 30 days, and 0% mortality was observed. The patient readmitted within 30 days received an FQ for a blood isolate with MIC 0.5. Overall, with the revised breakpoints, we observed a 4.2% decrease in the number of Enterobacteriaceae that would be susceptible to ciprofloxacin (Figure 1).

Conclusion. The new FQ breakpoints for Enterobacteriaceae will have a marginal impact on overall FQ susceptibility rates at our medical center. In this single-center study, patients that received FQ antibiotics for Enterobacteriaceae with MIC values now considered intermediate or resistant did not appear to experience poor outcomes.

Table 1: Observed Outcomes for Patients That Received FQ for Non-susceptible Isolates (Ciprofloxacin MIC 0.5 and 1)

	All Isolates (n=18)	Urine Isolates (n=14)	Blood Isolates (n=4)
LOS (days), median	4	4	3
30d Readmission, n (%)	1 (5.5)	0 (0)	1 (25)
Mortality, n (%)	0 (0)	0 (0)	0 (0)

Figure 1: Percentage of Susceptible *Enterobacteriaceae* Isolates



Disclosures. **All authors:** No reported disclosures.

1550. PK-PD Relationship and PK Driver of Efficacy of the Novel Antibacterial Lysin Exebacase (CF-301) in Pre-Clinical Models

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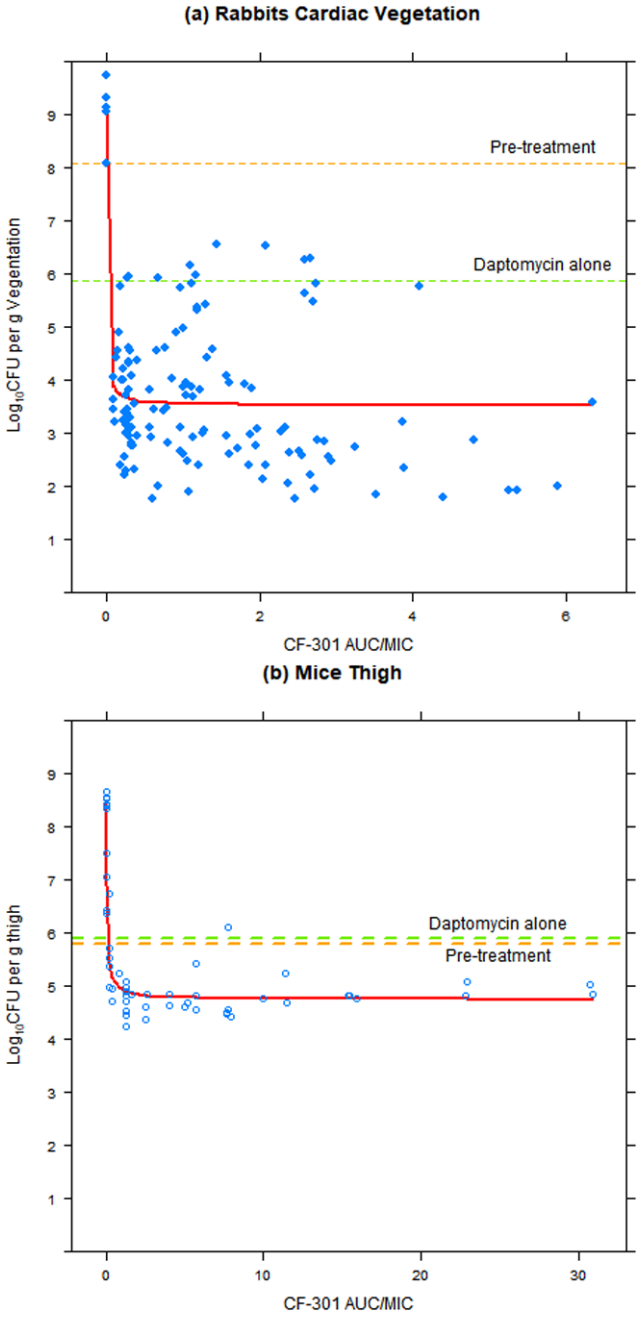
Background. Exebacase (CF-301) is a novel lysin with rapid bacteriolytic and anti-biofilm activity against *S. aureus*, pronounced synergy with antibiotics and low propensity for resistance. Exebacase has undergone Phase 1–2 trials. This work was to develop pharmacokinetic (PK) model in animal and determine the relationship between exebacase exposure and efficacy in animals.

Methods. PK data in 592 animals (4 species) included in population PK model. A range of linear and nonlinear mammillary models with allometric scaling fitted to the

PK data using NONMEM and the most parsimonious model was selected by improvement in objective function value ($P < 0.01$). To evaluate efficacy, 349 animals with 177 mice (neutropenic thigh infection) and 172 rabbits (aortic valve infective endocarditis were treated with exebacase in addition to suboptimal doses of daptomycin (DAP). Full PK profiles were simulated for individual animals. Fifty-nine dosing regimens of exebacase in mice (0–90 mg/kg) and 18 regimens in rabbits (0–1.4 mg/kg) with q24h, q12h and q8h frequencies. Relationship between AUC/MIC, Cmax/MIC, T> MIC, and log-CFU was examined using a range of functions by comparing residual standard error (RSE).

Results. 3-compartment model with allometric scaling best described the PK data and was validated by bootstrap and Goodness of Fit. Maximum drop in $\log_{10}$CFU/g in target tissues was at AUC/MIC< 0.2 for exebacase when added to DAP that was associated with CF reduction of -5 logs in rabbits (Figure (a)) with similar magnitudes in cardiac vegetations, kidney and spleen, and -4 logs in mice (Figure (b)). Treatment with DAP alone had $\log_{10}$CFU reduction of -1 in mice; and -2 in rabbits. AUC/MIC was an appropriate predictor of CFU reductions.

Conclusion. PK model adequately described the data for 4 animal species. Exebacase addition to DAP has a synergistic effect on efficacy measured by CFU reductions in target tissues in the animal models. Results support previously presented determinations of AUC/MIC as predictor of efficacy. Maximum reductions in CFU in rabbits and mice were observed at AUC/MIC ratios <0.2. These results further indicate that rabbit is the most appropriate efficacy model with MICs and antibacterial activity reflective of previously reported observations in human serum.



Disclosures. **All authors:** No reported disclosures.

1551. Systemic Tobramycin Absorption Resulting from Antibiotic-Impregnated Cement Spacers for the Treatment of Prosthetic Joint Infection

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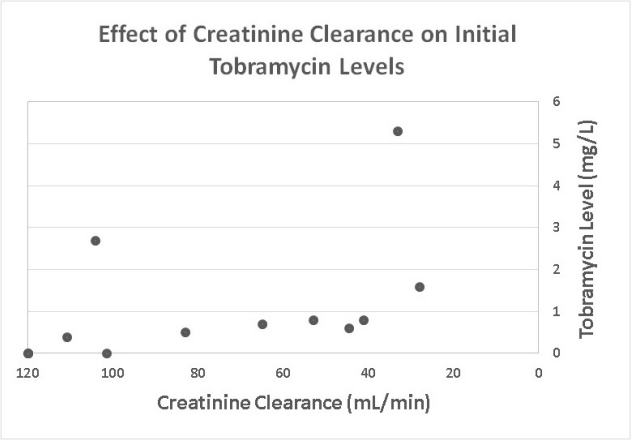
Background. Antibiotic-impregnated cement spacer (ACS) placement has been a cornerstone of two-stage surgical management of prosthetic hip and knee infection for decades. Utilized antibiotics have included aminoglycosides and vancomycin. Pharmacokinetic modeling studies have described peak systemic levels within the first 24–48 hours post-operatively, followed by rapid clearance. While this systemic exposure was previously felt insufficient to cause organ toxicity, a few studies have described antibiotic-induced nephrotoxicity.

Methods. We prospectively enrolled patients with prosthetic hip or knee infection, and subsequent ACS placement, containing vancomycin and tobramycin, from October 2017 to February 2019, at Allegheny General Hospital. Risk factors for post-operative nephrotoxicity, including patient comorbidities, receipt of potentially nephrotoxic medications, estimated creatinine clearance (CrCl), perioperative hypotension, total spacer tobramycin dosage, and post-operative day 1 (POD1) and 3 (POD3) serum tobramycin levels were recorded. Patients who had antibiotic cement spacer exchange, or had received systemic aminoglycoside therapy, were excluded.

Results. Thirteen patients were enrolled, comprising 4 hip and 9 knee ACS, with respective median (interquartile range (IQR)) tobramycin cement dosages of 3.8 (2.86–4.58) and 4.8 (4.8–9.6) grams. Tobramycin levels were measured at a median 16.5 and 60.7 hours on POD1 and POD3, respectively. Three hip and six knee ACS had respective, detectable POD1 median serum tobramycin levels of 0.6 (0.38–1.20) and 0.8 (0–0.8) µg/mL; three knees, but no hip ACS had detectable POD3 serum tobramycin levels. Six of the nine patients with detectable POD1 serum tobramycin levels had a CrCl of less than or equal to 65 mL/minute (figure), while each patient with detectable POD3 levels had a CrCl of less than 45 mL/minute. No significant changes in baseline CrCl were identified. A relationship between tobramycin cement dosage and detectable serum tobramycin levels was not observed.

Conclusion. Low baseline CrCl, but not the total tobramycin dosage or other nephrotoxicity risk factors, may be the single most reliable predictor of detectable postoperative systemic tobramycin levels in patients who have received hip or knee ACS.



Disclosures. **All authors:** No reported disclosures.

1552. Correlation Between Vancomycin Serum Trough Concentrations and Area Under the Curve in Pediatric Patients

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Background. Despite years of experience with vancomycin (VAN), the optimal method to monitor VAN therapy in pediatric patients is still unknown. Recent pediatric data indicate serum trough concentrations lower than 10–20 mg/L or 15–20 mg/L based on indication may achieve an AUC_{24} > 400 mg hours/L. The primary study objective was to compare AUC_{24} to goal VAN serum trough concentrations (STC).

Methods. A retrospective chart review of pediatric patients who received intravenous VAN June 1, 2018 to December 31, 2018 was completed. AUC_{24} was calculated using a trapezoidal method with 2 steady-state serum concentrations. A serum peak concentration was drawn 1 hour and 15 minutes following the end of infusion and an STC was drawn 30 minutes prior to infusion.