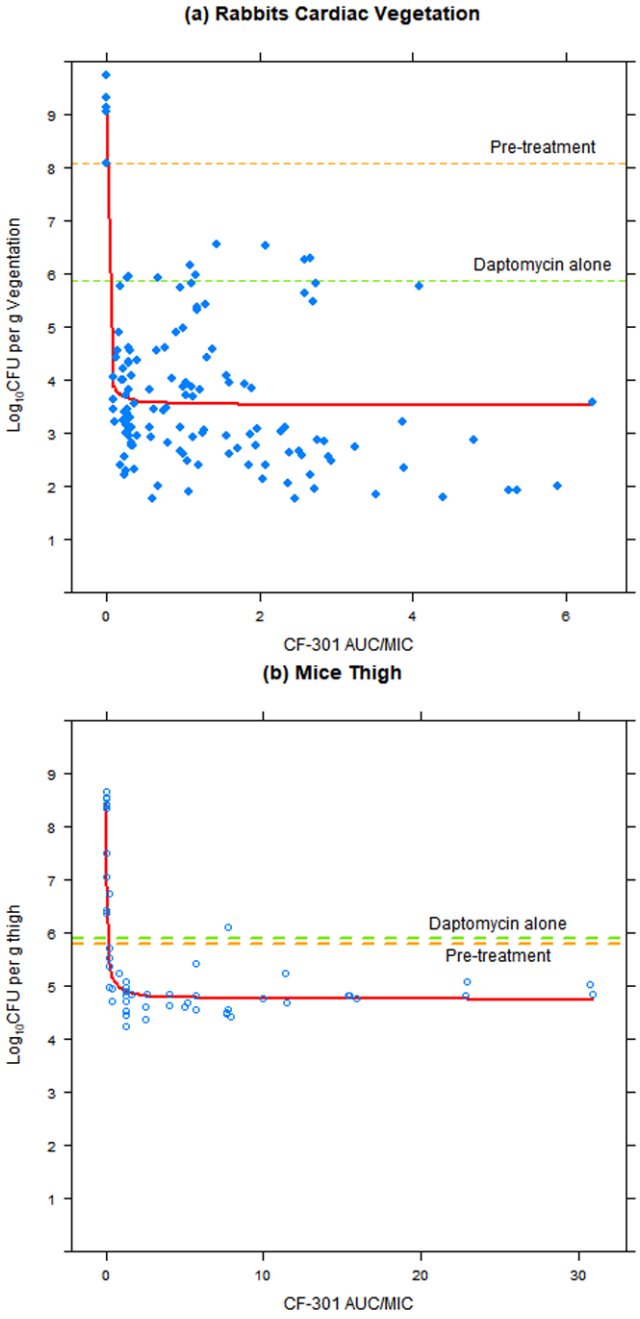
PK data using NONMEM and the most parsimonious model was selected by improvement in objective function value ($P < 0.01$). To evaluate efficacy, 349 animals with 177 mice (neutropenic thigh infection) and 172 rabbits (aortic valve infective endocarditis were treated with exebacase in addition to suboptimal 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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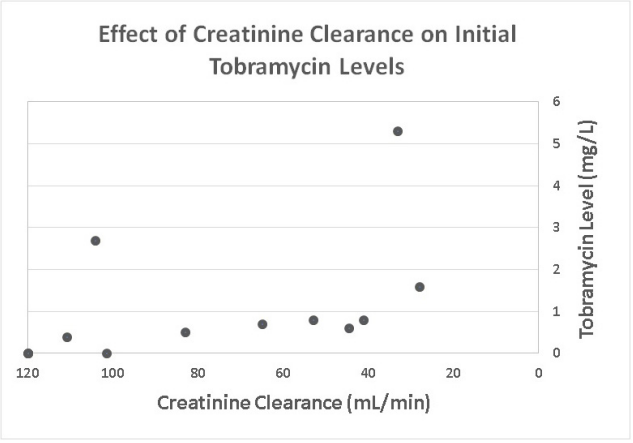
Background. Antibiotic-impregnated cement spacer (ACS) placement has been a cornerstone of two-stage surgical management of prosthetic hip and knee infection for decades. Utilized antibiotics have included aminoglycosides and vancomycin. Pharmacokinetic modeling studies have described peak systemic levels 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.