median weight was 112.7 kg (IQR 99.8 - 126.2) and the median BMI was 36.8 kg/m² (IQR 33.1 - 41). The median total daily vancomycin dose at initiation was 28.7 mg/kg/day (IQR 25.4 - 31.2). Vancomycin accumulation occurred in 99 patients (61.1%) within the first 10 days of therapy and AKI occurred in 21 patients (14.9%). No factors studied, including age, gender, obesity class, initial dose, SCr, or frequency were associated with accumulation.

**Conclusions.** Most patients with obesity experienced vancomycin accumulation within the first 10 days of therapy. Providers should be cautious when assessing a vancomycin concentration early in the treatment course.

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

1103. Minocycline (MIN) Pharmacodynamics (PD) against Stenotrophomonas maltophilia (STM) in a Neutropenic Murine Thigh Infection Model. Andrew J. Fratoni, PharmD; David P. Nicolau, PharmD; Joseph L. Kuti, PharmD; 1Hartford Hospital, Hartford, Connecticut; 2Center for Anti-Infective Research and Development, Hartford Hospital, Hartford, Connecticut

**Session:** P-62. PK/PD Studies

**Background.** Antibiotic treatment options for serious STM infections are limited. MIN displays in vitro activity against STM; however, limited data supports optimal dosing for STM. Herein, we employed the murine neutropenic thigh infection model to assess MIN PD against STM.

**Methods.** Four clinical STM isolates with MIN MICs 0.25 - 1 mg/L were included. Both thighs of neutropenic ICR mice were inoculated with bacterial suspensions at 10, 2, or 0.2 mL forming units (CFU)/mL. Mice received unanesthetized intravenous injections on Day 3 to provide predictable renal impairment. Two hours after inoculation, MIN or control was administered subcutaneously. Pharmacokinetic (PK) studies of 2.5, 25, and 100 mg/kg were conducted. Previously reported protein binding of 78.1% was used to define free exposure. Dose ranging studies were conducted on all STM to assess in vivo activity against a range of MIC exposures. MIN total daily doses (TDD) of 10, 20, and 50 mg/kg were fractionated q4h, q12h, and q6h against a single STM to determine the PK index best correlated with reductions in CFU/mL. Efficacy was measured in log₂ CFU/thigh at 24h compared with 0h controls. Composite CPU data were fitted to an E₀ model to determine the AUIC/MIC exposure for stasis and 1 log reduction.

**Results.** MIN PK was linear up to 50 mg/kg and well described by a 1 compartment model with first order absorption and elimination. Mean PK parameters across the linear range were: Vd, 2.97 L/kg; K₀1, 10.62 l/h; and K₁0, 0.35 l/h. Mean ± SD bacterial growth at 0h across all isolates was 6.17 ± 0.20 log CFU/mL. In 24h controls, bacterial growth was 7.90 ± 0.85 log CFU/thigh. A dose response was observed across all isolates using TDD of 2-300 mg/kg. PD indices correlated with CFU reductions as follows: Vd, 2.97 L/kg; K₀1, 10.62 l/h; and K₁0, 0.35 l/h. Mean ± SD bacterial burden at 0h across all isolates was 6.17 ± 0.20 log CFU/mL. Mice received uranyl nitrate on Day -3 to provide predictable renal impairment.

**Conclusion.** These are the first data describing MIN PD against STM. Against these STM, MIN/AUC/MIC was the PD index best correlated with CFU reductions. The exposure thresholds defined in this study will be useful in designing optimal MIN dosing regimens for treating STM infections and re-assessment of the current susceptibility breakpoint.

The study was funded under FDA Contract 75F40120C00171.

**Disclosures.** David P. Nicolau, PharmD; Abbie, Cepheid, Merck, Paratek, Pfizer, Wuhan, BioMérieux; I have been a consultant, speaker, and/or received research funding from the following companies: I. J. Kuti, PharmD, Allergan (Speaker's Bureau), BioMérieux (Consultant, Research Grant or Support, Speaker's Bureau), Merck (Scientific Research Study Investigator), GSK (Consultant, Research Grant or Support), Paratek (Speaker's Bureau), Roche Diagnostics (Consultant or Support), Shionogi (Research Grant or Support).

**Figure 1.** Methods for relating whole blood vancomycin concentrations collected via VAMS to plasma concentrations and measure to evaluate predictive performance.

**Table:** Predictive performance measure

| Method | Technique for predicting plasma from VAMS | Equation |
|--------|------------------------------------------|----------|
| Uncorrected VAMS | 1. Predicted plasma calculated from Passing-Bablok regression of measured plasma on uncorrected VAMS | Bias, calculated as median percentage predictive error (MPPE) |
| Hematocrit-corrected VAMS | 1. Hct-corrected VAMS = VAMS / (1 - Hct/100) | Imprecision, calculated as median absolute percentage predictive error (MAPE) |
| Lab-corrected VAMS | 1. Lab-corrected VAMS = VAMS / 0.718 | Accuracy, calculated as proportion of samples with MAPE < 20% |

**Results.** Paired samples were collected from 31 enrolled subjects (Figure 2), with a median age of 3.3 years (range 0.1-17.9). Measured P concentrations ranged from 4.6 - 54.9 mg/L. 11 C samples (29%) and 3 V samples (10%) were excluded due to collection issues. Prediction results are shown in Figure 3. The 3 prediction techniques had similar performance characteristics, with each method displaying minimal bias (0.4-2.0%) and reasonable imprecision (13.7-20.2%). The accuracy of prediction of P concentrations using VAMS was better for V than C samples.

**Figure 2.** Flow diagram from sample collection to evaluation.

**Abbreviations:** C-P, capillary VAMS-plasma; V-P, venous arterial VAMS-plasma; VAMS, volumetric absorptive microsampling.

1104. Comparison of Antibiotic Sampling Techniques: Predicting Plasma Vancomycin Concentrations Using Volumetric Absorptive Microsampling (VAMS) from Capillary and Venous/Arterial Whole Blood. Kevin J. Downes, MD; 1Derrick Tam, BS; 2Anna Sharova, MPH; Christina Vedaz, BS; Julie C. Fitzgerald, MD, PhD, MSCE; 1Abbas F. Jawad, PhD, MSCE; 1Ganneh S. Moorby, PhD; 3Athena F. Zuppa, MD, MSCE; 1Children's Hospital of Philadelphia, Philadelphia, Pennsylvania

**Session:** P-62. PK/PD Studies

**Background.** Therapeutic drug monitoring (TDM) is paramount to optimize the safety and efficacy of vancomycin (VAN). In children, TDM is challenged by difficulty in obtaining venous samples, impeding timely sampling. We assessed the ability of sampling using whole blood collected via VAMS to provide predictable renal impairment. Two hours after inoculation, MIN or control were administered subcutaneously. Pharmacokinetic studies of 2.5, 25, and 100 mg/kg were conducted. Previously reported protein binding of 78.1% was used to define free exposure. Dose ranging studies were conducted on all STM to assess in vivo activity against a range of MIC exposures. MIN total daily doses (TDD) of 10, 20, and 50 mg/kg were fractionated q4h, q12h, and q6h against a single STM to determine the PK index best correlated with reductions in CFU/mL. Efficacy was measured in log₂ CFU/thigh at 24h compared with 0h controls. Composite CPU data were fitted to an E₀ model to determine the AUIC/MIC exposure for stasis and 1 log reduction.

**Results.** MIN PK was linear up to 50 mg/kg and well described by a 1 compartment model with first order absorption and elimination. Mean PK parameters across the linear range were: Vd, 2.97 L/kg; K₀1, 10.62 l/h; and K₁0, 0.35 l/h. Mean ± SD bacterial burden at 0h across all isolates was 6.17 ± 0.20 log CFU/mL. In 24h controls, bacterial growth was 7.90 ± 0.85 log CFU/thigh. A dose response was observed across all isolates using TDD of 2-300 mg/kg. PD indices correlated with CFU reductions as follows: Vd, 2.97 L/kg; K₀1, 10.62 l/h; and K₁0, 0.35 l/h. Mean ± SD bacterial burden at 0h across all isolates was 6.17 ± 0.20 log CFU/mL. Mice received uranyl nitrate on Day -3 to provide predictable renal impairment. Two hours after inoculation, MIN or control was administered subcutaneously. Pharmacokinetic studies of 2.5, 25, and 100 mg/kg were conducted. Previously reported protein binding of 78.1% was used to define free exposure. Dose ranging studies were conducted on all STM to assess in vivo activity against a range of MIC exposures. MIN total daily doses (TDD) of 10, 20, and 50 mg/kg were fractionated q4h, q12h, and q6h against a single STM to determine the PK index best correlated with reductions in CFU/mL. Efficacy was measured in log₂ CFU/thigh at 24h compared with 0h controls. Composite CPU data were fitted to an E₀ model to determine the AUIC/MIC exposure for stasis and 1 log reduction.

**Conclusion.** These are the first data describing MIN PD against STM. Against these STM, MIN/AUC/MIC was the PD index best correlated with CFU reductions. The exposure thresholds defined in this study will be useful in designing optimal MIN dosing regimens for treating STM infections and re-assessment of the current susceptibility breakpoint.

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**Figure 2.** Flow diagram from sample collection to evaluation.

**Abbreviations:** C-P, capillary VAMS-plasma; V-P, venous arterial VAMS-plasma; VAMS, volumetric absorptive microsampling.

**Figure 3.** Performance of 3 techniques to predict plasma vancomycin concentrations using whole blood collected via VAMS.