Results. During 25 admissions, 12 patients had a first AUC$_{24}$ to goal and 13 patients had a first AUC$_{24}$ below goal. Of 41 AUC$_{24}$ calculations, 27 AUC$_{24}$ were 400 mg hours/L (group 1), and 14 AUC$_{24}$ were <400 mg hours/L (group 2). Median AUC$_{24}$ was 561 mg hours/L for group 1 vs. 344.5 mg hours/L for group 2 (P = 0.001). Correlating Cmin and Ctrough (Ct) for group 1 and group 2 were 12 mg/L and 13.5 mg/L vs. 6.4 mg/L and 7.3 mg/L, respectively (P < 0.001). Figure 1 shows the pharmacokinetic parameters for each group. Spearman correlation between AUC$_{24}$ and Cmin was 0.87. Of the 35 subtherapeutic VAN STCs, 20 (57.1%) achieved an AUC$_{24}$ > 400 mg hours/L (P = 0.08). Subgroup analysis of AUC$_{24}$ > 400 mg hours/L showed a median AUC$_{24}$, of 519 mg hours/L, with corresponding Cmin and Ctrough of 10.6 mg/L and 11.9 mg/L, respectively. The MIC was <1 in 90.9% of cases (Figure 2). The mean dose AUC$_{24}$ required to achieve an AUC$_{24}$ = 400 mg hours/L was 77.7 mg/kg/day; dosing frequency did not appear to affect AUC$_{24}$ outcome. Time to culture clearance was 2 days in group 1 and 6.5 days in group 2 (P = 0.24). No cases of nephrotoxicity were identified despite AUC$_{24}$ values ranging from 265–1294 mg hours/L.

Conclusion. AUC$_{24}$ monitoring using a 2-sample trapezoidal method was successfully implemented at this institution. The results of this study align with previous pediatric studies, supporting the use of lower serum trough concentration goals of 10–15 mg/L.

Results. Observed murine-free plasma concentrations ± 95% CI of CFDC and MEM are overlaid with simulated human and murine profiles in the figure. In both models, these regimens approximated human exposures after clinical doses. For all time points and both drugs, concentrations were not significantly different (P > 0.05) between models with or without iron overload.

Conclusion. Iron overload did not significantly alter PK profiles of a siderophore-β-lactam conjugate, CFDC, or a non-siderophore β-lactam, MEM. These data support the use of CFDC and MEM HSR for pharmacodynamic studies utilizing both iron-overloaded and standard murine thigh infection models.

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

1554. Nebulized Liposomal Amphotericin B for Treatment of Murine Pulmonary Mucormycosis
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Background. Pulmonary mucormycosis, a life-threatening infection of immunocompromised individuals, can have a 95% mortality rate, even with treatment. Intravenous (IV) liposomal amphotericin B (AmBisome, AmB) is used to treat the infection, but rapid growth of the pathogen can limit the drug's effectiveness. In the present study we investigated whether nebulized (nebz) AmB could improve treatment outcome using a neutropenic murine model of pulmonary mucormycosis.

Methods. *Rhizopus oryzae* (ATCC MYA621) was grown on Potato Dextrose Agar for 3–7 days, followed by spore harvesting, and determination of spore viability. Male ICR mice were immunosuppressed with 200 mg/kg of cyclophosphamide d-2, d-0, d+2, d+4, and d+7 challenged intranasally with 1 × 10$^6$ spores. In Study 1, mice (n = 16 mice/gp) were given AmBi at 7.5 or 10 mg/kg IV for 6 days, or nebz AmBi for 20 minutes (1.3 mg/mL AmBi in reservoir) for 4 days. In Study 2, 16 mice/gp were given AmBi at 15 mg/kg IV for 6 days or nebz AmBi for 7 days. PBS was the control. Lung and kidneys were collected d+6 to determine drug concentration by a bioassay (n = 7–8 mice/gp) and morbidity (n = 8 mice/gp) monitored to d+21.

Results. In Study 1, survival was significantly better with nebz AmBi for 4 days (50%) or 10 mg/kg IV AmBi (33%) vs. 7.5 mg/kg IV AmBi (0%) (P < 0.003). In Study 2 with 13% survival in the PBS mice, 7 days of nebz AmBi produced 100% survival and 15 mg/kg IV AmBi gave 83% survival (P < 0.02 vs. PBS), underscoring the need for more intensive treatments. In Study 2, we also observed that average lung drug levels with nebz AmBi were significantly lower (3 μg/g lung) than with 15 mg/kg AmBi IV (19 μg/g lung) (P = 0.003), even though both treatments were comparably effective. Kidney drug levels with 15 mg/kg AmBi IV were 13 μg/g and in comparison, nebz AmBi produced no detectable drug.

Conclusion. Daily nebulization of AmBi for one week or a high dose of IV AmBi at 15 mg/kg for 6 days protected the mice from severe pulmonary mucormycosis caused by *R. oryzae*, delivering effective drug levels to the lungs. The IV treatment yielded elevated levels of drug in the kidneys, while nebulization with AmBi produced less nephrotoxic drug in the kidneys but suggested that nebz AmBi would be a less nephrotoxic, but still very effective route for drug delivery.

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