**Background.** Vancomycin dosing guidelines recommend loading doses (LDs) (25–30 mg/kg TIVB), and a maintenance regimen, usually started after a time period equal to the dosing interval. Studies of vancomycin exposure and nephrotoxicity conclude that a 0 to 24-hour area under the serum concentration–time (0–24 AUC) > 677 mg·h/L results in a 3- to 4-fold increased risk of nephrotoxicity (Zasowski EJ, Antimicrob Agents Chemother 2018). For vancomycin LDs we compare the calculated LD and the maintenance dose, and delay initiation of the maintenance regimen when the LD exceeds the daily maintenance dose by > 50%. This study assessed the pharmacokinetics of two different regimens: daily 10 mg/kg IV AmBi and daily 200 mg/day IV AmBi.

**Methods.** We retrospectively reviewed 68 consecutive adult patients receiving therapeutic doses of vancomycin. Patient age, sex, height, serum creatinine, and indication were used to calculate the daily dose/intervals for a steady-state 24-hr AUC of 400 or 600 mg·h/L. The total 0–24 AUC was calculated by adding the 0–24 AUC from a 25 mg/kg LD (max 3 gm) to the 0–24 AUC(s) for the maintenance dose(s) within the first 24 hours. We compared the total 0–24 AUC when the first maintenance dose was timed for the next dosing interval (“scheduled”) to that when the maintenance dose was delayed according to our protocol (“delayed”). We tested the proportion of patients who would be exposed to a vancomycin 0–24 AUC > 677 mg·h/L using the “scheduled” process and in none of the patients using the “delayed” protocol. However, for patients with a goal AUC of 600, the 0–24 AUC was > 677 mg·h/L in 22/52 patients vs. 4/52 patients via the “scheduled” process vs. 4/52 patients via the “delayed” protocol. Conclusion. For patients with severe gram-positive bacterial infections requiring aggressive dosing of vancomycin, delaying the start of maintenance dosing following a large LD is an effective way to ensure attainment of therapeutic AUC within the first 24 hr without placing the patient at increased risk for nephrotoxicity.

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

**1577. Particle Characterization of Nebulized Liposomal Amphotericin B and Its Use in the Treatment of Murine Pulmonary Aspergillosis Janam J. Dave, MS; Adliene Sandoval, MS; Jon Olson, MS; Jill Adler-Moore, PhD; Cal Poly Pomona, Pomona, California, California**

**Session:** 162. PK/PD and Susceptibility Testing **Friday, October 4, 2019: 12:15 PM**

**Background.** Immunocompromised patients are very susceptible to pulmonaryaspergillosis causing 50% mortality with present treatments, indicating a need for improved therapy. To address this, we standardized a nebulization method for effective delivery of liposomal amphotericin B (AmBisome®, AmB) into lungs of Aspergillus fumigatus–infected mice.

**Methods.** AmB particle characterization was done with a Cascade particle implanter and a Schuco S5000 nebulizer containing 1.33 mg/mL AmB. For patients with a goal AUC of 400 mg·h/L, 87% of neb AmB particles were between 0.43 mm to 3.3 mm allowing for good drug penetration into 1°, 2° and terminal bronchi, bronchioles, and alveoli. This resulted in very good protection, with 20 min daily neb treatments (Gp1) giving 100% survival and 100% colony formation.

**Results.** 16/68 patients were diagnosed with SSTI (goal 24 hr AUC: 400 mg·h/L) and 52/68 with sepsis, bacteremia/endocarditis, or pneumonia (24 hr AUC: 600 mg·h/L). Median daily maintenance dose was 1750 mg (range: 675–4000 mg). For patients with a goal AUC of 600, the 0–24 AUC was > 677 mg·h/L in 22/52 patients vs. 4/52 patients via the “scheduled” process vs. 4/52 patients via the “delayed” protocol. Conclusion. For patients with severe gram-positive bacterial infections requiring aggressive dosing of vancomycin, delaying the start of maintenance dosing following a large LD is an effective way to ensure attainment of therapeutic AUC within the first 24 hr without placing the patient at increased risk for nephrotoxicity.

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

**1578. Rifampicin Reduces Tedizolid Concentrations When Co-Administered in Healthy Volunteers Lawrence Lee, MBBS, PhD; Kim Hor Hee, PhD; Nicholas Patton, MD, FRCP; National University of Singapore, Singapore**

**Session:** 162. PK/PD and Susceptibility Testing **Friday, October 4, 2019: 12:15 PM**

**Background.** Tedizolid is an oxazolidinone used to treat skin and soft-tissue infections. Rifampicin is a rifamycin antibiotic which can also treat skin and soft-tissue infections, such as those caused by Staphylococcus aureus. Tedizolid and rifampicin could be therefore used concurrently to treat infections. There is currently no clinical data on whether rifampicin affects tedizolid concentrations. Rifampicin is known to be a potent inducer of cytochrome P450s and transporters. Tedizolid is not known to be cleared by cytochrome P450s, but could be affected by other clearance mechanisms. Therefore we conducted a pharmacokinetic drug interaction study to investigate whether 2 weeks of rifampicin can affect tedizolid concentrations.

**Methods.** We conducted a healthy volunteer study in 8 subjects. Subjects were first given linezolid 600 mg on day 1, tedizolid 200 mg on day 4, rifampicin 600 mg daily from day 1 to day 19 (25 mg/kg of rifampicin), and an additional dose of tedizolid 200 mg on day 19. Blood was obtained at pre-dose, 1, 2, 3, 4, 5, 6, 8, and 24 hours post dose on days 4 and 19. Concentrations of tedizolid were measured using a validated liquid chromatography / mass spectrometry method.

**Pharmacokinetic parameters were calculated by Non-Compartmental Analyses using Phoenix WinNonLin version 8.0. The bioequivalence module was used to obtain ratios of PK parameters pre- and post-rifampicin.**

**Results.** Eight subjects were included in the study. Median age (range) and weight were 34.2 (22–45) years and 79 (58–90) kg, respectively. Tedizolid concentrations were 34.5 (29–44) years and 64 (58.4–90.8) kg, respectively. Tedizolid was well tolerated in the study. Tedizolid AUC (0–24 hours) was reduced after 2 weeks of rifampicin (GMR 0.80, 90% confidence interval 0.73–0.88), as was Cmin (0.54, 0.44–0.66) and Cmax (0.85, 0.79–0.91). Clearance/P of tedizolid was significantly increased after rifampicin (1.35, 1.21–1.50).

**Conclusion.** Rifampicin given for 2 weeks has the potential to reduce tedizolid concentrations, especially trough levels, which was reduced by 46%. Caution is recommended when using tedizolid together with rifampicin, especially when tedizolid MIC is high or treating difficult infections.

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

**1579. Multidrug-Resistant Candida auris Isolates From New York Hospitals and Healthcare Facilities Are Susceptible to Antifungal Combinations Britany O’Brien, MS; Sudha Chaturvedi, PhD; Vishnu Chaturvedi, PhD; New York State Department of Health Wadsworth Center, Albany, New York**

**Session:** 162. PK/PD and Susceptibility Testing **Friday, October 4, 2019: 12:15 PM**

**Background.** Candida auris outbreak continues unabated in New York with the current case counts exceeding 300 patients. We used a modification of standard CLSI broth microdilution method (BMD) if two-drug combinations are efficacious against C. auris isolates with high-resistance to fluconazole (FZ, MIC90 > 256 mg/L), and variable resistance to other broad-spectrum antifungal drugs.

**Methods.** BMD plates were custom-designed and quality controlled by TREK Diagnostic System. The combination tests of 15 drug-resistant C. auris involved microtiter wells with the initial 144 two-drug combinations and their two-fold dilutions (1/2–1/32) to get 864 two-drug combinations finally. We utilized MIC90 endpoints for the drug combination endpoints as reported earlier for the intra- and inter-laboratory agreements obtained against Candida species and Aspergillus fumigatus (Antimicrob Agents Chemother. 2015; 59:1759–1766). We also tested minimum fungicidal concentrations (MFC).

**Results.** We tested all possible 864 two-drug antifungal combinations for nine anti-fungal drugs in use to yield 12,960 MIC90 readings, and MFC readings for 15 C. auris isolates. Fluconazole (FLC) at 20 mg/L potentiated most successful combinations with other drugs. Micafungin (MFG), Anidulafungin (AFG), Caspofungin (CAS) at individual concentrations of 0.25 mg/L combined well with FLC (20 mg/L) to yield MIC90 for 14, 13, and 12 of 15 C. auris isolates tested, respectively. MFG/FLC combination was also fungicidal for 4 of 15 isolates. AMB / FLC (0.25/1.0 mg/L) yielded MIC90 for 13 isolates and MFC for three test isolates. Posaconazole (POS), and Isavuconazole (ISA) and Voriconazole (VRC) also combined well with FLC (0.25/20 mg/L) to yield MIC90 for 12, 13, and 12 isolates, respectively. POS/FLC combination was fungicidal for three isolates.

**Conclusion.** We identified seven two-drug combinations of antifungals efficacious against drug-resistant C. auris strains. The modified BMD combination susceptibility testing could be used by the clinical laboratories to assist providers with the selection of optimal treatment for C. auris candidemia.

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