Conclusion. Penicillin allergies can be removed with a pharmacy-driven algorithm that prioritizes direct challenges when appropriate even when the index reaction was moderate to severe. Risks of a reaction are low, and reactions tend to be mild. Given well-documented benefits of desensitizing patients for the patient and the institution, more hospitals should consider starting such services.

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1094. Determination of Plasma Protein Binding of Dalbavancin
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Background. Dalbavancin is a semi-synthetic glycopeptide with a long half-life, making it a promising alternative for infections requiring prolonged therapy such as complicated Staphylococcus aureus bacteremia. A critical pharmacokinetic consideration with prolonged treatment is the unbound or “free” concentration-time profile, as free antibiotic concentrations may correlate with tissue penetration and therapeutic effects better than total drug. Dalbavancin’s plasma protein binding (PB) remains poorly studied and has been reported to range between 93-99%. A reliable and validated free drug assay is needed to link dalbavancin concentrations with patient outcomes.

Methods. The ultracentrifugation technique was used to determine free dalbavancin concentrations in plasma at two concentrations (50 and 200 µg/mL) in duplicate. Centrifugation tubes and pipette tips were treated for 24 hours before use with Tween 80 to assess adsorption. PB centrifugation conditions: 400,000 g (106,000 RPM in TLA-120.1 rotor) for 4 hours at 37°C. Dalbavancin concentrations were analyzed from the plasma samples (total) and middle layer samples (free) by liquid chromatography–tandem mass spectrometry (LC/MS/MS) with isotopically labeled internal standard. Warfarin served as a positive control with known protein binding.

Results. Measurement of free dalbavancin was sensitive to adsorption onto plastic. Treatment of tubes and pipette tips with ≥2% Tween 80 effectively prevented drug loss during PB experiments (Figure 1). Addition of 2% Tween 80 did not affect PB results of warfarin. In PB experiments with 2% Tween 80 coated tubes, the free fraction of dalbavancin was 0.96% (95% CI: 0.94-0.98) at 50 µg/mL and 1.11% (95% CI: 1.08-1.13) at 200 µg/mL.

Figure 1. Percent Free Dalbavancin vs Varying Concentrations of Tween 80 for Pretreatment of Tubes

Conclusion. By the ultracentrifugation method, dalbavancin’s PB was estimated to be approximately 99%. Given dalbavancin’s high PB, accurate measurement of free dalbavancin concentrations should be a key consideration in future exposure-response studies, especially clinical trials. Future investigations should also determine if the active fraction is best predicted by the free or total fraction, as this remains a subject of debate.

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1095. Pharmacokinetics-Pharmacodynamics Evaluation of Tebipenem Pivoxil Hydroxideimine Using the 10-Day Hollow-Fiber In Vitro Infection Model
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Methods. Three Enterococcus coli clinical isolates (ESBL +, Sequence Type -131) (tebipenem MIC = 0.008 to 0.03 mg/L) were subjected to concentration-time profiles simulating free-drug plasma concentrations after oral administration of tebipenem regimens in a hollow-fiber in vitro infection model. Dose-ranging studies were completed using two isolates at an initial burden of 10^9 CFU/mL and with exposures for tebipenem regimens ranging from 4.69 to 1200 mg administered every eight hours (q8h). An additional isolate was subjected to only the tebipenem 600 mg q8h regimen evaluated in the Phase 3 trial. Samples were collected for the enumeration of bacterial burden and evaluation of the simulated pharmacokinetic profile. Each sample for bacterial enumeration was suspended onto drug-free and tebipenem-supplemented agar plates in order to observe the density of the total- and drug-resistant subpopulations over the 10-day period.

Results. A full dose response, ranging from treatment failure to reductions in bacterial burden from baseline, were observed in the dose-ranging studies for the two E. coli isolates. Tebipenem consistently lowered bacterial burdens below that of the initial inoculum at a dose of 600 mg q8h for all three E. coli isolates. Amplification of resistance was observed intermittently for all regimens, but was never equal to that of the total population at the 600 mg q8h clinical dose. Tebipenem MIC values for isolates collected from the drug-supplemented agar ranged from 0.06 to 0.25 mg/L, representing four two-fold dilutions from baseline.

Conclusion. The selection of tebipenem dosing regimens that minimize the potential for on-therapy drug-resistance amplification.

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1096. Evaluation of Vancomycin Pharmacokinetics in Intravenous Drug Users
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Session P-62: PK/PD Studies

Background. People who inject illicit drugs (PWID) are 16 times more likely to develop methicillin-resistant Staphylococcus aureus (MRSA) infections including severe infections like bacteremia and endocarditis. Vancomycin is recommended as the drug of choice for empiric and targeted coverage in both severe and non-severe MRSA infections. Pharmacokinetic literature has suggested up to 31% higher renal clearance in PWID population compared to non-PWID population.

Aim. To examine the vancomycin pharmacokinetics in PWID population compared to non-PWID population.

Methods. This was a single-center, prospective chart review that examined vancomycin pharmacokinetics in patients treated with vancomycin between January 1, 2015 through July 31, 2020. Patients were identified as either IVDU or non-IVDU groups based on ICD-9/10 codes. The primary outcome was the difference between the two groups in vancomycin steady state trough levels.

Results. A total of 158 patients were included in the analysis (77 IVDU vs 81 non-IVDU). Mean first vancomycin steady state trough were significantly less in IVDU population. There is a paucity of data examining vancomycin pharmacokinetics in PWID population.

Implications. Vancomycin is the drug of choice for empiric and targeted coverage in both severe and non-severe MRSA infections. Pharmacokinetic literature has suggested up to 31% higher renal clearance in PWID population compared to non-PWID population. This increased clearance may theoretically lead to more frequent sub-therapeutic troughs compared to standard dosing schemes. There is a paucity of data examining vancomycin pharmacokinetics in PWID population.

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