penetration using the ratio of ELF:serum AUC₀–∞ was 33.0% for ASN-1 and 20.3% for ASN-2 following the selected clinical dose of 3,600 mg.

**Conclusion.** A population PK model adequately described the time-course of ASN-1 and ASN-2 in ELE ELF penetration was 20–33% following administration of the ASN100 clinical dose. These results should be interpreted with caution given the limited sample size (six subjects per dose group) and limitations of area-based normalization of BALF to ELF volume.

**Results.** For the reference strain, a clinical regimen of 4 g piperacillin and 0.5 g tazobactam administered every 8 hours resulted in a $T > MIC$ of 39.6% and bacterial regrowth. An exposure equivalent to 1.5 g tazobactam ($T > MIC$ of 55.1%) was needed to suppress growth. These regrowth findings were validated with the two other ESBL-producers with tazobactam exposures characterized by $T > MIC$ of 36.8 and 43.8%.

**Conclusion.** Improved bacterial killing was observed with increasing tazobactam exposures. As a novel PK/PD index, $T > MIC$ may be used to characterize response to a β-lactamase inhibitor and provide efficacy targets to guide the development and clinical dosing of these inhibitors.

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1410. Novel Framework to Compare the Effectiveness of Tazobactam, Relebactam and Avibactam Against Extended-Spectrum β-Lactamase-Producing Enterobacteriaceae

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**Background.** Resistance mediated by extended-spectrum β-lactamasases (ESBLs) presents a serious challenge in the treatment of Gram-negative pathogens. ESBLs confer resistance to most β-lactams which may be reversed with the addition of an active β-lactamase inhibitor (such as tazobactam, relebactam and avibactam). However, various ESBLs may display different susceptibilities to these inhibitors, which could impact efficacy. We propose a framework for comparing the efficacy of these inhibitors when combined with the same β-lactam.

**Methods.** Three clinical isolates of *K. pneumoniae* harboring CTX-M-15 and one *E. coli* with SHV-12 were used. The susceptibility of each isolate to piperacillin was determined by broth dilution using escalating concentrations of tazobactam, relebactam and avibactam. Similar experiments were subsequently conducted with cefazidime. The resulting minimum inhibitory concentrations (MICs) were mapped as response to inhibitor concentration using an inhibitory $I_{max}$ model. The best-fit model parameters were compared for each isolate–inhibitor combination.

**Results.** In all scenarios, MIC reductions were observed in the presence of increasing inhibitor concentrations. The MIC reduction for each isolate was well fitted to inhibitor concentrations ($r^2 ≥ 95%$). $I_{max}$ estimates reflected the sensitivity of the isolates to each inhibitor, while $I_{50}$ captured the maximum extent of MIC reduction. With piperacillin, $I_{max}$ values ranged from 1.36 to 35.2/µg/mL for tazobactam, 2.32–15.82 µg/mL for relebactam and 0.62–2.37 µg/mL for avibactam.

**Conclusion.** We illustrated a simple structural model capable of comparing the performance of different inhibitors. This platform may be used to identify the optimal pairing of various β-lactams and β-lactamase inhibitors for individual isolates.

**Disclosures.** Y. Tam, European Union’s Seventh Framework Programme: Grant Investigator, Research grant.

1411. Tecioplanin (TEI) vs. Vancomycin (VAN) in Combination with Piperacillin-Tazobactam (TZP) or Meropenem (MER) as a Cause of Acute Kidney Injury (AKI)

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**Background.** VAN has been shown to cause increased incidence of AKI when combined with TZP. The reason is unknown. TEI is a glycopeptide which may be less nephrotoxic. We compared both glycopeptides in combination with TZP or MER for causing AKI.

**Methods.** A retrospective cohort study was performed between May 2015 and December 2017 in a large tertiary care setting. Evaluation of AKI was made by using RIFLE criteria. Patients ≥18 years were included if they had a baseline serum creatinine available and received one of the combinations tested for at least 48 hours.

**Results.** Overall 456 patients were screened and 379 included in the study. After controlling for residual differences (age, Charlson comorbidity index score, presence of AKI, GFR value, presence of sepsis or septic shock, residing in intensive care unit at the time of antibiotic therapy and number of days of antibiotic therapy), AKI incidence was significantly higher in patients receiving TZP-VAN than those receiving TZP-TEI and also in patients receiving TZP-VAN than those with MER-VAN. No difference
in AKI was detected between patients with MER-VAN and with MER-TEI (table). Mortality at 7 and 30 days and resolution of AKI at discharge were similar in all groups.

### Table: Comparison of various antibiotic combinations causing AKI

| Variable | Combination | Unadjusted OR (95% CI) | P-value | Adjusted OR (95% CI) | P-value |
|----------|-------------|------------------------|---------|----------------------|---------|
| TAZ-VAN  | TAZ-TEI     |                        |         |                      |         |
| All      |             |                        |         |                      |         |
| Risk     |             |                        |         |                      |         |
| TAZ      | 2.69 (1.33-5.49) | .023                   | 3.31 (1.43-7.55) | .004 |
| TAZ      | 3.14 (1.82-5.41) | .001                   | 2.14 (1.02-4.50) | .046 |

**Conclusion.** TAZ causes increased nephrotoxicity when combined with VAN. Combination with TEI may offset this side effect. Additionally, the higher AKI incidence with TAZ-VAN may suggest a particular nephrotoxic synergy between TAZ and VAN. Randomized controlled trials should confirm this observation.

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

### 1412. Caspofungin and Anidulafungin Behave as Fungistatic Agents Against Candida auris

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**Background.** Candida auris is an emerging multiresistant nosocomial pathogen responsible for outbreaks around the world. It is associated with therapeutic failure and high mortality rates. Echinocandins are the empiric treatment choice for C. auris infections. However, clinical reports show that some patients respond poorly to this therapy. The aim of this study was to determine the in vitro activity of Caspofungin and Anidulafungin against C. auris by time–kill curve methods.

**Methods.** Twenty C. auris strains were studied. They were isolated from patients with proven invasive fungal infection. Susceptibility testing was performed following the Clinical and Laboratory Standards Institute (CLSI) M27-A3 and S4 documents. Time–killing experiments were conducted for 10 of the 20 isolates (in duplicate on 2 separate days) using RPMI-1640 buffered with MOPS. Caspofungin and anidulafungin tested concentrations were 0.12, 0.25, 0.50, 1.00 and 8.00 µg/mL. The inoculum was tested concentrations were 0.12, 0.25, 0.50, 1.00 and 8.00 µg/mL. The inoculum was the Clinical and Laboratory Standards Institute (CLSI) M27-A3 and S4 documents. Anidulafungin against C. auris infections. The aim of this study was to determine the in vitro activity of Caspofungin and Anidulafungin against C. auris by time–kill curve methods. Additionally, the higher AKI incidence with TAZ-VAN may suggest a particular nephrotoxic synergy between TAZ and VAN. Randomized controlled trials should confirm this observation.

**Results.** CAMB was well tolerated by all four patients, and all are currently on the extension phase (Figure 3). There was significant improvement in clinical severity symptom scores of esophageal and oropharyngeal symptoms: CAMB01 achieved reduction in clinical symptoms by 57% (800 mg/day), CAMB02 by 85% (400 mg/day), CAMB03 50% (800 mg/day) and CAMB04 50% (800 mg/day). CAMB02 maintained higher plasma PK exposure throughout the study compared with CAMB01, a possible explanation for clinical response at a lower 400 mg/day dose. Reported adverse events were grade 1, mostly nausea and dizziness. There were no signs of liver, kidney or hematologic toxicity in any of the patients, with CAMB01 and CAMB02 receiving study drug for ~1 year.

**Conclusion.** CAMB was well tolerated in patient volunteers with long-standing symptomatic azole-resistant CMC. All four patients have met the primary endpoint of achieving 30% clinical response. CAMB is a promising oral therapy for patients with history of CMC, with potential use in treatment and prophylaxis of invasive fungal infections.

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### 1414. Inoculum Effect of Piperacillin/Tazobactam Concentration on Emergence of Resistance in Klebsiella aerogenes

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**Background.** Current oral therapeutic options for chronic mucocutaneous candidiasis (CMC) are often associated with resistance and toxicity. Amphotericin B (AMB) has broad fungicidal activity and markedly resists emergence of resistance but requires parenteral administration and monitoring for significant nephrotoxicity, which worsens with chronic treatment. Encocohleated amphotericin B (CAMB) is a novel oral formulation of AMB. In animal models, CAMB demonstrates antifungal activity with similar efficacy as intraperitoneal AMB deoxyscholute, but without the associated toxicity. This ongoing patient volunteer study assesses the efficacy, safety, tolerability and PK of CAMB in patients with CMC who are refractory or intolerant to standard oral azole antifungals.

**Methods.** Four patients have completed the clinical protocol treatment period: 3 patients with STAT3 deficient Hyper Igl syndrome and CMC, and one patient with chronic esophageal candidiasis. Eligible patients were dose escalated (Figure 1), with option of enrolling in an extension phase. Serial plasma PK samples were collected over 24 hours over the study period, with data available from two patients (Figure 2).

**Results.** CAMB was well tolerated by all four patients, and all are currently on the extension phase (Figure 3). There was significant improvement in clinical severity symptom scores of esophageal and oropharyngeal symptoms: CAMB01 achieved reduction in clinical symptoms by 57% (800 mg/day), CAMB02 by 85% (400 mg/day), CAMB03 50% (800 mg/day) and CAMB04 50% (800 mg/day). CAMB02 maintained higher plasma PK exposure throughout the study compared with CAMB01, a possible explanation for clinical response at a lower 400 mg/day dose. Reported adverse events were grade 1, mostly nausea and dizziness. There were no signs of liver, kidney or hematologic toxicity in any of the patients, with CAMB01 and CAMB02 receiving study drug for ~1 year.

**Conclusion.** CAMB was well tolerated in patient volunteers with long-standing symptomatic azole-resistant CMC. All four patients have met the primary endpoint of achieving 30% clinical response. CAMB is a promising oral therapy for patients with history of CMC, with potential use in treatment and prophylaxis of invasive fungal infections.