penetration using the ratio of ELF/serum AUC_{0-t} 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.

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### 1409. Evaluation of Alternative Piperacillin-tazobactam Dosing Strategies Against ESBL-Producing Enterobacteriaceae Using a Hollowfiber Infection Model

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**Background.** Extended-spectrum β-lactamase (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 using escalating concentrations of tazobactam, relebactam and avibactam. Similar experiments were subsequently conducted with ceftazidime. The resulting minimum inhibitory concentrations (MICs) were mapped as response to inhibitor concentration using an inhibitory E_{inhib} 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%). IC_{50} estimates captured the sensitivity of the isolates to each inhibitor, while IC_{max} captured the maximum extent of MIC reduction. With piperacillin, IC_{50} values ranged from 1.36 to 25.25 μg/mL for tazobactam, 2.32–15.82 μg/mL for relebactam and 0.62–2.37 μg/mL for avibactam. IC_{max} values were 4.75–6.99, 6.56–9.77 and 7.83–11.22 for tazobactam, relebactam and avibactam, respectively. Similar trends in IC_{50} and IC_{max} were observed with ceftazidime as the β-lactam.

**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.

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### 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 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 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

**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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