1592. In Vitro Activity of Ceftolozane-Tazobactam (C/T) Against Enterobacteriaceae and Pseudomonas aeruginosa Circulating in Chile
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Session: 162. PK/PD and Susceptibility Testing
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**Background.** The widespread dissemination of carbapenem-resistant (CR) *P. aeruginosa* and *Enterobacteriaceae* has created a major global public health crisis. C/T is a recently approved therapeutic which consists of the combination of a novel cephalosporin (ceftolozane) and tazobactam (a β-lactamase inhibitor). C/T has shown good activity against a wide range of multidrug-resistant (MDR) Gram negatives, being particularly interesting as an alternative for MDR *P. aeruginosa*. We aimed to determine the activity of C/T against clinical strains of Enterobacteriaceae and *P. aeruginosa* recovered in 4 large clinical centers from Chile.

**Methods.** We analyzed 434 isolates of *Enterobacteriaceae* (347 *E. coli, 66 K. pneumoniae, 21 E. cloacae complex* and 57 *P. aeruginosa* collected during 2017 from 4 tertiary care institutions in Santiago, Chile. Identification was performed as per each local clinical microbiology lab. Susceptibility testing was performed by broth microdilution using customized Sensititre plates (Trek). Carba-NP was performed to screen for carbapenemase production. Susceptibilities were analyzed as per 2019 CLSI breakpoints.

**Results.** The MIC50/90 for C/T against *Enterobacteriaceae* and *P. aeruginosa* were 1/4 µg/mL and 2/16 µg/mL, respectively. In *Enterobacteriaceae*, susceptibility to C/T reached 92% in *E. coli* (Figure 1A), 91% in *E. cloacae* complex (Figure 1B) and 70% in *K. pneumoniae* (Figure 1C). Remarkably, C/T remained active against 38% (33/57) of *CR P. aeruginosa* (Figure 2A). Among Carba-NP-negative CR isolates (46%, 26/57), susceptibility to C/T was 54% (Figure 3 A–C). In *P. aeruginosa*, the overall susceptibility to C/T was 81% (Figure 1D), maintaining activity against 69% (25/36) of CR strains (Figure 2B). Importantly, susceptibility to C/T in CR *P. aeruginosa* isolates with a negative Carba-NP (67%, 24/36) was 83% (20/24) (Figure 3D).

**Conclusion.** In this multicenter study, we observed that C/T was highly active against clinical isolates of *Enterobacteriaceae* and *P. aeruginosa*. Of note, C/T remained active against a large proportion of CR clinical strains. Moreover, the activity of C/T was particularly high against CR *P. aeruginosa* isolates with a negative Carba-NP.

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1593. Analysis of Hospital Antimicrobial Susceptibility Test Results for Patterns of Antibiotic Resistance
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**Background.** Antimicrobial susceptibility tests (ASTs) are routinely performed on pathogens isolated from clinical samples. ASTs are used by clinicians to select the most appropriate treatment for antibiotic-resistant microorganisms. In aggregate, ASTs offer insight into the rise and spread of antibiotic resistance across hospitals. Here, we used ASTs to identify patterns of antibiotic resistance across drugs and microorganisms.

**Methods.** We conducted a retrospective analysis of 364,813 AST results from the University of Pittsburgh Medical Center from 2015 to 2018. Data regarding infection site, hospital laboratory testing, organism identification, and antibiotic susceptibilities were extracted from the laboratory information system and anonymized prior to use. The pathogens studied included *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Staphylococcus aureus, Proteus mirabilis*, and *Enterococcus faecalis*.

We identified 21 antibiotic-pathogen combinations where resistance was found in less than 1% of AST results. Concordant susceptibility results of levofloxacin and ciprofloxacin occurred the most frequently among antibiotic pairs. Additionally, discordant susceptibility results were more common within antibiotics belonging to the same antibiotic class than between classes. *P. aeruginosa* had the highest rate of overall concordant results with concordance occurring within all -lactam classes. In contrast, *K. pneumoniae* and *P. mirabilis* showed the least concordance, suggesting that their resistance profiles are less predictable. Notably, we did not identify any pairs of antibiotics that strongly exhibited discordant susceptibility results regardless of the microorganism.

**Conclusion.** Using routinely collected clinical microbiological data, we were able to characterize pathogen-antibiotic combinations where resistance is rarely seen. Additionally, we identified rare pairs of antibiotics that frequently exhibited discordant susceptibilities both within and between classes. Lastly, we were unable to find evidence of discordant susceptibility results, indicating that more clinical research is needed to determine the efficacy of collateral sensitivity treatment techniques.

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1594. Ceftolozane–Tazobactam Demonstrates Higher In Vitro Susceptibility than Ceftazidime–Avibactam Against Pseudomonas aeruginosa Isolated from Respiratory Tract of Adult Cystic Fibrosis Patients
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**Background.** *Pseudomonas aeruginosa* is a commonly isolated pathogen in adults with cystic fibrosis (CF). Antimicrobial resistance is an escalating problem due to chronic colonization and frequent antimicrobial exposure. Ceftolozane-tazobactam (C/T) and ceftazidime–avibactam (CZA) exhibit promising activity against antimicrobial-resistant organisms, including *P. aeruginosa*. In this study, we compared in vitro activity of C/T and CZA against *P. aeruginosa* isolated from respiratory cultures obtained from adult patients with CF.

**Methods.** This is a retrospective study of respiratory cultures positive for *P. aeruginosa* collected from adult CF patients between January 1, 2015 to November 30, 2018. The first isolate per patient per year that underwent susceptibility testing for C/T, CZA, and colistin were included in the study. All isolates underwent in-house susceptibility testing for 9 anti-pseudomonal agents according to the methodology established by the Clinical Laboratory Standards Institute (CLSI). Susceptibility testing of C/T, CZA, and colistin were performed by a reference lab. Isolates were classified into 3 drug-resistant
categories using the following definition: multidrug-resistant (MDR) non-susceptible (NS) to ≥2 agent in ≥2 different antimicrobial classes, extensive drug-resistant (XDR) NS to 4 or ≥5 different classes, and pan drug-resistant (PDR) NS to all 6 classes except colistin.

**Results.** Forty-two P. aeruginosa respiratory isolates from 32 patients with CF were included. The overall susceptibility to C/T and CZA was 59.5% and 42.9%, respectively. Thirty-eight (90%) isolates were considered MDR with susceptibility of 55.3% to C/T and 44.7% to CZA. Among the 11 XDR isolates, susceptibility to C/T was 81.8% vs. CZA 72.7%. Susceptibility to C/T vs. CZA was also higher (37.5% vs. 25%) among the 24 PDR isolates.

**Conclusion.** Among P aeruginosa isolated from CF respiratory cultures, C/T appears to have better in vitro activity compared with CZA, and remained true among isolates considered XDR and PDR. These results suggest using C/T while awaiting susceptibilities when standard anti-pseudomonal agents cannot be used. Future studies evaluating clinical outcomes for the treatment of pulmonary CF exacerbations are needed to assess the applicability of in vitro susceptibility data.

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### 1595. Comparative In Vitro Activity of Imipenem–Relebactam Against Drug-Resistant Gram-Negative Isolates from Pediatric Patients

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**Session:** 162. PK/PD and Susceptibility Testing

**Background.** Drug resistance in Gram-negative bacteria is of particular concern in children. Relebactam, a novel diazabicycloundecane inhibitor, coupled with imipenem has broad-spectrum activity against β-lactamase producing organisms. Here, we compare the in vitro activity of imipenem-relebactam to 10 standard comparator drugs against resistant Gram-negative isolates from two US pediatric hospitals.

**Methods.** We tested 100 isolates (50 per site) from pediatric clinical specimens tested during 2015–2017. All isolates were extended-spectrum cephalosporin-resistant (ESC-R); more than half were multidrug resistant (67%). Selected ESC-R isolates included Enterobacteria coli (90), Klebsiella pneumoniae (8), Klebsiella oxytoca (1), and Enterobacter cloacae (1) that were resistant or intermediate to ≥1 cephalosporins and/or aztreonam. A 0.5 McFarland suspension was prepared from colonies grown on blood agar plates (Thermo Scientific) at 35 ± 1°C for 18–24 hours. A final inoculum of 5 × 10^5 CFU/mL was prepared in Mueller-Hinton broth. Sensititre plates (Thermo Fisher Scientific) containing graded concentrations of imipenem/relebactam and 10 comparator drugs were inoculated and incubated at 35 ± 1°C for 18–24 hours. The minimum inhibitory concentration (MIC) was determined using the Sensititre Vibrio system (Thermo Fisher Scientific) and endpoints were interpreted using CLSI (2019) breakpoint criteria, with the exception of colistin (EUCAST 2019).

**Results.** Selected ESC-R isolates had high rates of resistance to cephalosporins (64%–97%), aztreonam (80%), and levofloxacin (61%). All isolates were susceptible to imipenem/relebactam, imipenem and meropenem (MIC ≤ 1 µg/mL for all). The imipenem/relebactam MIC50 (0.06 µg/mL) and MIC90 (0.12 µg/mL) values were lower for ESC-R isolates than within any dilution of MICs of imipenem alone (0.12 µg/mL and 0.25 µg/mL). Among the comparators, colistin, amikacin, and piperacillin/tazobactam demonstrated comparable activities with 100%, 99%, and 94% susceptibility, respectively.

**Conclusion.** Meropenem, imipenem alone and in combination with relebactam exhibited 100% susceptibilities against ESC-R Enterobacteriaceae isolated from pediatric specimens, demonstrating the high potency of carbapenems.

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### 1596. Impact of Vancomycin Area Under Curve Below Current Persistent Methicillin-Resistant Staphylococcus aureus (MRSA) Bloodstream Infections (BSI)

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**Session:** 162. PK/PD and Susceptibility Testing

**Background.** Persistent Methicillin-resistant Staphylococcus aureus (MRSA) bloodstream infections (BSI) are associated with significant morbidity, mortality, and healthcare expenditures. Vancomycin (VAN) remains the treatment of choice for invasive MRSA BSI. Current guidelines for the treatment of MRSA BSI recommend a VAN AUC0–24/MIC ratio ≥400. The Detroit Medical Center (DMC) implemented an AUC-guided dosing strategy. However, data on the association between AUC0–24 and clinical outcomes in MRSA BSI are limited. We aimed to evaluate the association between VAN AUC0–24 and persistent bacteremia (PB) among patients with BSI.

**Methods.** Multi-center, retrospective cohort study from January 2015 to November 2018. We included adult patients with MRSA bacteremia treated with VAN for which AUC0–24 monitoring was performed. AUC was measured using 2-level guided dosing. The primary outcome was PB defined as continued positive cultures >72 hours after VAN initiation. Classification and Regression Tree (CART) analysis was performed to determine the best PB (competing mortality) prediction model for the cohort.

**Conclusion.** VAN AUC0–24 BP of <400.25 was independently associated with PB in patients with MRSA BSI. Our findings underscore the importance of VAN dose optimization to achieve timely bacterial clearance in MRSA bacteremia.

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