This displays the difference (cefotaxime/tazobactam minus polymyxin) in mean partial credit scores (black line) and associated 95% confidence bands (gray lines) as a function of the partial credit score assigned to an individual having at least one adverse event (range 0 – 100). A score of 100% is assigned to patients alive with no adverse events and a score of 0% is assigned to patients who die. A difference in mean partial credit scores of approximately zero suggests there was no difference observed between treatment groups.

**Conclusion.** These findings support the recent Infectious Diseases Society of America guidance favoring C/T over polymyxin for treatment of CRPA infections.

**Disclosures.** David van Duijn, MD, PhD, Entasis (Advisor or Review Panel member)/genentech (Advisor or Review Panel member)/Karius (Advisor or Review Panel member)/Merck (Grant/Research Support, Advisor or Review Panel member)/Pfizer (Consultant, Advisor or Review Panel member)/Qurex (Advisor or Review Panel member)/Shionogi (Grant/Research Support, Scientific Research Study Investigator, Advisor or Review Panel member)/Utility (Advisor or Review Panel member) Scott R. Evans, PhD, Abbvie (Consultant)/Advantagene (Consultant)/Alexion (Consultant)/Amgen (Consultant)/AstraZeneca (Consultant)/Atricure (Consultant)/Breast International Group (Consultant)/Cardinal Health (Consultant)/Clever (Consultant)/FHI Clinical (Consultant)/Genentech (Consultant)/Gilead (Consultant)/Horizon (Consultant)/International Drug Development Institute (Consultant)/Lung Biotech (Consultant)/Microbiotix (Consultant)/NeoRocs (Consultant)/Novartis (Consultant)/Nuvelution (Consultant)/Pfizer (Consultant)/Rakuten (Consultant)/Roche (Consultant)/Roivant (Consultant)/SAB Biopharm (Consultant)/Shire (Consultant)/Stryker (Consultant)/SVB Leerink (Consultant)/Takeda (Consultant)/Teva (Consultant)/Tracor (Consultant)/Vir (Consultant).

1220. Is MIC all that matters? MIC Distributions of Ceftazidime and Cefepime in Ceftriaxone-Resistant E. coli and Klebsiella spp.

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**Session:** P-72. Resistance Mechanisms

**Background.** The Clinical and Laboratory Standards Institute (CLSI) lowered MIC breakpoints for many beta-lactam antibiotics to enhance detection of resistance among Enterobacteriaceae. This shift was also meant to eliminate the need for routine testing for extended-spectrum beta-lactams (ESBLs). The recommended treatment for ESBL-producing Enterobacteriaceae is carbapenems. The IDSA guidelines for MDR-GN organisms recommend using ceftazidime (CRO) resistance as a proxy for ESBL production and thus carbapenem treatment. Under CLSI guidelines, alternative beta-lactams such as ceftazidime (CAZ) and cefepime (FEP) may still be reported as susceptible and thus used by clinicians even in light of IDSA recommendations. The aim of this project was to characterize the MIC distributions of CAZ and FEP stratified by CRO susceptibility.

**Methods.** Clinical E. coli, K. pneumoniae, and K. oxytoca isolates from blood cultures in adult patients from Nov 2016-Dec 2018 that had MICs tested by the Vitek-2 automated susceptibility testing system for CRO, FEP and CAZ were identified. Descriptive statistics were used to compare MIC distributions across the antibiotics of interest (SPSS).

**Results.** 573 isolates were included, of these, 17.3% were CRO resistant. Most (53%) CRO-R isolates had FEP MICs ≤2, which is considered S by CLSI. Using the EUCAST breakpoint of ≤4, which is considered S-DD by CLSI, 19% had FEP MICs of 4-8 which would be considered S-DD by CLSI. Using the EUCAST breakpoint of ≤8, which is considered S- by EUCAST, 19% had FEP MICs of ≤4. Using the EUCAST breakpoint of ≤16, which is considered S-DD by CLSI, 19% had FEP MICs of ≤2.

**Conclusion.** Of CRO-R isolates had CAZ MICs ≤4, which is considered S by CLSI. Using the EUCAST breakpoints for CRO-R isolates from blood cultures in adult patients from Nov 2016-Dec 2018 that had MICs tested by the Vitek-2 automated susceptibility testing system for CRO, FEP and CAZ were identified. Descriptive statistics were used to compare MIC distributions across the antibiotics of interest (SPSS).

1221. Genomic Factors Affecting the Efficacy of Antimicrobial Therapy in Daptomycin-, Linezolid-, Vancomycin-Resistant Enterococcus faecium (DLVRE) Samuel W. Gatesy, M.S.1; Nathan B. Pincus, B.S.1; William Justin Moore, PharmD2; Omar Al-Heeti, MD2; Tejas Joshi, MS1; Kelly E. R. Ratcha, MD, PhD2; Northwestern University, Libertyville, Illinois; Northwestern Medicine, Chicago, Illinois; Northwestern Feinberg School of Medicine, Chicago, Illinois

**Session:** P-72. Resistance Mechanisms

**Background.** Nosocomial acquisition of vancomycin-resistant Enterococcus (VRE) is one of the most challenging problems in healthcare. As Enterococcus isolates are increasingly resistant to vancomycin, clinicians now rely on alternative antimicrobial therapies including linezolid and daptomycin (DAP) to treat infections. For multidrug-resistant (MDR) VRE, combination therapy with beta-lactams and daptomycin has been shown to be effective.

**Methods.** Following initiation of empiric DAP and celaroline (CPT) for an MDR E. faecium bloodstream infection (VRE_001), we aimed to determine if there existed in vitro synergy between both agents that supported their clinical use. Combination synergy testing was performed using E-test strips and minimal inhibitory concentrations (MICs) were read at 24 hours. For whole genome sequence-based analysis (WGS), genomic DNA from VRE_001 was used for both short read (Illumina MiSeq) and long read sequencing (MinION, Nanopore). The complete genome was assembled and the NCBI AMRFinderPlus program used to identify known resistance mechanisms.

**Results.** Original MICs of VRE_001 from the clinical microbiology laboratory at Northwestern Memorial revealed an MDR E. faecium (Table 1). Combination synergy testing in the experimental laboratory revealed only modest amounts of synergy between CPT and DAP (Table 2). Following WGS, VRE_001 was identified as an ST-584 E. faecium with a 3.2 Mbp genome, including a single chromosome and five plasmids. WGS analysis revealed several mechanisms of antimicrobial resistance (Table 3) genetically supporting the observed MDR-DLVRE phenotype.

![Image](image.png)

**Table 1:** Minimal Inhibitory Concentrations (MICs) from the Northwestern Memorial Hospital Clinical Microbiology Laboratory

| Antibiotic | MIC Interpretation |
|------------|-------------------|
| Amikacin | 12 μg/mL |
| Daptomycin | 12 μg/mL |
| Linezolid | ≥2 μg/mL |
| Vancomycin | 32 μg/mL |
| Ceftazidime | 32 μg/mL |

| Table 2: Synergistic MIC Investigational Laboratory E-Testing

| Antibiotic | Daptomycin MIC Interpretation |
|------------|-------------------------------|
| CPT | 16 μg/mL |

| Table 3: Genomic mechanisms of antimicrobial resistance identified in VRE_001 using NCBI AMRFinderPlus

| Antibiotic | Point Mutations |
|------------|----------------|
| Daptomycin | s65, I124 |
| Vancomycin | s59, s60 |
| Fluoroquinolones | aac(3)-I |
| Aminoglycosides | aprA, aprB |
| Tetracyclines | tetM |

This displays the difference (cefotaxime/tazobactam minus polymyxin) in mean partial credit scores (black line) and associated 95% confidence bands (gray lines) as a function of the partial credit score assigned to an individual having at least one adverse event (range 0 – 100). A score of 100% is assigned to patients alive with no adverse events and a score of 0% is assigned to patients who die. A difference in mean partial credit scores of approximately zero suggests there was no difference observed between treatment groups.

**Conclusion.** These findings support the recent Infectious Diseases Society of America guidance favoring C/T over polymyxin for treatment of CRPA infections.

**Disclosures.** Emily Heil, PharmD, MS, BCIDP, Nothing to disclose Kimberley C. Caeys, PharmD, GenMark (Speaker’s Bureau)