Disclosures. Cecilia G. Carvalhaes, MD, PhD, Abbvie (formerly Allergan) (Research Grant or Support); Cipla Therapeutics, Inc. (Research Grant or Support); GlaxoSmithKline, plc (Research Grant or Support); Melinta Therapeutics, LLC (Research Grant or Support); Pfizer, Inc. (Research Grant or Support); Spero Therapeutics (Research Grant or Support); Wayne State University (Individual(s) Involved: Self): Research Grant or Support; Rhode Island Hospital (Individual(s) Involved: Self): Research Grant or Support; Rhode Island Hospital (Individual(s) Involved: Self): Research Grant or Support; Spero Therapeutics (Individual(s) Involved: Self): Research Grant or Support; Rhode Island Hospital (Individual(s) Involved: Self): Research Grant or Support; cervical HPV, was evaluated against a large collection of MDR Enterobacterales clinical isolates from US hospitals.

Results. PLZ inhibited 93.0% of the MDR isolates (MIC$_{50}$, 0.5/1 mg/L) and showed >99% S rates when tested against AME producers. PLZ had >50% S rates against ESBL- and/or CPE-producers (Table). AMK S rates were >90.0% for meropenem, 88.4% for tigecycline, 49.3% for piperacillin-tazobactam, and 17.8% for cefepime; only the carbapenems and tigecycline were active against all 97.6% of the MDR isolates. PLZ was active against 99.0% of ESBL producers, while AMK S rates were 96.2%/87.0% as per the US FDA/EUCAST against these organisms. PLZ and AMK showed similar S rates when tested against GEN-NS isolates. GEN and TOB exhibited limited activity against XDR (93.2% S; Table). AMK S rates were 84.6% and 69.3% when EUCAST (≤4 mg/L) and USCAST (≤8 mg/L) breakpoints were applied, respectively. Among agents from other classes, S rates were 85.5% for meropenem, 88.4% for tigecycline, 49.3% for piperacillin-tazobactam, and 17.8% for cefepime; only the carbapenems and tigecycline were active against all 97.6% of the MDR isolates.

Conclusion. Despite co-resistance to aminoglycosides and other classes of antibiotics observed with MDR Enterobacterales isolates, PLZ remained highly active against these isolates including AME-, ESBL-, and/or CPE-producers that cause infections in US hospitals.

Table

| Resistant subset | MIC (mg/L) | S (%) |
|------------------|-----------|-------|
| Plazomix         | 0.016      | 90.3  |
| Aminoglycoside   | 0.025      | 90.3  |
| Gentamicin       | 0.036      | 90.3  |
| Tobramycin       | 0.041      | 90.3  |

P-72. Resistance Mechanisms

Background. Multidrug-resistant (MDR) Enterobacterales isolates have increased in recent years and are a major public health threat in many US hospitals. Aminoglycoside (AMG) resistance often co-exist with resistance to other classes of antibiotics. A newer aminoglycoside, plazomix, was evaluated against a large collection of MDR Enterobacterales clinical isolates from US hospitals.

Methods. A total of 356 MDR isolates (1/patient) were collected from 32 US medical centers located in 23 states in 2018-2020 and susceptibility tested by broth microdilution method at a central laboratory. MDR was defined as nonsusceptible (NS) to ≥3 antimicrobial classes and extensively drug-resistant (XDR) as susceptible (S) to ≤2 classes. Isolates resistant to aminoglycosides and/or-broad-spectrum cephalosporins were screened for aminoglycoside-modifying enzymes (AME), 16S rDNA methyltransferases, and β-lactamases by whole genome sequencing.

Results. PLZ inhibited 93.0% of the MDR isolates (MIC$_{50}$, 0.5/1 mg/L) and showed >99% S rates when tested against AME producers. PLZ retained activity against isolates NS to AMK (83.9%), gentamicin (GEN; 89.3%), and/or tobramycin (TOB; 92.4%). PLZ showed markedly higher S rates than AMK against XDR (93.3% vs. 71.7%), AME producers (97.6% vs. 90.2%), and carbapenemase (CPE) producers (98.1% vs. 67.9%). PLZ was active against 99.0% of ESBL producers, while AMK S rates were 96.2%/87.0% as per the US FDA/EUCAST against these organisms. PLZ and AMK showed similar S rates when tested against GEN-NS isolates. GEN and TOB exhibited limited activity against MDR and all resistant subsets.

Conclusion. Despite co-resistance to aminoglycosides and other classes of antibiotics observed with MDR Enterobacterales isolates, PLZ remained highly active against these isolates including AME-, ESBL-, and/or CPE-producers that cause infections in US hospitals.
into Kp 23, a wild-type clinical isolate, and KPM 20, a clinical isolate deficient in OmpK35/36 and PhoE. MICs to cefotaxime/tazobactam, cefotaxime, cefazidime, ceftazidime, and meropenem were determined by E-test. Kp 23 and KPM 20 were characterized by Western blot and whole genome sequencing.

**Results.** Production of CMY-2 alone led to a resistant phenotype for cefotaxime/tazobactam, cefotaxime, and ceftazidime regardless of porin production (Figure 1). CMY-2 production in KPM 20 resulted in non-susceptibility to meropenem. Both clones were susceptible to ceftazidime. Production of CTX-M-14 and CTX-M-15 in Kp 23 resulted in only ceftazidime resistance. Production of CTX-M-14 and CTX- M-15 in KPM 20 resulted in non-susceptibility to all subsets.

Figure 1. MICs of K. pneumoniae clones against panel of β-lactam antibiotics.

**Conclusion.** When evaluating clinical isolates, it is impossible to determine the contribution of individual resistance mechanisms in the susceptibility pattern. This study demonstrated that resistance is not solely dependent on the β-lactamase produced and that the impact of porin deficiency varies with the antibiotic being evaluated. These data suggest that antibiotic selection may be more nuanced and that a broader range of therapeutic agents may be available given the appropriate diagnostic tools. Understanding the contributions of all resistance mechanisms is necessary to inform selection of the most appropriate antibiotic therapy.

**Disclosures.** Nancy D. Hanson, PhD, Merck

**1231. In Vitro Activity of Aztreonam-AVibatam and Comparator Agents Against Enterobacteriaceae from Patients with Lower Respiratory Tract Infections Collected During the ATLAS Global Surveillance Program, 2017-2019**

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

**Background.** β-lactamase-producing Enterobacteriaceae (Ebach) frequently co-carry resistance to antimicrobials from other classes, limiting treatment options. Avibactam (AVI) inhibits class A, C, and class D serine β-lactamases, while aztreonam (ATM) is refractory to hydrolysis by class B metallo-β-lactamases (MBLs). ATM-AVI is being developed for use against drug-resistant isolates of Ebact, especially those co-producing MBLs and serine β-lactamases. This study evaluated the in vitro activity of ATM-AVI and comparators against Ebact collected in 2017-2019 from patients with lower respiratory tract infections (LRTI) as part of the Antimicrobial Testing Leadership and Surveillance (ATLAS) program.

**Methods.** Non-duplicate clinical isolates were collected in 52 countries in Europe, Latin America, Asia/Pacific (excluding mainland China and India), and Middle East/Africa. Susceptibility testing was performed by CLSI broth microdilution and CFDC testing used iron-depleted media. CLSI/FDA breakpoints were used. Isolates displaying MIC values ≥4 µg/mL for imipenem (except for P. mirabilis, P. penneri and indole-positive Proteus) or meropenem (MER) were subjected to genome sequencing and screening of β-lactamase genes.

**Results.** A total of 36 (0.9%) CRE were detected, and represented mostly by isolates of P. aeruginosa (75.0%; 27/36, Table 1). A small number of ENT (11.1%; 4/36) carried other carbapenemase genes (1 each of blaKPC, blaNDM-1, and blaOXACA). Whereas 80.9% (29/36) of CRE were non-susceptible to all antibiotics tested, 19.1% (7/36) were susceptible to ≥1 antibiotic.

**Table 1. Activity of ATM-AVI and Comparator Agents against Molecularly Characterized Carbapenem-resistant Isolates COLlected in 2017-2019 from Patients with Lower Respiratory Tract Infections (LRTI) as Part of the SENTRY Antimicrobial Surveillance Program in the USA.**

**Conclusion.** The in vitro activity of ATM-AVI warrants further development of this combination for treatment of LRTI caused by drug-resistant Ebact.

**Disclosures.** Sibylle Lob, PhD, IHMA (Employee)/Pfizer, Inc. (Independent Contractor) Krystyna Kazmierczak, PhD, IHMA (Employee)/Pfizer, Inc. (Independent Contractor) Francis Arhin, PhD, Pfizer, Inc. (Employee) Daniel F. Sahn, PhD, IHMA (Employee)/Pfizer, Inc. (Independent Contractor)

**1232. In Vitro Activity of Cefiderocol and Comparator Agents Against Molecularly Characterized Carbapenem-resistant Enterobacteriaceae Clinical Isolates Causing Infection in United States Hospitals (2020)**

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

**Background.** Cefiderocol (CFDC) represents a new addition to the antimicrobial armamentarium with broad activity against Gram-negative bacteria (GNB). CFDC remains stable to hydrolysis in the presence of serine β-lactamases (ESBLs, KPC and OXA-type carbapenemases) and metallo-β-lactamases. The CFDC and comparator activities were analyzed against Enterobacteriaceae (ENT), including molecularly characterized carbapenem-resistant isolates (CRE), as a part of the SENTRY Antimicrobial Surveillance Program in the USA.

**Methods.** 4,053 ENT were collected from 31 sites in 2020. Susceptibility testing was performed by broth microdilution and CFDC testing used iron-depleted media. CLSI/FDA breakpoints were used. Isolates displaying MIC values ≥2 µg/mL for imipenem (except for P. mirabilis, P. penneri and indole-positive Proteus) or meropenem (MER) were subjected to genome sequencing and screening of β-lactamase genes.

**Results.** A total of 36 (0.9%) CRE were detected, and represented mostly by isolates of P. aeruginosa (75.0%; 27/36, Table 1). A small number of ENT (11.1%; 4/36) carried other carbapenemase genes (1 each of blaKPC, blaNDM-1, and blaOXACA). Whereas 80.9% (29/36) of CRE were non-susceptible to all antibiotics tested, 19.1% (7/36) were susceptible to ≥1 antibiotic.