into Kp 23, a wild-type clinical isolate, and KPM 20, a clinical isolate deficient in OmpK35/36 and PhoE. MICs to cefotaxime/tazobactam, ceftazidime, ceftriaxone, cefepime, 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, ceftazidime, and ceftriaxone regardless of porin production (Figure 1). CMY-2 production in KPM 20 resulted in non-susceptibility to meropenem. Both clones were susceptible to cepfuncillin. 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 all non-susceptibility to all isolates.

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 therapeutics 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.

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1231. In Vitro Activity of Aztreonam-Avibactam 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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**Background.** β-lactamase-producing Enterobacteriaceae (Ebot) frequently co-carry resistance to antimicrobials from other classes, limiting treatment options. Avibactam (AVI) inhibits class A, class 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 Enterobacteriaceae, especially those co-producing MBLs and serine β-lactamases. This study evaluated the in vitro activity of ATM-AVI and comparators against Ebot collected in 2017-2019 from patients with lower respiratory tract infections (LRTI) as part of the Antimicrobial Surveillance Program in the USA.

**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 using iron-depleted media. CLSI/FDA breakpoints were used. Isolates displaying MIC values ≤2 µg/mL for imipenem (excluding 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 determined and represented by isolates carrying blacarbapenemase-1 (75.0%; 27/36; Table). A small number of ENT (11.1%; 4/36) carried other carbapenemase genes (1 each of blactB, blaslb, blasla, and blaslb), whereas 13.9% (5/36) of isolates did not carry any known carbapenemases. CFDC (99.8% susceptible [S]), imipenem-relebactam (IMR; 99.7-99.9%S), meropenem-velbesibactam (VBL; 99.9-100%S), ATM-AVI (CZA; 99.8-100%S), and MER (99.9-100%S) were active against all ENT and the non-CRE subset. CFDC (MIC<sub>90</sub> 0.54 µg/mL; 97.2%S) and CZA (MIC<sub>90</sub> 1/8 µg/mL; 94.4%S) were the most active agents against CRE, whereas CFDC, IMR, MEV and CZA were active (100%) against the KPC subset. Finally, CFDC (MIC<sub>90</sub> 0.54-µg/mL; 100%S) was the most active agent against CRE inhibitory activity other than blacarbapenemase and blaslb, whereas CZA (1-8 µg/mL; 100%) was most active with CRE against no known carbapenemases, followed by CFDC (0.5-8 µg/mL; 80.0%).

**Conclusion.** The CFDC activity was consistent, regardless of phenotypes or genotypes, including against isolates carrying genes other than blacarbapenemase, where approved β-lactam/β-lactamase inhibitor combinations showed limited activity. These data confirm CFDC as an important option for the treatment of infections caused by ENT and resistant subsets.

**Table**

| MIC (µg/mL) | Cefiderocol | Comparator 1 | Comparator 2 | Comparator 3 |
|------------|-------------|---------------|---------------|--------------|
| Enterobacteriaceae | 2 | 4 | 8 | 16 |
| Enterococcus faecalis | 2 | 4 | 8 | 16 |
| Staphylococcus aureus | 2 | 4 | 8 | 16 |

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