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2125. Activity of Novel β-Lactam/β-Lactamase Inhibitor Combinations against Serine-Carbapenemase producing Carbapenem-Resistant Pseudomonas aeruginosa
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Background. Antimicrobial resistance in Pseudomonas aeruginosa is complex and multifaceted. While the novel β-lactamase inhibitors (BLI), avibactam, relebactam, and vaborbactam inhibit serine-based β-lactamases, the comparative potency of the novel β-lactam (BL)/BLI combinations against serine-carbapenemase producing P. aeruginosa is unknown. The present study sought to compare the in vitro activity of ceftazidime/avibactam, ceftazidime, imipenem/relebactam, imipenem, meropenem/vaborbactam, and meropenem against serine-β-lactamase producing P. aeruginosa.

Methods. Carbapenem-resistant P. aeruginosa were collated through the Enhancing Rational Antimicrobials against Carbapenem-resistant P. aeruginosa (ERACE-PA) Global Surveillance. Isolates positive for serine-based carbapenemases were assessed. Minimum inhibitory concentrations (MICs) were determined by broth microdilution to each novel-BL/BLI and BL alone. In vitro potency was assessed by MIC50/90 and percent of isolates susceptible per CLSI guidance.

Results. GES was the most common carbapenemase identified (n=59) followed by KPC (n=8). Ceftazidime/avibactam had MIC50/MIC90 values of 4/8 mg/L and 91% of isolates were susceptible. Conversely, ceftazidime alone was active against only 3% of isolates. The MIC50/MIC90 of imipenem/relebactam were 16/>16 mg/L and 13% of all isolates were defined as susceptibility. Against the KPC-producing isolates, 38% were susceptible to imipenem/relebactam compared with 0% for imipenem. The meropenem/vaborbactam MIC50/MIC90 were >16/>16 mg/L, and 6% of isolates were susceptible which was similar to meropenem alone (MIC50/90, >8/>8 mg/L; 3% susceptible) suggesting the addition of vaborbactam cannot overcome co-expressed, non-enzymatic resistance mechanisms.

Conclusion. Among the novel BL/BLIs, ceftazidime/avibactam displayed better in vitro activity and thus is a rational treatment option for serine-carbapenemase harboring P. aeruginosa. While imipenem/relebactam displayed some activity particularly against isolates with blabKPC, meropenem/vaborbactam exhibited poor activity with MICs similar to meropenem alone. These data can be integrated with rapid molecular diagnostics to guide empiric therapy.