### Results

The MIC distributions of C/T and CAZ/AVI against 1,138 *P. aeruginosa* isolates are shown below. The mode MIC value for C/T was 22 doubling dilutions lower than that for CAZ/AVI, and it was 23 dilutions lower than the C/T CLSI susceptible breakpoint, whereas the modal MIC value for CAZ/AVI was 2 dilutions lower than its susceptible breakpoint. Among all *P. aeruginosa* isolates, percentages of susceptibility were 96.6% (1,088/1,138) (C/T), 76.6% (CAZ/AVI), 67.0% (imipenem [IMI]), 74.0% (meropenem [MEM]), 71.5% (piperacillin–tazobactam [TZP]), and 64.9% (aztreonam). Among subsets of nonsusceptible isolates, susceptibilities to C/T and CAZ/AVI were 83.5% and 74.4%, respectively (CAZ/NS subset, *n* = 266), 91.0% and 85.1% (IMI-NS, *n* = 296), 87.5% and 80.1% (MEM-NS, *n* = 296), 87.0% and 79.6% (TZP-NS, *n* = 324), and 72.4% and 57.8% among isolates nonsusceptible to all tested β-lactams (*n* = 11).

**Conclusion.** The activity of C/T exceeded that of CAZ/AVI and other tested comparators against a recent collection of clinical isolates of *P. aeruginosa*, including subsets of isolates nonsusceptible to other β-lactams. Susceptibilities to C/T were 6–14 percentage points higher than observed for CAZ/AVI among β-lactam-NS subsets. C/T promises to be an important treatment option for patients with antimicrobial-resistant *P. aeruginosa* infections.

### Table 1: TEAs and Postbacterial Endocarditis Changes in Patients at Risk for Cardiac Safety Concerns

| Patients with history of hypertension, n (%) | LEF (n=246) | MOX (n=292) |
|---------------------------------------------|-------------|-------------|
| TEAs in cardiac SCC | 8.0 (3.3) | 8.6 (3.2) |
| TEAs in QT prolongation category | 1.0 (4.0) | 4.1 (6.2) |
| Patient baseline and postbacterial values of QTcF | 215 (88.8) | 223 (88.8) |
| Increase in QTcF | 45 (16.4) | 57 (22.7) |
| Increase in QTcF | 4.1 (6.3) | 9.3 (6.3) |
| Value QTcF >480 msec | 10 (4.1) | 9 (3.6) |
| Value QTcF >500 msec | 10 (4.1) | 2 (0.8) |
| Baseline QTcF >480 msec and postbacterial QTcF >480 msec | 9 (3.7) | 7 (2.6) |
| Baseline QTcF >500 msec and postbacterial QTcF >500 msec | 1 (0.4) | 2 (0.7) |

### Table 2: Nephrotobitory TEAs and Postbacterial Liver Enzyme Changes in Patients at Risk for Hepatic Safety Concerns

| Patients with baseline liver enzyme elevation (AST or ALT >ULN) | LEF (n=119) | MOX (n=144) |
|-------------------------------------------------------------|-------------|-------------|
| TEAs in nephrotobitory SCC | 10.0 (3.8) | 9.7 (4.3) |
| n (%) | 2 (1.7) | 2 (1.4) |
| Any postbacterial value, n (%) | 3 (2.5) | 3 (2.1) |
| AST > ULN | 234 (88.2) | 234 (86.3) |
| In QTcF | 52 (15.0) | 49 (16.9) |
| Increase in QTcF | 4.1 (7.2) | 6 (6.2) |
| Value QTcF >480 msec | 11 (4.1) | 14 (3.5) |
| Value QTcF >500 msec | 10 (4.1) | 6 (1.5) |
| Baseline QTcF >480 msec and postbacterial QTcF >480 msec | 10 (3.6) | 10 (4.0) |
| Baseline QTcF >500 msec and postbacterial QTcF >500 msec | 1 (0.4) | 1 (0.1) |

### Table 3: Patients aged 266 y, n (%) with C/T and CAZ/AVI

| Patients aged 266 y with postbacterial values, n (%) | C/T | CAZ/AVI |
|----------------------------------------------------|-----|--------|
| n (%) | 2 (1.7) | 2 (1.4) |
| Any postbacterial value, n (%) | 3 (2.5) | 3 (2.1) |
| AST > ULN | 11 (9.0) | 22 (15.3) |
| ALT > ULN | 30 (25.1) | 40 (28.5) |
| ALT > ULN | 1020 (4.0) | 1024 (4.0) |
| ALT > ULN | 5000 (23.4) | 1020 (4.0) |
| ALT > ULN | 1020 (4.0) | 1024 (4.0) |
| Total bilirubin value > ULN | 1502 (12.0) | 1504 (12.0) |
| ALT > AST + 3 ULN and total bilirubin value > 2 ULN | 1505 (12.5) | 1506 (12.5) |

### Discussion

All authors: No reported disclosures.

### 719. Cefiderocol Retains Anti-Biofilm Activity in MDR Gram-Negative Pathogens

Christine A. Pybus, MS;1 David E. Greenberg, MD;1 UT Southwest Medical Center, Dallas, Texas; 2UT Southwest Medical Center, Dallas, Texas

**Session:** 68: Novel Antimicrobials and Approaches Against Resistant Bugs

**Thursday, October 3, 2019: 12:15 PM**

**Background.** Cefiderocol is a siderophore cephalosporin with potent antibacterial activity against a broad range of Gram-negative pathogens. Microorganisms form biofilms, e.g., cUTI, utilize bacterial siderophores to access free iron. A siderophore antibiotic may have unique antimicrobial properties in the setting of biofilm. In this study, we compared antimicrobial activity of cefiderocol to comparator antibiotics in well-characterized multi-drug-resistant pathogens. We determined the activity of cefiderocol and comparator antibiotics in the biofilm setting.

### Methods

Minimum inhibitory concentrations (MICs) in Mueller–Hinton II broth (MHII) and iron-depleted cation-adjusted MHII (ID-CAMHB) were measured. Among subsets of nonsusceptible isolates, susceptibilities to C/T and CAZ/AVI were 83.5% and 74.4%, respectively (CAZ/NS subset, *n* = 266), 91.0% and 85.1% (IMI-NS, *n* = 296), 87.5% and 80.1% (MEM-NS, *n* = 296), 87.0% and 79.6% (TZP-NS, *n* = 324), and 72.4% and 57.8% among isolates nonsusceptible to all tested β-lactams (*n* = 11).

**Conclusion.** The activity of C/T exceeded that of CAZ/AVI and other tested comparators against a recent collection of clinical isolates of *P. aeruginosa*, including subsets of isolates nonsusceptible to other β-lactams. Susceptibilities to C/T were 6–14 percentage points higher than observed for CAZ/AVI among β-lactam-NS subsets. C/T promises to be an important treatment option for patients with antimicrobial-resistant *P. aeruginosa* infections.

### Disclosures

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### Methods

Minimum inhibitory concentrations (MICs) in Mueller–Hinton II broth (MHII) and iron-depleted cation-adjusted MHII (ID-CAMHB) were measured for cefiderocol and seven comparator antibiotics in multidrug-resistant isolates of *P. aeruginosa*, *Burkholderia cepacia* complex (Bcc), *Klebsiella pneumoniae*, *Escherichia coli*, and *Acinetobacter baumannii*. MBC (minimum biofilm eradication concentration) assays were used to test cefiderocol’s activity in biofilms formed on pegs. Total biofilm biomass and viable cell number were measured.

### Results

The MIC<sub>90</sub> of cefiderocol ranged from 0.125 μg/mL (Bcc) to 1 μg/mL (P. aeruginosa) in ID-CAMHB. MIC<sub>90</sub> values were consistently lower for cefiderocol in all strains tested compared with other agents (cefotaxime–tobramycin, cefidazime–arvabactam, cefazidime, piperacillin–tazobactam, imipenem–ciprofloxacin, clarithromycin, meropenem–rifampin, meropenem). Among subsets of nonsusceptible isolates, susceptibilities to C/T and CAZ/AVI were 83.5% and 74.4%, respectively (CAZ/NS subset, *n* = 266), 91.0% and 85.1% (IMI-NS, *n* = 296), 87.5% and 80.1% (MEM-NS, *n* = 296), 87.0% and 79.6% (TZP-NS, *n* = 324), and 72.4% and 57.8% among isolates nonsusceptible to all tested β-lactams (*n* = 11).

**Conclusion.** Cefiderocol effectively reduces biofilm in multidrug-resistant strains of *P. aeruginosa* and is a potent inhibitor of planktonic growth across a range of Gram-negative medically important pathogens.

### Disclosures

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