Methods. A total of 2831 Carb-NS GN respiratory isolates collected from 2014 to 2017 were tested centrally (IHMA, Inc., Schaumburg, IL). Minimum inhibitory concentrations (MICs) were determined for CFDC, cefepime (FEP), ceftazidime–avibactam (CZA), ceftolozane-tazobactam (C/T), ciprofloxacin (CIP), colistin (CST), and meropenem (MEM) by broth microdilution and interpreted according to the 2018 CLSI guidelines. CFDC MICs were tested in iron-depleted and iron-replete Mueller–Hinton broth, and interpretive according to the 2018 CLSI provisional breakpoints. Carb-NS strains were defined as MEM of ≤ 4 µg/mL for Enterobacteriaceae (ENB) and ≤ 2 µg/mL for nonfermenters (NF).

Results. CFDC exhibited predictable in vitro activity against 2807 clinically relevant Carb-NS GN isolates (214 ENB, 1066 P. aeruginosa, 794 S. maltophilia, and 20 Burkholderia cepacia) isolated from respiratory infections. CFDC was the most active agent against Carb-NS ENB with 97.7% susceptibility followed by 78.0% CZA, 59.4% CST, and 16.6% CIP. Against Carb-NS P. aeruginosa complex, CFDC demonstrated 94% susceptibility vs. 97% for C/T. CFDC was the most active agent against Carb-NS P. aeruginosa with 99.9% susceptibility followed by 97.8% CST, 77.6% C/T, and 77.5% CZA. 99.7% of S. maltophilia and 100% of B. cepacia isolates had CFDC MICs of ≤ 4 µg/mL. The MIC₅₀ of tested compounds for clinically relevant pathogens are shown in the table.

Conclusion. In a multinational collection of Carb-NS GN respiratory isolates, CFDC demonstrated potent in vitro activity with MIC₅₀ of ≤ 4 µg/mL for all clinically relevant ENB and NF. These findings suggest that CFDC can be a potential option for the treatment of respiratory infections caused by Carb-NS ENB, A. baumannii complex, P. aeruginosa, S. maltophilia, and B. cepacia.

Disclosures. All authors: No reported disclosures.

2014–2017

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Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs Thursday, October 3, 2019: 12:15 PM

Background. Avibactam (AVI) is a β-lactamase inhibitor with potent inhibitory activity against Class A, Class C, and some Class D serine β-lactamases. The combination of ceftazidime (CAZ) with AVI has been approved in Europe and in the United States for several indications. This study evaluated the in vitro activity of CAZ-AVI and comparators against Enterobacteriaceae (Ebs) and Pseudomonas aeruginosa (Pae) isolates collected from patients with bloodstream infections as part of the ATLAS surveillance program in 2014–2017.

Methods. A total of 53416 Ebs and 15050 Pae non-duplicate clinically significant isolates, including 5155 Ebs and 845 Pae isolated from bloodstream infections, were collected by 167 hospital laboratories in 36 countries in Europe, Latin America, Asia, Pacific (excluding China), and the Middle East/Africa region. Susceptibility testing was performed by CLSI broth microdilution. CAZ-AVI was tested at a fixed concentration of 4 µg/mL. AVI meropenem–non-susceptible (MEM-NS) Ebs and Pae isolates were screened for the presence of β-lactamase genes.

Results. Susceptibility data are shown in the Table. Percentages of susceptibility (% S) to the tested agents were 0.2–2.8% lower among Ebs and Pae from bloodstream infections compared with isolates from combined sources in most cases. CAZ-AVI showed potent in vitro activity against all Ebs bloodstream isolates and subsets of CAZ-Ns and colistin-resistant (CST-R) isolates (MIC₅₀ 0.5–2 µg/mL, 96.0–100% S). Reduced activity against MEM-NS Ebs was attributable to carriage of class B metallo-β-lactamases (MBLs) because all MEM-NS MBL-negative isolates were susceptible to CAZ-AVI. CAZ-AVI also showed good in vitro activity against the majority of Pae bloodstream isolates (MIC₅₀ 16 µg/mL, 89.5% S). Activity was reduced against CAZ-Ns, MEM-NS, and CST-R subsets (53.7–85.0% S), which included isolates carrying MBLs, but exceeded the activity of CAZ and MEM against these subsets by 15–63%. CST- and AMK susceptible were the only tested comparators that demonstrated comparable or greater activity against Pae bloodstream isolates.

Conclusion. CAZ-AVI provides a valuable therapeutic option for treating bloodstream infections caused by MBL-negative Ebs and Pae isolates.

694. In vitro Antibacterial Activity of Sulbactam–Durbactam (ETX2514SUL) Against 121 Recent Acinetobacter baumannii Isolated From Patients in India Alita Miller, PhD1; Sarah McLeod, PhD2; Tarun Mathur, PhD3; Ian Morrisey1; 1Entasis Therapeutics, Waltham, Massachusetts; 2IHMA Inc., Gurugram, Haryana, India; 3IHMA Europe, Monthey; Valais, Switzerland

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Background. The incidence of infections caused by multidrug-resistant Acinetobacter baumannii is increasing at alarming rates in Southeast Asia and other parts of the world. Sulbactam (SUL) has intrinsic antibacterial activity against A. baumannii; however, the prevalence of β-lactamases in this species has limited its therapeutic use. Durbactam (ETX2514, DUR) is a novel β-lactamase inhibitor with broad-spectrum activity against Ambler classes A, C, and D β-lactamases. DUR restores SUL in vitro activity against multidrug-resistant A. baumannii. Against >3,600 globally diverse, clinical isolates from 2012–2017, addition of 4 µg/mL DUR reduced the SUL MIC₉₀ from >32 to 2 µg/mL. SUL-DUR is currently in Phase 3 clinical development for the treatment of infections caused by multidrug-resistant Acinetobacter spp.
The goal of this study was to determine the activity of SUL-DUR and comparator antibiotics (amikacin (AMK), ampicillin-sulbactam (AMP-SUL), cefoperazone-sulbactam (CFS-SUL), and meropenem (MEM)) against A. baumannii isolated from hospitalized patients in India.

Methods. A total of 121 clinical A. baumannii isolates from multiple hospital settings and infection sources were collected between 2016–2019 from six geographically diverse hospitals in India. Species identification was performed by MALDI-TOF. Susceptibility of these isolates to SUL-DUR (10µg/10µg) and comparator antibiotics was determined by disk diffusion using CLSI methodology and interpretive criteria, except for CFS-SUL, for which resistance was defined using breakpoints from the CFS-SUL package insert.

Results. As shown in Table 1, resistance of this collection of isolates to marketed agents was extremely high. In contrast, based on preliminary breakpoint criteria, only 11.5% of isolates were resistant to SUL-DUR.

Conclusion. The in vitro antibacterial activity of SUL-DUR was significantly more potent than comparator agents against multidrug-resistant A. baumannii isolates collected from diverse sites in India. These data support the continued development of SUL-DUR for the treatment of antibiotic-resistant infections caused by A. baumannii.

Table 1. Percent Resistant A. baumannii (% N = 121)

| Antibiotic | SUL-DUR | AMP-SUL | MEM | AMK | CFS-SUL |
|-----------|---------|---------|-----|-----|---------|
| 11.5%     | 99.0%   | 95.9%   | 88.4% | 79.3% |

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695. Activity of Imipenem–Relebactam and Ceftolozane–Tazobactam Against a Contemporary Collection of Gram-Negative Bacteria from New York City Alejandro Iregui, MD; Zeb Khan, MD; David Landman, MD; John M. Quale, MD; SUNY Downstate Medical Center, Brooklyn, New York

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Background. Carbapenem-resistant Gram-negative bacteria are important nosocomial pathogens, and therapeutic options are often limited.

Methods. Clinical isolates were gathered during a surveillance study in 2017 involving 7 hospitals in Brooklyn, NY. Isolates underwent susceptibility testing using the agar dilution method; for the combination of imipenem-relebactam and ceftolozane-tazobactam, the concentration and ratios of relebactam to tazobactam were fixed at 4 µg/mL. Breakpoints were defined according to CLSI criteria; for imipenem-relebactam, the breakpoint of imipenem was utilized. Isolates were screened by PCR for common carbapenemases.

Results. Overall susceptibility patterns are given in the Table. Of 1805 isolates of E. coli (including 4 with blaKPC), 100% were susceptible to imipenem and imipenem-relebactam. Of 503 isolates of K. pneumoniae (including 19 isolates with bladur), all were susceptible to imipenem-relebactam. Of 171 isolates of Enterobacter spp. (including 3 with bladur), 100% were susceptible to imipenem-relebactam. Of 260 isolates of P. aeruginosa, 96% were susceptible to imipenem-relebactam and nearly all to ceftolozane-tazobactam. Against A. baumannii, the activity of imipenem-relebactam was the same as imipenem and the ceftolozane-tazobactam MIC was ≤ 4 µg/mL in 65% of isolates.

Conclusion. Imipenem-relebactam possesses promising activity against multidrug-resistant Enterobacteriaceae endemic to New York City. Ceftolozane-tazobactam demonstrated excellent activity against P. aeruginosa, including isolates resistant to carbapenems.

Table 1

| Organism | Source | Carbapenem Activity | Imipenem–relebactam | Ceftolozane–Tazobactam |
|----------|--------|---------------------|----------------------|------------------------|
| E. coli (includes 4 with bladur) | 100% | 100% | 100% |
| K. pneumoniae (including 19 isolates with bladur) | All | 100% | 100% |
| Enterobacter spp. (including 3 with bladur) | 100% | 100% | 100% |
| P. aeruginosa | 96% | 96% | 96% |

Disclosures. All authors: No reported disclosures.