

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 (MIC) 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 cation-adjusted Mueller-Hinton broth, and interpreted according to the 2018 CLSI provisional breakpoints. Carb-NS strains were defined as MEM MIC of ≥ 2 $\mu\text{g/mL}$ for Enterobacteriaceae (ENB) and of ≥ 4 $\mu\text{g/mL}$ for nonfermenters (NF).

Results. CFDC exhibited predictable *in vitro* activity against 2807 clinically relevant Carb-NS GN isolates (214 ENB, 1086 *A. baumannii* complex, 693 *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 16.4% CIP. Against Carb-NS *A. baumannii* complex, CFDC demonstrated 94% susceptibility vs. 83.7% for CST. 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 $\mu\text{g/mL}$. The MIC₉₀ 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 MIC₉₀ of ≤ 4 $\mu\text{g/mL}$ 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*.

Organism	N	MIC ₉₀ ($\mu\text{g/mL}$)						
		CFDC	FEP	CZA	C/T	CIP	CST	MEM
Enterobacteriaceae	214	4	>64	>64	>64	>8	>8	>64
<i>P. aeruginosa</i>	693	1	64	64	>64	>8	2	64
<i>A. baumannii</i> complex	1086	2	>64	>64	>64	>8	>8	>64
<i>S. maltophilia</i>	794	0.25	>64	>64	>64	8	8	NA
<i>B. cepacia</i>	20	0.5	>64	32	>64	>8	NA	16

Disclosures. All authors: No reported disclosures.

693. In Vitro Activity of Ceftazidime-Avibactam and Comparator Agents Against Enterobacteriaceae and Pseudomonas aeruginosa Collected From Patients with Bloodstream Infections as Part of the ATLAS Global Surveillance Program, 2014–2017

Krystyna Kazmierczak, PhD¹; Gregory Stone, PhD²; Daniel F. Sahn, PhD¹; IHMA, Inc., Schaumburg, Illinois; ²Pfizer, Inc., Groton, Connecticut

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 (*Eba*) 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 *Eba* and 15050 *Pae* nonduplicate clinically significant isolates, including 5155 *Eba* 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 $\mu\text{g/mL}$ AVI. Meropenem-nonsusceptible (MEM-NS) *Eba* 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 *Eba* and *Pae* from bloodstream infections compared with isolates from combined sources in most cases. CAZ-AVI showed potent *in vitro* activity against all *Eba* bloodstream isolates and subsets of CAZ-NS and colistin-resistant (CST-R) isolates (MIC₉₀, 0.5–2 $\mu\text{g/mL}$, 96.0–100% S). Reduced activity against MEM-NS *Eba* 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 (MIC₉₀, 16 $\mu\text{g/mL}$, 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 15–65%. CST and amikacin 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 *Eba* and *Pae* isolates.

Source	Organism/Phenotype (n)	Drug (MIC ₉₀ [$\mu\text{g}/\text{mL}$] % S) susceptible									
		CAZ-AVI MIC ₉₀ % S	CAZ MIC ₉₀ % S	MEM MIC ₉₀ % S	AMK MIC ₉₀ % S	CST MIC ₉₀ % S					
All	Enterobacteriaceae, All (53416)	0.5 99.1	64 75.4	0.12 96.2	8 97.1	>4 83.2					
	All (5155)	0.5 98.9	64 72.6	0.12 94.9	8 96.7	>4 87.5					
	CAZ-NS (1413)	1 96.0	>128 0.0	>8 82.1	32 89.6	2 90.5					
	MEM-NS (262)	>128 78.6	>128 3.4	>8 0.0	>32 67.6	>4 72.9					
	MEM-NS, MBL-negative (206)	2 100	>128 4.4	>8 0.0	>32 71.4	>4 72.8					
	CST-R (1407)	2 98.6	>128 55.0	>8 60.7	32 86.0	>4 0.0					
Blood	<i>P. aeruginosa</i> , All (15050)	8 91.2	64 78.1	>8 72.7	32 89.8	2 97.1					
	All (845)	16 89.5	64 77.3	>8 70.5	32 87.9	2 97.6					
	CAZ-NS (192)	128 53.7	>128 0.0	>8 23.4	>32 56.8	2 96.9					
	MEM-NS (249)	128 65.5	>128 41.0	>8 0.0	>32 63.9	2 96.8					
	MEM-NS, MBL-negative (201)	32 80.6	>128 50.3	>8 0.0	>32 74.6	2 96.5					
	CST-R (29)	32 85.0	32 70.9	>8 60.0	>32 80.0	4 0.0					

CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; AMK, amikacin; CST, colistin; NS, non-susceptible; R, resistant; MBL, metallo- β -lactamase. % Susceptible was determined using CLSI 2019 breakpoints.
*Excludes isolates of Protease and Serratia spp., which are intrinsically resistant.

Disclosures. All authors: No reported disclosures.

694. In vitro Antibacterial Activity of Sulbactam-Durlobactam (ETX2514SUL) Against 121 Recent Acinetobacter baumannii Isolated from Patients in India
Alita Miller, PhD¹; Sarah McLeod, PhD¹; Tarun Mathur, PhD²; Ian Morrissey³; ¹Entasis Therapeutics, Waltham, Massachusetts; ²IHMA Inc., Gurugram, Haryana, India; ³IHMA Europe, Monthey, Valais, Switzerland

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

Background. The incidence of infections caused by multidrug-resistant *Acinetobacter baumannii* is increasing at an alarming rate 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. Durlobactam (ETX2514, DUR) is a novel β -lactamase inhibitor with broad-spectrum activity against Ambler class 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 mg/L DUR reduced the SUL MIC₉₀ from >32 to 2 mg/L. SUL-DUR is currently in Phase 3 clinical development for the treatment of infections caused by carbapenem-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), ceftoperazone-sulbactam (CFP-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 (10 $\mu\text{g}/10\mu\text{g}$) and comparator antibiotics was determined by disk diffusion using CLSI methodology and interpretive criteria, except for CFP-SUL, for which resistance was defined using breakpoints from the CFP-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)

SUL-DUR	AMP-SUL	MEM	AMK	CFP-SUL
11.5%	90.9%	95.9%	88.4%	79.3%

Disclosures. All authors: No reported disclosures.

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

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

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 concentrations of relebactam and tazobactam were fixed at 4 $\mu\text{g/mL}$. 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 bla_{KPC}), 100% were susceptible to imipenem and imipenem-relebactam. Of 503 isolates of *K. pneumoniae* (including 19 isolates with bla_{KPC}), all were susceptible to imipenem-relebactam. Of 171 isolates of *Enterobacter* spp. (including 3 with bla_{KPC}), 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 $\mu\text{g/mL}$ 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.

	MIC ₅₀	MIC ₉₀	Range	Susceptible (%)
	$\mu\text{g}/\text{mL}$	$\mu\text{g}/\text{mL}$		
<i>E. coli</i> (n=1805)				
Imipenem	0.25	0.25	≤ 0.12 - 4	100%
Imipenem/relebactam	0.125/4	0.25/4	$\leq 0.125/4$ - 0.5/4	100%
Ceftolozane/tazobactam	$\leq 0.25/4$	$\leq 0.25/4$	$\leq 0.25/4$ - >16/4	99.8%
Piperacillin/tazobactam	2/4	4/4	$\leq 0.25/4$ - >128/4	98.8%
<i>K. pneumoniae</i> (n=503)				
Imipenem	0.25	0.5	≤ 0.12 - >4	96%
Imipenem/relebactam	0.25/4	0.25/4	$\leq 0.125/4$ - 0.5/4	100%
Ceftolozane/tazobactam	1/4	1/4	$\leq 0.25/4$ - >16/4	96%
Piperacillin/tazobactam	4/4	8/4	$\leq 0.25/4$ - >128/4	96%
<i>P. aeruginosa</i> (n=260)				
Imipenem	0.5	1	≤ 0.12 - >4	98%
Imipenem/relebactam	0.25/4	0.5/4	0.08/4 - 0.5/4	100%
Ceftolozane/tazobactam	0.5/4	2/4	$\leq 0.25/4$ - >16/4	92%
Piperacillin/tazobactam	4/4	32/4	1/4 - >128/4	89%
<i>A. baumannii</i> (n=49)				
Imipenem	0.5	>4	0.25 - >4	61%
Imipenem/relebactam	0.5/4	>4/4	0.125/4 - >4/4	62%
Ceftolozane/tazobactam	1/4	16/4	$\leq 0.25/4$ - >16/4	65%
Piperacillin/tazobactam	32/4	>128/4	$\leq 0.25/4$ - >128/4	45%

Disclosures. All authors: No reported disclosures.