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 µg/mL for Enterobacteriaceae (ENB) and of ≥4 µg/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 µg/mL. The MIC_{90}s 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 MIC_{90} 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*.

Table.

	MIC_{90} (µg/mL)							
Organism	**N**	**CFDC**	**FEP**	**CZA**	**C/T**	**CIP**	**CST**	**MEM**
Enterobacteriaceae	214	4	>64	>64	>64	>8	>8	>64
P. aeruginosa	693	1	64	64	>64	>8	2	64
***A. baumannii* complex**	1086	2	>64	>64	>64	>8	>8	>64
S. maltophilia	794	0.25	>64	>64	>64	8	8	NA
B. cepacia	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

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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 µg/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 (MIC_{90}, 0.5–2 µg/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 (MIC_{90}, 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 15–65%. 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} [µg/ml]/% Susceptible)									
		CAZ-AVI		CAZ		MEM		AMK		CST	
		MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S
All	*Enterobacteriaceae*, All (53416)	0.5	99.1	64	75.4	0.12	96.2	8	97.1	>4	83.2
Blood	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 (140)[a]	2	98.6	>128	35.0	>8	60.7	32	85.0	>4	0.0
All	*P. aeruginosa*, All (15050)	8	91.2	64	76.1	>8	72.7	32	89.8	2	97.1
Blood	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 (20)	32	85.0	32	70.0	>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 determine using CLSI 2019 breakpoints.
[a]Excludes isolates of Proteeae 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

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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 MIC_{90} 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), cefoperazone-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 (10µg/10µg) 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

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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 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 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 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.

	MIC50	MIC90	Range	Susceptible (%)
	µg/ml			
E. coli (n=1805)				
Imipenem	0.25	0.25	≤ 0.12 - 1	100%
Imipenem/relebactam	0.125/4	0.25/4	≤ 0.015/4 – 0.5/4	100%
Ceftolozane/tazobactam	≤ 0.25/4	≤ 0.25/4	≤ 0.25/4 – >16/4	99.8%
Piperacillin/tazobactam	2/4	4/4	≤ 0.25/4 – >128/4	98.8%
K. pneumoniae (n=503)				
Imipenem	0.25	0.5	≤ 0.12 - >4	96%
Imipenem/relebactam	0.25/4	0.25/4	≤ 0.015/4 – 0.5/4	100%
Ceftolozane/tazobactam	≤ 0.25/4	1/4	≤ 0.25/4 – >16/4	96%
Piperacillin/tazobactam	4/4	8/4	≤ 0.25/4 – >128/4	96%
Enterobacter spp. (n=171)				
Imipenem	0.5	1	≤ 0.12 - 2	98%
Imipenem/relebactam	0.25/4	0.5/4	0.06/4 – 0.5/4	100%
Ceftolozane/tazobactam	0.5/4	2/4	≤ 0.25/4 – >16/4	92%
Piperacillin/tazobactam	4/4	32/4	1/4 – >128/4	89%
P. aeruginosa (n=260)				
Imipenem	2	>4	≤ 0.12 - >4	75%
Imipenem/relebactam	0.5/4	2/4	0.03/4 – >4/4	96%
Ceftolozane/tazobactam	1/4	2/4	≤ 0.25/4 – >16/4	98.8%
Piperacillin/tazobactam	8/4	128/4	2/4 – >128/4	76%
A. baumannii (n=49)				
Imipenem	0.5	>4	0.25 - >4	61%
Imipenem/relebactam	0.5/4	>4/4	0.12/4 – >4/4	
Ceftolozane/tazobactam	1/4	16/4	≤ 0.25/4 – >16/4	
Piperacillin/tazobactam	32/4	>128/4	≤ 0.25/4 – >128/4	45%

Disclosures. **All authors:** No reported disclosures.