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Activity of Ceftazidime-Avibactam Tested Against Contemporary (2012) Pathogens from Urinary Tract and Intraabdominal Infections from Patients in the USA **RK FLAMM, HS SADER, RN JONES** JMI Laboratories, North Liberty, Iowa, USA

Abstract

Background: The investigational antimicrobial combination of ceftazidime (CAZ) and the non β -lactam β -lactamase inhibitor avibactam (AVI) is undergoing Phase III clinical development. In this report, we present the results of testing CAZ-AVI and comparators against a recent collection of pathogens from patients with urinary tract (UTI) or intraabdominal (IAI) infections.

Methods: UTI and IAI isolates (one per patient episode) were collected during 2012 at 73 USA medical centers. Isolates were processed at the medical centers and forwarded to a central laboratory for confirmatory identification and susceptibility (S) testing using CLSI methods.

Results: CAZ-AVI demonstrated potent activity against Enterobacteriaceae (ENT) isolated from both UTI and IAI (MIC₉₀, 0.25 μ g/mL for both). The most active agent against ENT for both UTI and IAI was meropenem (MER; MIC_{50/90}, ≤0.06/0.06 µg/mL, S = 98.8% and MIC_{50/90}, ≤0.06/0.06 µg/mL, S = 97.8%, respectively). ENT levofloxacin-resistance (LEV-R) was at 16.1/16.6%, respectively for UTI/IAI. The ESBLphenotype rate for *E. coli* (EC) for UTI/IAI was 8.5/10.4% and for Klebsiella spp. (KSP), 13.0/16.3%, respectively. The CAZ-AVI MIC₉₀ for ESBL-positive-phenotype EC and KSP from UTI was at 0.25 and 1 μ g/mL, respectively. From IAI, the MIC₉₀ values were at 0.5 and 2 µg/mL, respectively. The LEV-R rates among ESBL-positive EC and KSP were 70.5/69.2% for UTI and 94.1/76.5% for IAI. CAZ-AVI inhibited 98.7 and 96.3% of Pseudomonas aeruginosa (PSA) from UTI and IAI at a MIC of ≤8 µg/mL. Amikacin-, colistin- and gentamicin-S ranged from 90.3-98.1% for UTI and 92.7-97.6% for IAI. A total of 93.8% of CAZ-non-S PSA isolates from UTI and 75.0% from IAI were inhibited at a CAZ-AVI MIC value of $\leq 8 \mu g/mL$. Amikacin and colistin against CAZ-non-S PSA in UTI and amikacin, colistin and gentamicin in IAI were the only agents exhibiting S at >90.0%. Against MER-non-S PSA, 97.0 and 76.9% of UTI and IAI isolates, respectively were inhibited at a CAZ-AVI MIC value ≤8 µg/mL.

Conclusions: CAZ-AVI demonstrated potent activity against contemporary Gram-negative pathogens including multidrugresistant isolates from patients with UTI and IAI in USA hospitals. These data may support CAZ-AVI as a new treatment option in these common hospital infections.

	Urinar	y tract	Intraabdominal				
		MIC in	μg/mL				
	Ceftaz	idime-	Cefazidime-				
Organism _	avibactam/	ceftazidime	avibactam/ceftazidime				
(no. tested UTI/IAI)	MIC ₅₀	MIC ₉₀	MIC ₅₀	MIC ₉₀			
Enterobacteriaceae (2,188/410)	0.06/0.12	0.25/2	0.12/0.25	0.25/32			
<i>E. coli</i> (913/164)	0.06/0.12	0.12/0.5	0.06/0.12	0.12/1			
ESBL-positive (78/17)	0.12/8	0.25/32	0.12/16	0.5/>32			
Klebsiella spp. (501/104)	0.12/0.12	0.25/8	0.12/0.12	0.5/32			
ESBL-positive (65/17)	0.5/>32	1/>32	0.5/>32	2/>32			
Enterobacter cloacae (112/60)	0.12/0.25	0.5/>32	0.12/0.5	0.5/>32			
CAZ-non-S E. cloacae (23/20)	0.5/>32	1/>32	0.5/>32	1/>32			
P. aeruginosa (155/82)	2/2	4/16	2/2	4/32			
CAZ-non-S P. aeruginosa (16/12)	2/32	8/>32	4/32	16/>32			
MER-non-S <i>P. aeruginosa</i> (33/13)	4/4	8/>32	4/8	16/>32			

Introduction

Avibactam is an investigational non- β -lactam β -lactamase inhibitor that displays a broad-spectrum inhibition profile against both class A and class C β -lactamases, including extended spectrum β -lactamases and KPC serine-carbapenemases, as well as activity against some class D enzymes. Avibactam alone has very limited intrinsic antibacterial activity. When combined with ceftazidime, the combination has shown potent in vitro activity against Enterobacteriaceae and Pseudomonas aeruginosa including multidrug-resistant strains.

The efficacy of the combination has been shown in Phase II clinical trials for complicated urinary tract (cUTI) and complicated intraabdominal infections (cIAI). In a Phase II clinical trial in the treatment of cUTI, ceftazidime-avibactam was shown to have efficacy and safety similar to the comparator imipenem-cilastatin. In a Phase II trial for cIAI in hospitalized adults, ceftazidimeavibactam plus metronidazole was shown to be effective and well tolerated, similar to meropenem. The ceftazidime-avibactam combination is currently undergoing further clinical development in Phase 3 studies of cUTI, cIAI and nosocomial pneumonia.

The aim of this study was to evaluate the activity of ceftazidimeavibactam and comparator agents against a contemporary collection of isolates from patients with UTI and IAI in the USA (2012).

Methods

Bacterial isolates: Isolates from patients with UTI or IAI (as protocol does not specify, these may be from either complicated or uncomplicated cases; one per patient episode) were processed at 73 USA medical centers during 2012 and forwarded to a central laboratory (JMI Laboratories, North Liberty, Iowa, USA) for confirmatory identification and susceptibility testing. Only clinically significant isolates were included in the study. A total of 2,879 isolates from UTI infections and 759 from IAI were collected. Of these, 2,188 were Enterobacteriaceae from UTI and 410 from IAI. For P. aeruginosa, the isolate totals were 155 from UTI and 82 from IAI.

Antimicrobial susceptibility testing: All isolates were susceptibility tested with dry-form panels using reference broth microdilution method as described by the Clinical and Laboratory Standards Institute (CLSI). Interpretations of susceptibility for antimicrobials were those found in CLSI M100-S23 (2013) and quality control (QC) was performed using Staphylococcus aureus ATCC 29213; Enterococcus faecalis ATCC 29212; Streptococcus pneumoniae ATCC 49619; Escherichia coli ATCC 25922; and P. aeruginosa ATCC 27853. All QC results were within ranges as published in CLSI (M100-S23, 2013) documents.

Results

- The MIC₅₀ and MIC₉₀ for ceftazidime-avibactam against Enterobacteriaceae were ≤0.06 and 0.25 µg/mL for UTI isolates and 0.12/0.25 µg/mL for IAI isolates (Table 1). For UTI isolates, the susceptibility for ceftazidime, piperacillintazobactam, meropenem, and tigecycline was 91.8, 94.5, 98.8, and 97.9%, respectively. For IAI isolates, susceptibility values were 86.1, 88.5, 97.8, and 97.8%, respectively (Table 2). Levofloxacin resistance for UTI and IAI isolates was 16.1 and 16.6%, respectively (Table 2)
- In UTI, the ESBL-positive-phenotype rate for *E. coli* was 8.5% and for IAI isolates 10.4% (Table 1). For *Klebsiella* spp. the ESBL-positive-phenotype rates were more elevated, 13.0 and 16.3%, respectively (Table 1). The ceftazidime-avibactam MIC₅₀ and MIC₉₀ for ESBL-positive-phenotype *E. coli* from UTI was 0.12 and 0.25 µg/mL (Tables 1 and 2). For ESBLphenotype *E. coli* isolates from IAI, the MIC₅₀ and MIC₉₀ were similar 0.12 and 0.5 µg/mL (Tables 1 and 2). Meropenem susceptibility rates were high among ESBL-positivephenotype E. coli at 98.7/100.0% for UTI/IAI isolates (Table 2). Tigecycline susceptibility was also high at 100.0% in UTI/IAI (Table 2). Piperacillin-tazobactam and levofloxacin susceptibility were low at 80.8/26.9% in UTI and 70.6/5.9% in IAI (Table 2)
- Ceftazidime-avibactam MIC₅₀ and MIC₉₀ values for ESBL positive-phenotype Klebsiella spp. from UTI were 0.5 and 1 µg/mL (Tables 1 and 2). For ESBL-positive-phenotype Klebsiella spp. isolates from IAI, the MIC_{50} and MIC_{90} were 0.5 and 2 µg/mL (Tables 1 and 2). Tigecycline susceptibility rates were high for ESBL-positive- phenotype *Klebsiella* spp. at 96.9/100.0% for UTI/IAI isolates (Table 2), but piperacillintazobactam, meropenem, and levofloxacin susceptibility were low at 30.8/64.6/24.6% in UTI and 11.8/58.8/23.5% in IAI (Table 2)
- Ceftazidime-avibactam inhibited 98.7 and 96.3% of *P*. aeruginosa isolates from UTI and IAI at a MIC of ≤8 µg/mL (Table 1). The MIC₅₀ and MIC₉₀ for isolates from either UTI or IAI were 2 and 4 μ g/mL, respectively (Tables 1 and 2). Against meropenem-non-susceptible isolates of *P*. aeruginosa, 97.0 and 76.9% of UTI and IAI isolates, respectively were inhibited at a ceftazidime-avibactam MIC value $\leq 8 \mu g/mL$ (Table 1). A total of 93.8 and 75.0% of ceftazidime-non-susceptible isolates from UTI/IAI were inhibited at a ceftazidime-avibactam MIC value of ≤8 µg/mL (Table 1). For all *P. aeruginosa*, amikacin susceptibility for UTI/IAI isolates was at 98.1/97.6% and for colistin, the rates were the same (Table 2). Susceptibility for most other antimicrobials was decreased against the meropenem-nonsusceptible and ceftazidime-non-susceptible P. aeruginosa isolates from either UTI or IAI. Amikacin and colistin were exceptions, their susceptibility remained >90.0% (Table 2).

from the USA (2012)

				No. of isolates (Cumulative %) MIC in µg/mL										
	Indication	No. of Isolates	≤0.06	0.12	0.25	0.5	1	2	4	8	16	≥32	MIC ₅₀	MIC ₉₀
Enterchasteriasea	UTI	2188	1,144 (52.3)	731 (85.7)	208 (95.2)	75 (98.6)	22 (99.6)	3 (99.8)	4 (>99.9)	1 (100.0)			≤0.06	0.25
Enterobacteriaceae	IAI	410	169 (41.2)	157 (79.5)	43 (90.0)	28 (96.8)	10 (99.3)	3 (100.0)					0.12	0.25
Escharichia cali	UTI	913	501 (54.9)	351 (93.3)	54 (99.2)	7 (100.0)							≤0.06	0.12
	IAI	164	88 (53.7)	64 (92.7)	9 (98.2)	2 (99.4)	1 (100.0)						≤0.06	0.12
ESPI phonotypo	UTI	78	17 (21.8)	41 (74.4)	17 (96.2)	3 (100.0)							0.12	0.25
ESBE-phenotype	IAI	17		12 (70.6)	3 (88.2)	1 (94.1)	1 (100.0)						0.12	0.5
Klabsiallasan	UTI	501	226 (45.1)	182 (81.4)	52 (91.8)	29 (97.6)	10 (99.6)	1 (99.8)	1 (100.0)				0.12	0.25
Nebsiella spp.	IAI	104	32 (30.8)	48 (76.9)	12 (88.5)	8 (96.2)	1 (97.1)	3 (100.0)					0.12	0.5
ESPI phonotypo	UTI	65	6 (9.2)	13 (29.2)	12 (47.7)	22 (81.5)	10 (96.9)	1 (98.5)	1 (100.0)				0.5	1
ESBE-phenotype	IAI	17	1 (5.9)	3 (23.5)	3 (41.2)	6 (76.5)	1 (82.4)	3 (100.0)					0.5	2
Klabsialla proumoniaa	UTI	445	197 (44.3)	166 (81.6)	44 (91.5)	26 (97.3)	10 (99.6)	1 (99.8)	1 (100.0)				0.12	0.25
Riebsiella priedmoniae	IAI	85	23 (27.1)	43 (77.6)	8 (87.1)	7 (95.3)	1 (96.5)	3 (100.0)					0.12	0.5
Entorobactor closeco	UTI	112	8 (7.1)	53 (54.5)	32 (83.0)	11 (92.9)	6 (98.2)	0 (98.2)	2 (100.0)				0.12	0.5
	IAI	60	4 (6.7)	26 (50.0)	13 (71.7)	11 (90.0)	6 (100.0)						0.12	0.5
Morgonolla morgonii	UTI	106	82 (77.4)	13 (89.6)	7 (96.2)	2 (98.1)	2 (100.0)						≤0.06	0.25
Morganena morgann	IAI	8	8 (100.0)										≤0.06	≤0.06
Sarratia maragagana	UTI	45	3 (6.7)	19 (48.9)	15 (82.2)	7 (97.8)	1 (100.0)						0.25	0.5
Serralia marcescens	IAI	11	1 (9.1)	6 (63.6)	2 (81.8)	2 (100.0)							0.12	0.5
Psoudomonas apruginosa	UTI	155				9 (5.8)	47 (36.1)	63 (76.8)	23 (91.6)	11 (98.7)	1 (99.4)	1 (100.0)	2	4
r seudomonas aeruginosa	IAI	82					35 (42.7)	30 (79.3)	11 (92.7)	3 (96.3)	2 (98.8)	1 (100.0)	2	4
MED Non S (MIC >4 ug/mL)	UTI	33					2 (6.1)	9 (33.3)	14 (75.8)	7 (97.0)	0 (97.0)	1 (100.0)	4	8
MER-NOII-3 (MIC, 24 µg/IIIL)	IAI	13					2 (15.4)	4 (46.2)	3 (69.2)	1 (76.9)	2 (92.3)	1 (100.0)	4	16
CAZ Non S (MIC > 16 u/m)	UTI	16					2 (12.5)	7 (56.3)	2 (68.8)	4 (93.8)	0 (93.8)	1 (100.0)	2	8
CAZ-NOIPS (MIC, 210 µg/IIIE)	IAI	12						4 (33.3)	4 (66.7)	1 (75.0)	2 (91.7)	1 (100.0)	4	16

Table 2. In vitro activity of ceftazidime-avibactam and comparator agents tested against UTI and IAI isolates from USA (2012)

Organism/antimicrobial agent (no. tested)
Enterobacteriaceae
Ceftazidime-avibactam
Ceftazidime
Piperacillin-tazobactam
Meropenem
Levofloxacin
Tigecvcline ^c
TMP-SMX ^d
Escherichia coli
Ceftazidime-avibactam
Ceftazidime
Piperacillin-tazobactam
Meropenem
Levofloxacin
Piperacillin-tazobactam
Meropenem
Levofloxacin
Tigecycline ^c
TMP-SMX ^a
<i>Klebsiella</i> spp.
Ceftazidime-avibactam
Ceftazidime
Piperacillin-tazobactam
Meropenem
Levofloxacin
Tigecycline ^c
TMP-SMX ^d
ESBL-phenotype
Ceftazidime-avibactam
Ceftazidime
Piperacillin-tazobactam
Meropenem
Levofloxacin
Tigecycline ^c
TMP-SMX ^d
Enterobacter cloacae
Ceftazidime-avibactam
Ceftazidime
Piperacillin-tazohactam
Meronenem
l evoflovacin

Table 1. Summary of ceftazidime-avibactam activity tested against select organisms from urinary tract and intrabdominal infections

	<u>UTI Isc</u>	lates		<u>IAI Iso</u>	lates			<u>UTI Is</u>	<u>olates</u>	IAI Isolates		
MIC (µ	ıg/mL)	%S / %I / %R	MIC (ug/mL)	%S / %I / %R	Organism/antimicrobial	MIC (µg/mL) %S / %I		%S / %I / %R	MIC (ug/mL)	%S / %I / %R
MIC ₅₀	MIC ₉₀	CLSI ^a	MIC ₅₀	MIC ₉₀	CLSI ^a	agent (no. tested)	MIC ₅₀	MIC ₉₀	CLSI ^a	MIC ₅₀	MIC ₉₀	CLSI ^a
	(2,18	38)		(41	0)	Morganella morganii		(106)			(8)	
0.06	0.25	_b / _ / _	0.12	0.25	- / - / -	Ceftazidime-avibactam	0.06	0.25	-/-/-	0.03	-	- / - / -
0.12	2	91.8 / 1.2 / 7.1	0.25	32	86.1 / 1.5 / 12.4	Ceftazidime	0.12	32	84.0 / 1.8 / 14.2	0.06	-	100.0 / 0.0 / 0.0
2	8	94.5 / 2.4 / 3.1	2	32	88.5 / 3.2 / 8.3	Piperacillin-tazobactam	≤0.5	8	92.5 / 2.8 / 4.7	≤0.5	-	100.0 / 0.0 / 0.0
≤0.06	≤0.06	98.8/<0.1/1.2	≤0.06	≤0.06	97.8 / 0.0 / 2.2	Meropenem	≤0.06	0.12	100.0 / 0.0 / 0.0	≤0.06	-	100.0 / 0.0 / 0.0
≤0.12	>4	81.7 / 2.2 / 16.1	≤0.12	>4	81.7 / 1.7 / 16.6	Levofloxacin	≤0.12	>4	69.8 / 6.6 / 23.6	≤0.12	-	87.5 / 0.0 / 12.5
0.25	1	97.9/2.1/0.0	0.25	1	97.8 / 2.2 / 0.0	Tigecvcline ^c	0.5	2	97.2 / 2.8 / 0.0	0.5	-	100.0 / 0.0 / 0.0
≤0.5	>4	77.8 / 0.0 / 22.2	≤0.5	>4	80.0 / 0.0 / 20.0	TMP-SMX ^d	≤0.5	>4	64.2 / 0.0 / 35.8	≤0.5	-	62.5 / 0.0 / 37.5
	(91)	3)		(16-	4)	Serratia marcescens		(4	5)		(11)	
0.06	0.12	-/-/-	0.06	0.12	, _ / - / -	Ceftazidime-avibactam	0.25	0.5	, _/-/-	0.12	0.5	-/-/-
0.12	0.5	94.6 / 1.2 / 4.3	0.12	1	92.1 / 1.9 / 6.1	Ceftazidime	0.25	1	100.0 / 0.0 / 0.0	0.25	0.5	100.0 / 0.0 / 0.0
2	8	97.5/1.4/1.1	2	8	94.5 / 0.6 / 4.9	Piperacillin-tazobactam	2	4	97.8 / 2.2 / 0.0	2	4	100.0 / 0.0 / 0.0
≤0.06	≤0.06	99.9 / 0.1 / 0.0	≤0.06	≤0.06	100.0 / 0.0 / 0.0	Meropenem	≤0.06	0.12	100.0 / 0.0 / 0.0	≤0.06	≤0.06	100.0 / 0.0 / 0.0
≤0.12	>4	76.9 / 0.8 / 22.2	≤0.12	>4	76.2 / 0.6 / 23.2	Levofloxacin	≤0.12	1	95.6 / 2.2 / 2.2	0.25	2	90.9 / 0.0 / 9.1
0.12	0.12	100.0 / 0.0 / 0.0	0.06	0.12	100.0 / 0.0 / 0.0	Tigecycline ^c	0.5	1	97.8 / 2.2 / 0.0	0.5	1	100.0 / 0.0 / 0.0
≤0.5	>4	71.5 / 0.0 / 28.5	≤0.5	>4	75.6 / 0.0 / 24.4		≤0.5	≤0.5	97.8 / 0.0 / 2.2	≤0.5	1	90.9 / 0.0 / 9.1
	(78	3)		(17	·)	Pseudomonas aeruginosa		(15	5)		(82))
0.12	0.25	, _/-/-	0.12	0.5	, _/-/-	Ceftazidime-avibactam	2	4	-/-/-	2	4	-/-/-
8	32	37.2 / 12.8 / 50.0	16	>32	23.5 / 17.7 / 58.8	Ceftazidime	2	16	89.7 / 3.8 / 6.5	2	32	85.4 / 1.1 / 13.4
8	64	80.8 / 10.2 / 9.0	8	>64	70.6 / 0.0 / 29.4	Cefepime	4	16	86.5 / 9.6 / 3.9	2	16	81.7 / 8.5 / 9.8
≤0.06	≤0.06	98.7 / 1.3 / 0.0	≤0.06	0.12	100.0 / 0.0 / 0.0	Piperacillin-tazobactam	8	32	81.9 / 12.8 / 5.2	8	>64	79.3 / 8.5 / 12.2
>4	>4	26.9 / 2.6 / 70.5	>4	>4	5.9 / 0.0 / 94.1	Meropenem	0.5	8	78.7 / 5.8 / 15.5	0.5	8	84.1 / 2.5 / 13.4
0.12	0.25	100.0 / 0.0 / 0.0	0.12	0.25	100.0 / 0.0 / 0.0	Levofloxacin	0.5	>4	65.8 / 3.2 / 31.0	0.5	>4	78.0 / 6.1 / 15.9
>4	>4	41.0 / 0.0 / 59.0	>4	>4	11.8 / 0.0 / 88.2	Amikacin	2	8	98.1 / 0.7 / 1.3	2	8	97.6 / 1.2 / 1.2
	(50	1)		(10)	4)	Gentamicin	2	4	90.3/2.7/7.1	≤1	4	92.7/2.3/4.9
0.12	0.25	-/-/-	0.12	0.5	-/-/-	Colistin	2	2	98.1 / 1.9 / 0.0	2	2	97.6 / 2.4 / 0.0
0.12	8	89.2 / 1.0 / 9.8	0.12	32	86.5 / 0.0 / 13.5	Ceftazidime-Non-S		(16	6)		(12)	
2	16	90.6 / 1.4 / 8.0	4	>64	80.8 / 6.7 / 12.5	Ceftazidime-avibactam	2	8	, _/-/-	4	16	-/-/-
≤0.06	≤0.06	95.4 / 0.0 / 4.6	≤0.06	≤0.06	93.3 / 0.0 / 6.7	Ceftazidime	32	>32	0.0 / 37.5 / 62.5	32	>32	0.0 / 8.3 / 91.7
≤0.12	>4	88.8 / 1.2 / 10.0	≤0.12	>4	84.6 / 1.0 / 14.4	Cefepime	16	>16	31.3 / 49.9 / 18.8	16	>16	8.3 / 50.0 / 41.7
0.25	0.5	99.6 / 0.4 / 0.0	0.25	1	98.1 / 1.9 / 0.0	Piperacillin-tazobactam	32	>64	18.8 / 49.9 / 31.3	>64	>64	0.0 / 25.0 / 75.0
≤0.5	>4	81.8 / 0.0 / 18.2	≤0.5	>4	82.7 / 0.0 / 17.3	Meropenem	2	>8	50.0 / 0.0 / 50.0	2	8	50.0 / 8.3 / 41.7
	(65	5)		(17	<i>(</i>)	Levofloxacin	>4	>4	12.5 / 12.5 / 75.0	2	>4	50.0 / 16.7 / 33.3
0.5	1	, _/-/-	0.5	2	, _/-/-	Amikacin	4	8	100.0 / 0.0 / 0.0	2	8	100.0 / 0.0 / 0.0
>32	>32	16.9 / 7.7 / 75.4	>32	>32	17.6 / 0.0 / 82.4	Colistin	2	2	100.0 / 0.0 / 0.0	2	2	91.7 / 8.3 / 0.0
>64	>64	30.8 / 9.2 / 60.0	>64	>64	11.8 / 17.6 / 70.6	Meropenem-Non-S		(33	3)		(13))
≤0.06	>8	64.6 / 0.0 / 35.4	≤0.06	>8	58.8 / 0.0 / 41.2	Ceftazidime-avibactam	4	8	- / - / -	4	16	- / - / -
>4	>4	24.6 / 6.2 / 69.2	>4	>4	23.5 / 0.0 / 76.5	Ceftazidime	4	>32	75.8 / 3.0 / 21.2	8	>32	53.8 / 7.7 / 38.5
0.5	1	96.9 / 3.1 / 0.0	0.5	1	100.0 / 0.0 / 0.0	Cefepime	8	>16	60.6 / 27.3 / 12.1	>16	>16	38.5 / 7.7 / 53.8
>4	>4	30.8 / 0.0 / 69.2	>4	>4	41.2 / 0.0 / 58.8	Piperacillin-tazobactam	16	>64	60.6 / 21.2 / 18.2	64	>64	38.5 / 15.3 / 46.2
	(11)	2)		(60))	Meropenem	8	>8	0.0 / 27.3 / 72.7	8	>8	0.0 / 15.4 / 84.6
0.12	0.5	, _/-/-	0.12	0.5	, _/-/-	Levofloxacin	>4	>4	21.2 / 6.1 / 72.7	>4	>4	30.8 / 15.4 / 53.8
0.25	>32	79.5 / 0.9 / 19.6	0.5	>32	66.7 / 3.3 / 30.0	Amikacin	4	16	93.9 / 0.0 / 6.1	4	16	92.3 / 7.7 / 0.0
2	64	86.6 / 8.9 / 4.5	4	>64	81.7 / 3.3 / 15.0	Colistin	2	2	97.0/3.0/0.0	2	2	92.3 / 7.7 / 0.0
≤0.06	≤0.06	99.1 / 0.0 / 0.9	≤0.06	0.12	98.3 / 0.0 / 1.7	a. Criteria as published by the (CLSI [2013]					
≤0.12	2	90.2 / 0.8 / 8.9	≤0.12	1	90.0 / 1.7 / 8.3	b, no CLSI interpretive criteria	a.					
0.25	1	99.1 / 0.9 / 0.0	0.25	1	96.7 / 3.3 / 0.0	c. US-FDA breakpoints were ap	plied when a	available [Ty	gacil Product Insert, 201	2].		
≤0.5	>4	87.5 / 0.0 / 12.5	≤0.5	>4	81.7 / 0.0 / 18.3	u. INIM-SINA=trimetnoprim-Sulf	ametnoxazol	е.				

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Conclusions

- Ceftazidime-avibactam demonstrated potent activity against contemporary Enterobacteriaceae including ESBL-positive phenotype and carbapenem-nonsusceptible isolates from patients with UTI and IAI in USA hospitals
- Ceftazidime-avibactam demonstrated potent activity against contemporary *P. aeruginosa* including carbapenem-non-susceptible and ceftazidime-nonsusceptible isolates from patients with UTI and IAI
- These data may support ceftazidime-avibactam as a potential treatment option in these types of hospital infections and indicate that further clinical study is warranted.

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