# Antimicrobial Activity of Ceftazidime/NXL-104 Tested Against Gram-Negative Organisms, Including Multidrug-Resistant Subsets, Causing Infections in USA and European Medical Centers

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### **Amended Abstract**

**Background**: NXL-104 (NXL) is a novel non-β-lactam β-lactamase (BL) inhibitor of Ambler class A, C, and some D enzymes. Ceftazidime (CAZ) combined with NXL is currently being evaluated in clinical trials for the treatment of serious hospital infections, including those caused by antimicrobialresistant (R) Gram-negative (GN) pathogens.

Methods: CAZ/NXL (NXL 4 µg/mL) and comparators were susceptibility (S) tested by CLSI broth microdilution methods against 5990 GN isolates cultured from 55 medical centers in the USA (27) and Europe (EU; 28) in 2009. The collection included: Escherichia coli (2170; 11.8% ESBL phenotype), *Klebsiella* spp. (KSP; 1156; 17.6% ESBL phenotype and 5.3% decreased S to carbapenems), *Pseudomonas aeruginosa* (PSA; 952; 24.6% imipenem [IMI]-R), Enterobacter spp. (ESP; 618; 23.4% CAZ-R), Acinetobacter spp. (ASP; 311; 47.9% IMI-R), Serratia spp. (272), Proteus mirabilis (234), Citrobacter spp. (120), indole-positive Proteae (109), and Salmonella spp (48).

**Results:** CAZ/NXL was highly active against all Enterobacteriaceae (ENT) species, with MIC<sub>50</sub> of 0.06–0.25 µg/mL and MIC<sub>oo</sub> of 0.5–1 µg/mL (main species listed in Table). ESBL phenotype and CAZ-R were more frequent among ENT from the EU compared with the USA, but CAZ/NXL was equally active against ENT from both regions. KSP with decreased S to carbapenems (5.0-5.9% resistance) were S to CAZ/NXL (96.8% inhibited at ≤4 µg/mL). NXL improved CAZ activity against PSA and CAZ/NXL inhibited >50% of IMI-R PSA at MIC of ≤4 µg/mL. All β-lactams tested had limited activity against ASP.

	Ci	umulati	ve % inf	nibited a	at CAZ/	NXL MIC	; (µg/m)	L) of:
Organism (no. tested)	≤0.06	0.12	0.25	0.5	1	2	4	8
E. coli (2170)	32.4	82.4	95.4	99.5	99.9	100.0	-	-
ESBL phenotype (256)	10.6	51.6	80.9	96.5	99.6	100.0	-	-
Klebsiella spp. (1156)	17.5	65.6	84.1	93.7	97.4	99.4	99.8	99.9
ESBL phenotype (204)	2.5	17.7	35.8	66.2	85.3	96.6	98.5	99.5
Decreased S to			05.0	54.0	70.0		~~~~	00 A
carbapenems (62)	8.1	14.5	25.8	54.8	72.6	91.9	96.8	98.4
Enterobacter spp. (618)	5.8	37.7	72.0	89.5	96.4	98.9	99.5	99.5
Ceftazidime-R (143)	0.7	4.2	20.3	62.2	87.4	96.5	97.9	97.9
P. aeruginosa (952)	0.0	0.1	0.7	3.0	17.2	68.6	83.7	93.4
Imipenem-R (234)	0.0	0.4	0.4	1.7	9.4	33.3	55.6	78.2

Conclusions: CAZ/NXL was very active against ENT, including ESBL, KPC, and AmpC producers. CAZ/NXL was also active against PSA, including many IMI-R strains, but had limited potency against ASP.

### Introduction

Bacterial isolates resistant to clinically available β-lactams present a challenge to successful treatment of serious infections. β-lactamasemediated resistance, in particular, represents a significant clinical threat because of the mobile nature of the genes encoding these enzymes. Two strategies have been used to restore the utility of  $\beta$ -lactam compounds: (i) the design/discovery of novel  $\beta$ -lactam molecules that are refractory to enzymatic inactivation, and (ii) the inhibition of  $\beta$ -lactamases, thereby allowing the  $\beta$ -lactam to retain target concentrations.

NXL-104 (NXL) is a non- $\beta$ -lactam  $\beta$ -lactamase inhibitor with promising activity against class A, C, and some D β-lactamases. β-lactamase enzymes are inactivated very efficiently by NXL, with low  $IC_{50}$  (concentration resulting in 50%) inhibition) values and low turnover numbers. NXL protects β-lactams from hydrolysis by a variety of enzymes.

In this study, we evaluated the activity of ceftazidime combined with NXL (CAZ/NXL) against a large collection of contemporary Gram-negative clinical isolates recovered in hospitals located in the USA and Europe during 2009.

### Material And Methods

Bacterial isolates: A total of 5,990 non-duplicate consecutive Gram-negative strains were collected during 2009 from medical centers located in the USA (27 sites) and Europe (28 sites). These isolates were collected from bloodstream, respiratory tract, or skin and soft tissue infections according to defined protocols. Only clinically significant isolates were included in the study (1 per patient episode). Species identification was confirmed by standard biochemical tests and/or use of the Vitek Systems (bioMérieux; Hazelwood, MO, USA), as necessary.

**Susceptibility testing:** Isolates were susceptibility tested by a reference broth microdilution procedure (Clinical Laboratory Standard Institute [CLSI]),<sup>1</sup> using validated microdilution panels manufactured by TREK Diagnostics (Cleveland, OH, USA). Susceptibility testing results were interpreted according to CLSI criteria.<sup>2</sup> Escherichia coli ATCC 25922 and Pseudomonas aeruginosa ATCC 27853 were concurrently tested for guality assurance; all results were in the published ranges.

E. coli and Klebsiella spp. isolates for which the MICs of ceftriaxone, ceftazidime, or aztreonam were ≥2 µg/mL were considered to be phenotype-positive for ESBL production.<sup>2</sup>

### Results

- All 2,170 E. coli strains were inhibited at ≤2 µg/mL of CAZ/NXL, and 100% were susceptible by CLSI breakpoint criteria for ceftazidime alone (Tables 1 and 2). Using the EUCAST<sup>3</sup> breakpoint for ceftazidime ( $\leq 1 \mu g/mL$  susceptible), CAZ/NXL susceptibility rates were 99.9%.
- Against *E. coli* strains displaying the ESBL phenotype, CAZ/NXL provided the best coverage (100% using ceftazidime CLSI breakpoint), followed by meropenem (99.2% susceptible; Table 2).
- Using the 4 µg/mL ceftazidime breakpoint established by the CLSI,<sup>2</sup> CAZ/NXL demonstrated the highest susceptibility rate among agents tested against *Klebsiella* spp. (99.8%; Table 2). Meropenem was also very active against this species (95.8–96.3% susceptible)
- Only 2 (0.1%) *Klebsiella* spp. strains had CAZ/NXL MIC >4 µg/mL: 1 KPC-producing K. pneumoniae from the USA (8 µg/mL), and a VIM-1-producing K. pneumoniae from Spain (32 µg/mL; Table 1). Both strains showed decreased susceptibility to carbapenems (meropenem MIC values of >8 and 2 µg/mL, respectively).

### Table 1. Frequency Distributions of Ceftazidime/NXL-104 When Tested Against Gram-Negative Isolates Collected in US and European Medical Centers During 2009

Organism group (no. tested)ª					Cumulative % of strains inhibite				
	<b>≤</b> 0.03	0.06	0.12	0.25	0.5	1	2		
Escherichia coli (2,170)	7.1	32.4	82.4	95.4	99.5	99.9	100.0		
ESBL phenotype (256)	3.5	10.6	51.6	80.9	96.5	99.6	100.0		
Klebsiella spp. (1,156)	1.6	17.5	65.6	84.1	93.7	97.5	99.5		
ESBL phenotype (204)	2.0	2.5	17.7	35.8	66.2	85.8	97.1		
Decreased carbapenem-S (62) <sup>b</sup>	6.5	8.1	14.5	25.8	54.8	72.6	91.9		
Enterobacter spp. (618)	1.3	5.8	37.7	72.0	89.5	96.4	98.9		
Ceftazidime-R (143)°	0.0	0.7	4.2	20.3	62.2	87.4	96.5		
Serratia spp. (272)	0.0	2.6	38.2	79.4	93.4	96.3	98.5		
Proteus mirabilis (234)	19.2	86.3	98.7	100.0					
Indole-positive Proteae (109)	11.0	67.9	88.1	95.4	97.2	99.1	100.0		
Citrobacter spp. (120)	0.8	20.0	58.3	85.0	95.8	98.3	100.0		
Salmonella spp. (48)	2.1	6.3	25.0	87.5	100.0				
Pseudomonas aeruginosa (952)	0.0	0.0	0.1	0.7	3.0	17.2	68.6		
Imipenem-R (234)d	0.0	0.0	0.4	0.4	1.7	9.4	33.3		
Acinetobacter spp. (311)	0.3	0.6	1.0	1.6	2.2	2.6	5.5		
Imipenem-R (149) <sup>d</sup>	0.0	0.0	0.0	0.7	0.7	0.7	0.7		

a. Single isolate from Spain (VIM-type metallo-β-lactamase). b. Defined as MIC ≥2 µg/mL to imipenem and/or meropenem

c. Defined as MIC ≥16 µg/mL to ceftazidime

### Table 2. Activity of Ceftazidime/NXL-104 and Comparator Agents Tested Against 5,990 Gram-Negative Clinical Isolates Collected in US and European Medical Centers During 2009

Organism (no. tested)/		ι	JSA			EUF	ROPE		
Antimicrobial agent	N	/IC	% Susc	ceptibility		MIC	% Sus	ceptibilit	
	50%	90%	CLSIª	EUCAST	50%	90%	CLSI <sup>a</sup>	EUCA	
Escherichia coli (2,170)									
Ceftazidime/NXL-104 <sup>b</sup>	0.12	0.25	100.0	99.9	0.12	0.25	100.0	99.9	
Ceftazidime	0.25	1	93.4	90.9	0.25	2	93.2	87.2	
Cefepime	≤0.12	0.5	95.5	92.1	≤0.12	2	93.8	88.7	
Meropenem	≤0.12	≤0.12	99.9	99.9	≤0.12	≤0.12	99.8	99.9	
Piperacillin/tazobactam	2	8	94.0	91.2	2	16	91.1	87.8	
ESBL-producers (256)	0.25	0.5	100.0	100.0	0.12	0.5	100.0	99.4	
Ceftazidime/NXL-104 <sup>b</sup> Ceftazidime	0.25	>32	31.5	100.0	0.12	0.5	49.4	99.4 8.5	
Cefepime	8	>16	53.3	22.8	8	>16	49.4 54.3	20.7	
Meropenem	≤0.12	≤0.12	98.9	98.9	≤0.12	≤0.12	99.4	100.	
Piperacillin/tazobactam	-0.12	64	72.8	55.4	8	>64	66.5	50.6	
Klebsiella spp. (1,156)	0	04	12.0	00.4	0	- 0-1	00.0	00.0	
Ceftazidime/NXL-104b	0.12	0.5	99.7	98.1	0.12	0.5	99.8	96.4	
Ceftazidime	0.12	16	88.8	88.1	0.25	>32	79.2	75.4	
Cefepime	≤0.12	2	92.4	89.9	≤0.12	>16	84.2	80.3	
Meropenem	≤0.12	≤0.12	95.1	95.3	≤0.12	≤0.12	96.6	97.7	
Piperacillin/tazobactam	4	32	88.4	82.6	4	>64	77.3	73.3	
ESBL-producers (204)									
Ceftazidime/NXL-104 <sup>b</sup>	0.5	2	98.8	85.7	0.5	2	99.2	85.8	
Ceftazidime	>32	>32	9.5	7.1	32	>32	17.5	9.2	
Cefepime	16	>16	38.1	19.0	>16	>16	37.5	21.7	
Meropenem	≤0.12	>8	60.7	61.9	≤0.12	2	86.7	90.8	
Piperacillin/tazobactam	>64	>64	23.8	19.0	64	>64	25.8	18.3	
Imipenem non-susceptible (62)	0.5	2	97.1	70 5	0.5	4	96.4	71.4	
Ceftazidime/NXL-104 <sup>b</sup> Ceftazidime	0.5 >32	>32	5.9	73.5 5.9	0.5 >32	4 >32	96.4 14.3	14.3	
Cefepime	>32	>32	5.9 14.7	5.9	>16	>32	25.0	14.3	
Meropenem	>8	>8	5.9	8.8	-10	>8	50.0	60.7	
Piperacillin/tazobactam	>64	>64	5.9	5.9	>64	>64	3.6	3.6	
Enterobacter spp. (618)	- 04	- 04	0.0	0.0	- 04	- 0-1	0.0	0.0	
Ceftazidime/NXL-104 <sup>b</sup>	0.25	0.5	100.0	97.0	0.25	1	95.6	98.8	
Ceftazidime	0.25	>32	78.9	74.8	0.25	>32	70.2	65.1	
Cefepime	≤0.12	2	95.9	85.8	≤0.12	2	96.8	87.4	
Meropenem	≤0.12	≤0.12	97.8	97.8	≤0.12	≤0.12	98.4	98.4	
Piperacillin/tazobactam	4	64	82.2	77.3	4	>64	72.7	68.0	
Ceftazidime-resistant (143)									
Ceftazidime/NXL-104 <sup>b</sup>	0.5	2	100.0	86.5	0.5	2	95.6	88.4	
Ceftazidime	>32	>32	0.0	0.0	32	>32	0.0	0.0	
Cefepime	2	>16	81.1	31.1	1	16	88.4	53.6	
Meropenem	≤0.12	4	89.2	89.2	≤0.12	0.5	94.2	94.2	
Piperacillin/tazobactam	64	>64	20.3	9.5	64	>64	13.0	5.8	
Serratia spp. (272) Ceftazidime/NXL-104 <sup>b</sup>	0.25	0.5	100.0	97.5	0.25	0.5	99.1	94.5	
Ceftazidime	0.25	0.5	95.1	94.5	0.23	0.5	99.1	94.0	
Cefepime	≤0.12	0.5	99.4	94.5	≤0.12	0.5	100.0	91.7	
Meropenem	≤0.12	≤0.12	97.5	97.5	≤0.12	≤0.12	100.0	100.2	
Piperacillin/tazobactam	2	4	98.2	95.7	2	32	89.9	84.4	
Citrobacter spp. (120)	-	-	00.2	00.1	-	02	00.0	04.4	
Ceftazidime/NXL-104 <sup>b</sup>	0.12	0.5	100.0	98.4	0.12	0.5	100.0	98.3	
Ceftazidime	0.25	32	87.3	85.7	0.25	32	80.7	78.9	
Cefepime	≤0.12	1	100.0	95.2	≤0.12	1	96.5	93.0	
Meropenem	≤0.12	≤0.12	100.0	100.0	≤0.12	≤0.12	100.0	100.	
Piperacillin/tazobactam	2	64	88.9	85.7	2	32	84.2	78.9	

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MIC (µg/	mL):				
4	8	16	32	>32	
99.8 99.0 96.8 99.5 97.9 99.6	99.9 99.5 98.4 99.5 97.9 100.0	99.9 99.5 98.4 99.5 97.9	100.0ª 100.0ª 100.0ª 99.5 97.9	100.0 <sup>b</sup> 100.0 <sup>b</sup>	
83.7 55.6 11.9 1.3	93.4 78.2 30.5 12.8	96.3 86.7 50.2 32.2	98.4 94.0 70.1 58.4	100.0 100.0 100.0 100.0	
foridime					

		RALL	
50%	90%	% Suse	EUCAST
0.12	0.25	100.0	99.9
0.12 0.25 ≤0.12 ≤0.12 2	0.25 2 1 ≤0.12 16	93.3 94.6 99.9 92.4	99.9 88.8 90.2 99.9 89.3
0.12 8 ≤0.12 8	0.5 32 >16 ≤0.12 >64	100.0 43.0 53.9 99.2 68.8	99.6 9.4 21.5 99.6 52.3
0.12	0.5	99.8	97.4
0.12	32	84.9	82.9
≤0.12	16	89.0	85.9
≤0.12	≤0.12	95.8	96.3
4	>64	83.8	78.8
0.5	2	79.9	72.5
>32	>32	14.2	8.3
>16	>16	37.7	20.6
≤0.12	>8	76.0	78.9
>64	>64	25.0	18.6
0.5	2	96.8	72.6
>32	>32	9.7	9.7
>16	>16	19.4	11.3
>8	>8	25.8	32.3
>64	>64	4.8	4.8
0.25	1	99.5	96.4
0.25	>32	75.4	70.8
≤0.12	2	96.3	86.4
≤0.12	≤0.12	98.1	98.1
4	64	78.3	73.5
0.5	2	97.9	87.4
32	>32	0.0	0.0
2	>16	84.6	42.0
≤0.12	0.5	91.6	91.6
64	>64	16.8	7.7
0.25	0.5	99.6	96.3
0.25	0.5	94.9	93.4
≤0.12	0.5	99.6	96.3
≤0.12	≤0.12	98.5	98.5
2	8	94.9	91.2
0.12	0.5	100.0	98.3
0.25	32	84.2	82.5
≤0.12	1	98.3	94.2
≤0.12	≤0.12	100.0	100.0
2	32	86.7	82.5

### Table 2. (continued)

Organism (no. tested)/		U				EUR	OPE			OVE	RALL	
Antimicrobial agent	N	lic	% Sus	ceptibility	N	IIC	% Suse	ceptibility	M	IC	% Sus	ceptibility
-	50%	90%	CLSI <sup>a</sup>	EUCAST	50%	90%	<b>CLSI</b> <sup>a</sup>	EUCAST	50%	90%	CLSI <sup>a</sup>	EUCAST
Proteus mirabilis (234)												
Ceftazidime/NXL-104 <sup>b</sup>	0.06	0.12	100.0	100.0	0.06	0.12	100.0	100.0	0.06	0.12	100.0	100.0
Ceftazidime	0.06	0.12	98.3	98.3	0.06	1	97.4	90.5	0.06	0.12	97.9	94.4
Cefepime	≤0.12	≤0.12	100.0	100.0	≤0.12	0.5	95.7	93.1	≤0.12	0.25	97.9	96.6
Meropenem	≤0.12	≤0.12	100.0	100.0	≤0.12	≤0.12	100.0	100.0	≤0.12	≤0.12	100.0	100.0
Piperacillin/tazobactam	≤0.5	1	100.0	100.0	≤0.5	1	100.0	100.0	≤0.5	1	100.0	100.0
Indole-positive Proteus spp. (109)												
Ceftazidime/NXL-104 <sup>b</sup>	0.06	0.25	100.0	97.5	0.06	0.12	100.0	100.0	0.06	0.25	100.0	99.1
Ceftazidime	0.12	8	87.5	82.5	0.12	8	88.4	76.8	0.12	8	88.1	78.9
Cefepime	≤0.12	≤0.12	100.0	97.5	≤0.12	0.25	98.6	97.1	≤0.12	0.25	99.1	97.2
Meropenem	≤0.12	≤0.12	100.0	100.0	≤0.12 ≤0.12	0.25	100.0	100.0	≤0.12	≤0.12	100.0	100.0
Piperacillin/tazobactam	≤0.12	2	97.5	97.5	≤0.5	2	98.6	97.1	<u>≤</u> 0.12 ≤0.5	2	98.2	97.2
Salmonella spp. (48)	-0.0	2	57.5	51.5	20.5	2	30.0	31.1	20.5	~	50.Z	51.2
Ceftazidime/NXL-104 <sup>b</sup>	0.25	0.5	100.0	100.0	0.25	0.5	100.0	100.0	0.25	0.5	100.0	100.0
Ceftazidime	0.25	0.25	100.0	100.0	0.25	0.5	100.0	100.0	0.25	0.5	100.0	100.0
	0.25 ≤0.12		100.0	100.0	0.25 ≤0.12	0.5	100.0	100.0	5 ≤0.12	0.5	100.0	100.0
Cefepime		≤0.12										
Meropenem	≤0.12	≤0.12	100.0	100.0	≤0.12	≤0.12	100.0	100.0	≤0.12	≤0.12	100.0	100.0
Piperacillin/tazobactam	2	4	100.0	100.0	4	8	100.0	100.0	4	8	100.0	100.0
Pseudomonas aeruginosa (952)	-											
Ceftazidime/NXL-104°	2	8	96.8	96.8	2	8	90.0	90.0	2	8	93.4	93.4
Ceftazidime	2	32	84.5	84.8	4	>32	72.8	72.8	2	32	78.6	78.6
Cefepime	2	16	84.5	84.5	4	>16	71.9	71.9	4	16	78.1	78.1
Meropenem	0.5	8	87.9	83.0	1	>8	73.6	67.2	0.5	>8	80.7	75.0
Piperacillin/tazobactam	8	>64	87.3	79.0	8	>64	81.7	65.5	8	>64	84.5	72.2
Imipenem-resistant (234)												
Ceftazidime/NXL-104°	4	8	61.0	61.0	4	32	71.7	71.7	4	32	78.2	78.2
Ceftazidime	8	>32	53.7	53.7	32	>32	40.8	40.8	16	>32	45.3	45.3
Cefepime	8	>16	50.0	50.0	16	>16	35.5	35.5	16	>16	40.6	40.6
Meropenem	8	>8	34.1	13.4	>8	>8	21.1	4.6	8	>8	25.6	7.7
Piperacillin/tazobactam	32	>64	64.6	41.5	64	>64	58.6	31.6	64	>64	60.7	35.0
Acinetobacter spp. (311)	02		00		0.	0.	00.0	01.0	• • •	0.	00.1	00.0
Ceftazidime/NXL-104 <sup>d</sup>	32	>32	30.5	_	16	>32	30.6	-	16	>32	30.6	_
Ceftazidime	8	>32	51.7	_	>32	>32	25.5	_	>32	>32	35.5	_
Cefepime	16	>16	49.2	_	>16	>16	29.5	_	>16	>16	37.0	_
	2	>8	62.7	56.8	>8	>8	45.6	40.9	-10	>8	52.1	46.9
Meropenem Piperacillin/tazobactam	64	>64	62.7 50.0		>64	>64	45.6 26.9		-4 >64	>64	35.7	
	04	~04	50.0	-	~04	~04	20.9	-	~04	~04	30.7	-
Imipenem-resistant (149)			1.0		00		40.4		00		40.7	
Ceftazidime/NXL-104d	>32	>32	4.6	-	32	>32	16.4	-	32	>32	12.7	-
Ceftazidime	>32	>32	20.9	-	>32	>32	3.8	-	>32	>32	8.7	-
Cefepime	>16	>16	4.7	-	>16	>16	4.7	-	>16	>16	4.7	-
Meropenem	>8	>8	0.0	0.0	>8	>8	1.9	0.9	>8	>8	1.3	0.7
Piperacillin/tazobactam	>64	>64	0.0	-	>64	>64	1.9	-	>64	>64	1.3	-

b. Breakpoints for ceftazidime/NXL-104 were those for ceftazidime versus Enterobacteriaceae according to CLSI, 2010 (≤4 µg/mL susceptible [S], 8 µg/mL intermediate [I], ≥16 µg/mL resistant [R]) and EUCAST, 2010 (≤1 µg/mL S, 2 µg/mL I, ≥4 µg/mL R). c. Breakpoints for ceftazidime/NXL104 were those for ceftazidime versus *Pseudomonas* spp. according to CLSI, 2010 (≤8 µg/mL S, 16 µg/mL I, ≥32 µg/mL R) and EUCAST, 2010

(≤8  $\mu$ g/mL S and ≥16  $\mu$ g/mL R).

d. Breakpoints for ceftazidime/NXL104 were those for ceftazidime versus Acinetobacter spp. according to CLSI, 2010 (≤8 µg/mL S, 16 µg/mL I, ≥32 µg/mL R).

- Among 618 Enterobacter spp. strains, 99.5% were inhibited by CAZ/NXL at ≤4 µg/mL. Three *E. cloacae* strains from Spain had CAZ/NXL MIC values ≥32 µg/mL and carried a metallo- $\beta$ -lactamase encoding gene (*bla*<sub>VIM</sub>).
- CAZ/NXL inhibited 99.6% of the Serratia spp. strains at  $4 \mu g/mL$  or lower (Tables 1 and 2); its activity was comparable to that of cefepime and meropenem (>98% susceptible; Table 2).
- All remaining Enterobacteriaceae species were inhibited at  $\leq 2 \mu g/mL$  of CAZ/NXL (Table 1), which demonstrated activity similar to that of cefepime and meropenem against *Proteus* mirabilis, Citrobacter spp., indole-positive Proteae, and Salmonella spp. isolates (100% susceptibility: Table 2).
- Using the CLSI breakpoint for ceftazidime (≤8 µg/mL), 93.4% of *P. aeruginosa* strains were categorized as susceptible to CAZ/NXL (MIC<sub>50/90</sub> 2 and 8 µg/mL, respectively).
- All β-lactams tested showed limited activity against Acinetobacter spp., regardless of imipenem resistance profile (Table 2). CAZ/NXL inhibited only 30.5% of isolates at ≤8 µg/mL (CLSI susceptible breakpoint for ceftazidime; Table 1).

## Conclusions

- CAZ/NXL demonstrated very good activity against Gramnegative isolates, including sets of challenging β-lactamaseproducing strains with various  $\beta$ -lactam resistance patterns.
- Activity of CAZ/NXL was only limited against Acinetobacter spp. and metallo- $\beta$ -lactamase-producing strains.
- The increase of community and nosocomial infections caused by  $\beta$ -lactamase-producing organisms (often multidrug-resistant) reduces antimicrobial therapy options. The use of NXL. a broad-spectrum  $\beta$ -lactamase inhibitor, in combination with a well-known,  $\beta$ -lactam such as ceftazidime, may offer a useful therapeutic alternative for these infections in the future.

# References

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