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Global Surveillance: Susceptibility of Ceftolozane-Tazobactam against *Pseudomonas aeruginosa*, *Klebsiella* spp., and *Escherichia coli* Isolates Collected in Asia-Pacific, North and Latin America, and Europe from 2011–2016

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Introduction

- Ceftolozane is a novel oxyimino-aminothiazolyl cephalosporin with potent activity against *Enterobacteriaceae* (similar to other oxyimino-aminothiazolyl cephalosporins) and has demonstrated greater activity than ceftazidime against *Pseudomonas aeruginosa*
  - Ceftolozane maintains its stability against many *P. aeruginosa* resistance mechanisms, including AmpC hyperproduction and efflux mechanisms
  - Porin deficiency has little effect on ceftolozane
  - As with other oxyimino-aminothiazolyl cephalosporins, however, ceftolozane's activity can be compromised in bacteria producing extended-spectrum β-lactamases (ESBLs), stably derepressed AmpC β-lactamases, and carbapenemases
- Tazobactam, a penicillanic acid sulfone, is a well-established β-lactamase inhibitor that extends the spectrum of β-lactam agents
- Ceftolozane-tazobactam was approved by the US Food and Drug Administration in 2014 and the European Medicines Agency in 2015 for the treatment of patients with complicated intra-abdominal infections in combination with metronidazole and for complicated urinary tract infections, including pyelonephritis
- For the past decade, nosocomial infections caused by *P. aeruginosa* and *Enterobacteriaceae*, as well as antimicrobial resistance to them, have increased in prevalence worldwide and associated morbidity and mortality rates have also risen
- Empiric and targeted therapies to treat infections caused by these organisms are becoming increasingly limited in efficacy
- In this study, the activity of C-T and comparators was assessed against *Pseudomonas aeruginosa*, *Klebsiella* spp. (*K. pneumoniae* and *K. oxytoca*), and *Escherichia coli* isolates collected in hospitals throughout Asia-Pacific, Australia-New Zealand, Europe, and North and Latin America participating in the Program to Assess Ceftolozane-Tazobactam Susceptibility (PACTS) from 2011–2016

Materials and Methods

- A total of 51,315 gram-negative isolates that include *Escherichia coli* (EC; 23,457), *Klebsiella pneumoniae* (KPN; 11,065), *K. oxytoca* (KOX; 2,353), and *Pseudomonas aeruginosa* (PSA;14,440), were collected in 2011–2016 from approximately 88 PACTS hospitals in Asia-Pacific (APAC), Australia and New Zealand (ANZ), Europe (EU), North America (NA), and Latin America (LA) and tested for susceptibility by the CLSI broth microdilution method in a central laboratory (JMI Laboratories, North Liberty, Iowa, USA)
- Isolates were from documented infections and only 1 isolate per patient-infection episode was included
- In addition to C-T, ceftazidime (CAZ), piperacillin-tazobactam (TZP), colistin (COL), and meropenem (MER) were tested
- Antibiotic-resistant phenotypes identified using CLSI (2017) clinical breakpoints included carbapenem-resistant (CRE) *E. coli, Klebsiella* spp.; extended-spectrum beta-lactamase phenotype (ESBL) *E. coli* and *Klebsiella* spp.; CAZ nonsusceptible (CAZ-NS), MER-NS, and COL-NS *P. aeruginosa*
  - The ESBL-phenotype isolates analyzed were non-carbapenem resistant (ESBL, non-CRE; ESBL criteria used were according to CLSI M100-S27), excluding the carbapenemase-producing *Enterobacteriaceae* that may be included in the ESBL phenotype
- CLSI (2017) C-T breakpoints for *Enterobacteriaceae* are ≤2 mg/L susceptible (S), 4 mg/L intermediate (I), and ≥8 mg/L resistant (R); *P. aeruginosa* C-T breakpoints are ≤4 mg/L S, 8 mg/L I, and ≥16 mg/L R
- EUCAST (2017) C-T breakpoints for *Enterobacteriaceae* are ≤1 mg/L S and >1 mg/L R; *P. aeruginosa* C-T breakpoints are ≤4 mg/L S and >4 mg/L R

Results

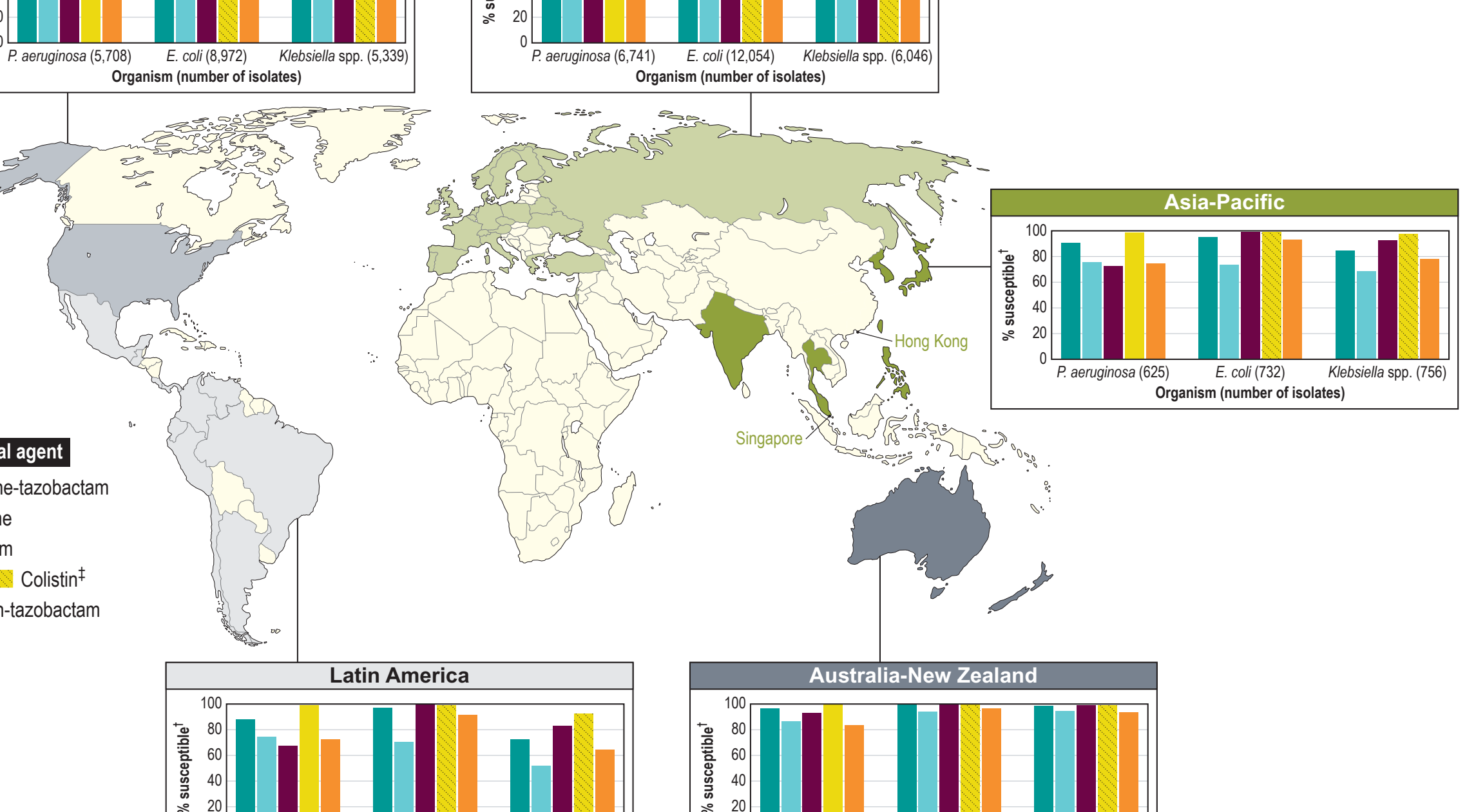
- Among the 51,315 isolates tested, 20,019 (39.0%) were from NA, 24,841 (48.4%) were from EU, 2,113 (4.1%) were from APAC, 1,592 (3.1%) were from ANZ, and 2,750 (5.4%) were from LA (Table 1)
- MIC distributions of C-T for *P. aeruginosa*, *E. coli*, *Klebsiella* spp. (KPN and KOX combined), and the resistant phenotypes are shown by geographic region in Table 1

Table 1 Cumulative frequency distribution of ceftolozane-tazobactam MIC results by continent (mg/L)

Organism / organism group	No. of isolates	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32	MIC_{50}	MIC_{90}
Australia / New Zealand																
P. aeruginosa	596		0 (0.0)	4 (0.7)	4 (1.3)	104 (18.8)	289 (67.3)	138 (90.4)	22 (94.1)	14 (96.5)	12 (98.5)	3 (99.0)	1 (99.2)	5 (100.0)	0.5	1
Ceftazidime-nonsusceptible	81				0 (0.0)	1 (1.2)	7 (9.9)	24 (39.5)	14 (56.8)	14 (74.1)	12 (88.9)	3 (92.6)	1 (93.8)	5 (100.0)	2	16
Meropenem-nonsusceptible	42					0 (0.0)	8 (19.0)	13 (50.0)	5 (61.9)	6 (76.2)	3 (83.3)	2 (88.1)	1 (90.5)	4 (100.0)	1	32
Colistin-nonsusceptible	1									0 (0.0)	1 (100.0)				N/A	N/A
Piperacillin-tazobactam-nonsusceptible	99				0 (0.0)	3 (3.0)	12 (15.2)	37 (52.5)	13 (65.7)	14 (79.8)	11 (90.9)	3 (93.9)	1 (94.9)	5 (100.0)	1	8
E. coli	653		0 (0.0)	35 (5.4)	345 (58.2)	225 (92.6)	39 (98.6)	6 (99.5)	1 (99.7)	0 (99.7)	1 (99.8)	1 (100.0)			0.12	0.25
CRE	0															
ESBL, nonCRE	76			0 (0.0)	10 (13.2)	31 (53.9)	27 (89.5)	5 (96.1)	1 (97.4)	0 (97.4)	1 (98.7)	1 (100.0)			0.25	1
Klebsiella spp.	343	0 (0.0)	1 (0.3)	5 (1.7)	101 (31.2)	158 (77.3)	48 (91.3)	17 (96.2)	8 (98.5)	1 (98.8)	0 (98.8)	1 (99.1)	0 (99.1)	3 (100.0)	0.25	0.5
CRE	3												0 (0.0)	3 (100.0)	>32	N/A
ESBL, nonCRE	30			0 (0.0)	1 (3.3)	6 (23.3)	7 (46.7)	7 (70.0)	7 (93.3)	1 (96.7)	0 (96.7)	1 (100.0)			1	2
North America (US)																
P. aeruginosa	5,708	0 (0.0)	3 (0.1)	7 (0.2)	33 (0.8)	508 (9.7)	2997 (62.2)	1359 (86.0)	390 (92.8)	234 (96.9)	94 (98.5)	22 (98.9)	10 (99.1)	51 (100.0)	0.5	2
Ceftazidime-nonsusceptible	891				0 (0.0)	1 (0.1)	38 (4.4)	188 (25.5)	264 (55.1)	224 (80.2)	93 (90.7)	22 (93.2)	10 (94.3)	51 (100.0)	2	8
Meropenem-nonsusceptible	1,100				0 (0.0)	13 (1.2)	246 (23.5)	386 (58.6)	187 (75.6)	130 (87.5)	62 (93.1)	19 (94.8)	9 (95.6)	48 (100.0)	1	8
Colistin-nonsusceptible	35					0 (0.0)	20 (57.1)	9 (82.9)	3 (91.4)	0 (91.4)	1 (94.3)	1 (97.1)	0 (97.1)	1 (100.0)	0.5	2
Piperacillin-tazobactam-nonsusceptible	1,170				0 (0.0)	4 (0.3)	118 (10.4)	366 (41.7)	294 (66.8)	225 (86.1)	88 (93.6)	20 (95.3)	7 (95.9)	48 (100.0)	2	8
E. coli	8,972	2 (<0.1)	7 (0.1)	223 (2.6)	3826 (45.2)	3662 (86.0)	828 (95.3)	207 (97.6)	89 (98.6)	41 (99.0)	30 (99.4)	19 (99.6)	18 (99.8)	20 (100.0)	0.25	0.5
CRE	22								0 (0.0)	3 (13.6)	4 (31.8)	6 (59.1)	5 (81.8)	4 (100.0)	16	>32
ESBL, nonCRE	1,286		0 (0.0)	2 (0.2)	98 (7.8)	393 (38.3)	430 (71.8)	174 (85.3)	83 (91.8)	38 (94.7)	26 (96.7)	13 (97.7)	13 (98.8)	16 (100.0)	0.5	2
Klebsiella spp.	5,339	0 (0.0)	8 (0.1)	64 (1.3)	1505 (29.5)	2087 (68.6)	783 (83.3)	302 (88.9)	103 (90.9)	52 (91.9)	47 (92.7)	47 (93.6)	85 (95.2)	256 (100.0)	0.25	2
CRE	303							0 (0.0)	3 (1.0)	1 (1.3)	14 (5.9)	24 (13.9)	64 (35.0)	197 (100.0)	>32	>32
ESBL, nonCRE	626		0 (0.0)	2 (0.3)	19 (3.4)	83 (16.6)	132 (37.7)	117 (56.4)	87 (70.3)	51 (78.4)	32 (83.5)	23 (87.2)	21 (90.6)	59 (100.0)	1	32
Europe																
P. aeruginosa	6,741		0 (0.0)	8 (0.1)	29 (0.5)	487 (7.8)	3199 (55.2)	1398 (76.0)	528 (83.8)	321 (88.6)	114 (90.3)	64 (91.2)	95 (92.6)	498 (100.0)	0.5	8
Ceftazidime-nonsusceptible	1,847				0 (0.0)	1 (0.1)	40 (2.2)	342 (20.7)	432 (44.1)	294 (60.0)	93 (65.1)	58 (68.2)	92 (73.2)	495 (100.0)	4	>32
Meropenem-nonsusceptible	1,995			0 (0.0)	1 (0.1)	27 (1.4)	323 (17.6)	441 (39.7)	295 (54.5)	202 (64.6)	87 (69.0)	59 (71.9)	88 (76.3)	472 (100.0)	2	>32
Colistin-nonsusceptible	49					0 (0.0)	18 (36.7)	13 (63.3)	9 (81.6)	2 (85.7)	1 (87.8)	0 (87.8)	0 (87.8)	6 (100.0)	1	>32
Piperacillin-tazobactam-nonsusceptible	2,100				0 (0.0)	7 (0.3)	129 (6.5)	464 (28.6)	449 (50.0)	306 (64.5)	114 (70.0)	63 (73.0)	89 (77.2)	479 (100.0)	4	>32
E. coli	12,054	2 (<0.1)	4 (<0.1)	196 (1.7)	4642 (40.2)	5194 (83.3)	1252 (93.7)	420 (97.1)	146 (98.4)	57 (98.8)	48 (99.2)	35 (99.5)	22 (99.7)	36 (100.0)	0.25	0.5
CRE	9									0 (0.0)	1 (11.1)	3 (44.4)	1 (55.6)	4 (100.0)	32	N/A
ESBL, nonCRE	2,384		0 (0.0)	5 (0.2)	151 (6.5)	738 (37.5)	779 (70.2)	384 (86.3)	140 (92.2)	56 (94.5)	46 (96.4)	32 (97.8)	21 (98.7)	32 (100.0)	0.5	2
Klebsiella spp.	6,046	1 (<0.1)	1 (<0.1)	44 (0.8)	1191 (20.5)	1937 (52.5)	927 (67.8)	442 (75.1)	262 (79.5)	214 (83.0)	102 (84.7)	90 (86.2)	128 (88.3)	707 (100.0)	0.25	>32
CRE	632					0 (0.0)	1 (0.2)	8 (1.4)	8 (2.7)	6 (3.6)	8 (4.9)	15 (7.3)	68 (18.0)	518 (100.0)	>32	>32
ESBL, nonCRE	1,758		0 (0.0)	1 (0.1)	21 (1.3)	196 (12.4)	369 (33.4)	311 (51.1)	240 (64.7)	208 (76.6)	94 (81.9)	72 (86.0)	60 (89.4)	186 (100.0)	1	>32
Latin America																
P. aeruginosa	770		0 (0.0)	2 (0.3)	6 (1.0)	71 (10.3)	380 (59.6)	132 (76.8)	53 (83.6)	34 (88.1)	18 (90.4)	15 (92.3)	10 (93.6)	49 (100.0)	0.5	8
Ceftazidime-nonsusceptible	199					0 (0.0)	6 (3.0)	36 (21.1)	41 (41.7)	27 (55.3)	17 (63.8)	14 (70.9)	9 (75.4)	49 (100.0)	4	>32
Meropenem-nonsusceptible	250		0 (0.0)	1 (0.4)	0 (0.4)	5 (2.4)	56 (24.8)	54 (46.4)	26 (56.8)	24 (66.4)	14 (72.0)	15 (78.0)	9 (81.6)	46 (100.0)	2	>32
Colistin-nonsusceptible	6					0 (0.0)	4 (66.7)	0 (66.7)	0 (66.7)	0 (66.7)	0 (66.7)	1 (83.3)	1 (100.0)		0.5	N/A
Piperacillin-tazobactam-nonsusceptible	213					0 (0.0)	12 (5.6)	47 (27.7)	46 (49.3)	34 (65.3)	14 (71.8)	13 (77.9)	5 (80.3)	42 (100.0)	4	>32
E. coli	1,046		0 (0.0)	24 (2.3)	369 (37.6)	382 (74.1)	164 (89.8)	57 (95.2)	21 (97.2)	6 (97.8)	4 (98.2)	8 (98.9)	2 (99.1)	9 (100.0)	0.25	1
CRE	3										0 (0.0)	1 (33.3)	0 (33.3)	2 (100.0)	>32	N/A
ESBL, nonCRE	377			0 (0.0)	17 (4.5)	110 (33.7)	146 (72.4)	57 (87.5)	21 (93.1)	6 (94.7)	4 (95.8)	7 (97.6)	2 (98.1)	7 (100.0)	0.5	2
Klebsiella spp.	934	0 (0.0)	1 (0.1)	12 (1.4)	163 (18.8)	260 (46.7)	126 (60.2)	78 (68.5)	35 (72.3)	19 (74.3)	27 (77.2)	23 (79.7)	35 (83.4)	155 (100.0)	0.5	>32
CRE	144	0 (0.0)	1 (0.7)	0 (0.7)	0 (0.7)	0 (0.7)	0 (0.7)	1 (1.4)	0 (1.4)	1 (2.1)	9 (8.3)	13 (17.4)	22 (32.6)	97 (100.0)	>32	>32
ESBL, nonCRE	350		0 (0.0)	1 (0.3)	6 (2.0)	51 (16.6)	78 (38.9)	63 (56.9)	34 (66.6)	18 (71.7)	18 (76.9)	10 (79.7)	13 (83.4)	58 (100.0)	1	>32
Asia-Pacific (APAC)																
P. aeruginosa	625	0 (0.0)	1 (0.2)	0 (0.2)	3 (0.6)	83 (13.9)	317 (64.6)	97 (80.2)	32 (85.3)	33 (90.6)	10 (92.2)	4 (92.8)	1 (93.0)	44 (100.0)	0.5	4
Ceftazidime-nonsusceptible	154					0 (0.0)	8 (5.2)	29 (24.0)	28 (42.2)	32 (63.0)	9 (68.8)	4 (71.4)	1 (72.1)	43 (100.0)	4	>32
Meropenem-nonsusceptible	172				0 (0.0)	5 (2.9)	42 (27.3)	31 (45.3)	14 (53.5)	26 (68.6)	9 (73.8)	4 (76.2)	0 (76.2)	41 (100.0)	2	>32
Colistin-nonsusceptible	10					0 (0.0)	3 (30.0)	2 (50.0)	1 (60.0)	1 (70.0)	0 (70.0)	0 (70.0)	0 (70.0)	3 (100.0)	1	>32
Piperacillin-tazobactam-nonsusceptible	159					0 (0.0)	9 (5.7)	35 (27.7)	30 (46.5)	32 (66.7)	10 (73.0)	4 (75.5)	1 (76.1)	38 (100.0)	4	>32
E. coli	732	0 (0.0)	1 (0.1)	17 (2.5)	260 (38.0)	261 (73.6)	115 (89.3)	29 (93.3)	14 (95.2)	6 (96.0)	4 (96.6)	4 (97.1)	7 (98.1)	14 (100.0)	0.25	1
CRE	9									0 (0.0)	1 (11.1)	0 (11.1)	3 (44.4)	5 (100.0)	>32	N/A
ESBL, nonCRE	267			0 (0.0)	20 (7.5)	82 (38.2)	98 (74.9)	27 (85.0)	14 (90.3)	6 (92.5)	3 (93.6)	4 (95.1)	4 (96.6)	9 (100.0)	0.5	2
Klebsiella spp	756	0 (0.0)	1 (0.1)	9 (1.3)	179 (25.0)	269 (60.6)	91 (72.6)	57 (80.2)	34 (84.7)	24 (87.8)	7 (88.8)	11 (90.2)	9 (91.4)	65 (100.0)	0.25	16
CRE	52					0 (0.0)	1 (1.9)	0 (1.9)	0 (1.9)	0 (1.9)	1 (3.8)	1 (5.8)	2 (9.6)	47 (100.0)	>32	>32
ESBL, nonCRE	216			0 (0.0)	4 (1.9)	31 (16.2)	39 (34.3)	44 (54.6)	33 (69.9)	24 (81.0)	6 (83.8)	10 (88.4)	7 (91.7)	18 (100.0)	1	32

[a] Criteria as published by CLSI [2017] and EUCAST [2017]

- Among *P. aeruginosa*, 22.0% were CAZ-NS (range 13.6% [ANZ] to 27.4% [EU]); 25.9% were TZP-NS (range 20.5% [NA] to 31.2% [EU]); 24.7% were MER-NS (range 7.1% [ANZ] to 32.4% [LA]); and 0.7% were COL-NS (range 0.2% [ANZ] to 1.6% [APAC]) (Table 1 and Table 2)
- Among all *E. coli* and *Klebsiella* spp. isolates, 0.2% and 8.5%, respectively, were CRE and 18.7% and 22.2%, respectively, were ESBL, non-CRE
- The modal MIC values for C-T were similar across geographic regions and species groups: 0.5 mg/L for *P. aeruginosa*; 0.25 mg/L for *Klebsiella* spp.; and 0.12-0.25 mg/L for *E. coli* (Table 1)
- The activities of C-T and 4 comparators against *P. aeruginosa*, *E. coli*, and *Klebsiella* spp. are shown in Table 2
- Overall, C-T had potent activity against *Klebsiella* spp. and *E. coli*; only COL and MER were more active
  - C-T had excellent activity against *E. coli* (98.3/97.2 %S [CLSI/EUCAST]), including ESBL, non-CRE *E. coli* (92.1/86.2 %S[CLSI/EUCAST])
  - Against *K. pneumoniae*, C-T was slightly less active (84.3/81.0%S [CLSI/EUCAST])
- For *P. aeruginosa*, C-T was the most active beta-lactam (92.2%S [CLSI and EUCAST])
  - Among comparators, only COL was more active (99.3%S [CLSI and EUCAST]), while 78.0% (CLSI and EUCAST) of isolates were S to CAZ and 75.3% (CLSI and EUCAST) were S to MER
  - For MER-NS *P. aeruginosa*, 72.1% (CLSI and EUCAST) were S to C-T; 65.9% (CLSI and EUCAST) CAZ-NS and 84.2% (CLSI and EUCAST) of COL-NS isolates were S to C-T
- Table 3 shows C-T and comparator %S for each continent and resistant phenotype
- More variability between regions was observed for *Klebsiella* spp., ranging from 64.7–93.%S for ESBL, non-CRE *Klebsiella* spp.
- For *P. aeruginosa*, the C-T %S range was 88.1–96.9%, and C-T activity against CAZ-NS ranged from 55.3–80.2% and for MER-NS ranged from 64.6–87.5%.



[†] CLSI [2017]
[‡] EUCAST [2017]

Table 2 Activity of ceftolozane-tazobactam and comparator antimicrobial agents when tested against 2011–2016 isolates

Organism group (no. tested) / antimicrobial agent	CLSI[†]		EUCAST[†]		$MIC_{50/90}$ (mg/L)
	%S	%R	%S	%R	
P. aeruginosa (14,440)					
Ceftolozane-tazobactam	92.2	6.0	92.2	7.8	0.5 / 4
Ceftazidime	78.0	16.8	78.0	22.0	2 / >16
Colistin	99.3	0.7	99.3	0.7	1 / 2
Meropenem	75.3	17.9	75.3	11.1	0.5 / >8
Piperacillin-tazobactam	74.1	13.7	74.1	25.9	8 / >64
Ceftazidime-nonsusceptible *P. aeruginosa* (3,172)					
Ceftolozane-tazobactam	65.9	27.0	65.9	34.1	4 / >32
Ceftazidime	0.0	76.6	0.0	100.0	>16 / >16
Colistin	98.9	1.1	98.9	1.1	1 / 2
Meropenem	35.7	53.8	35.7	37.9	8 / >8
Piperacillin-tazobactam	7.5	58.1	7.5	92.5	>64 / >64
Meropenem-nonsusceptible *P. aeruginosa* (3,559)					
Ceftolozane-tazobactam	72.1	23.0	72.1	27.9	2 / >32
Ceftazidime	42.7	46.4	42.7	57.3	16 / >16
Colistin	98.9	1.1	98.9	1.1	1 / 2
Meropenem	0.0	72.7	0.0	45.0	8 / >8
Piperacillin-tazobactam	32.8	37.1	32.8	67.2	64 / >64
Colistin-nonsusceptible *P. aeruginosa* (101)					
Ceftolozane-tazobactam	84.2	12.9	84.2	15.8	1 / 32
Ceftazidime	65.3	24.8	65.3	34.7	4 / >16
Colistin	0.0	100.0	0.0	100.0	4 / >4
Meropenem	62.4	25.7	62.4	13.9	1 / >8
Piperacillin-tazobactam	64.4	18.8	64.4	35.6	8 / >64
Piperacillin-tazobactam-nonsusceptible *P. aeruginosa* (3,741)					
Ceftolozane-tazobactam	71.8	21.9	71.8	28.2	2 / >32
Ceftazidime	21.6	62.8	21.6	78.4	>16 / >16
Colistin	99.0	1.0	99.0	1.0	1 / 2
Meropenem	36.0	53.6	36.0	37.2	8 / >8
Piperacillin-tazobactam	0.0	52.6	0.0	100.0	>64 / >64
E. coli (23,457)					
Ceftolozane-tazobactam	98.3	1.2	97.2	2.8	0.25 / 0.5
Ceftazidime	87.0	10.6	82.8	13.0	0.25 / 16
Colistin			99.5	0.5	≤0.5 / ≤0.5
Meropenem	99.8	0.2	99.8	0.1	≤0.06 / ≤0.06
Piperacillin-tazobactam	93.2	3.7	89.7	6.8	2 / 16
CRE *E. coli* (43)					
Ceftolozane-tazobactam	0.0	93.0	0.0	100.0	32 / >32
Ceftazidime	2.3	95.3	0.0	97.7	>32 / >32
Colistin			97.7	2.3	≤0.5 / ≤0.5
Meropenem	2.3	86.0	14.0	37.2	8 / >8
Piperacillin-tazobactam	2.3	95.3	0.0	97.7	>64 / >64
ESBL, nonCRE *E. coli* (4,390)					
Ceftolozane-tazobactam	92.1	5.5	86.2	13.8	0.5 / 2
Ceftazidime	31.8	55.6	9.2	68.2	16 / >16
Colistin			99.3	0.7	≤0.5 / ≤0.5
Meropenem	99.9	0.0	100.0	0.0	≤0.06 / ≤0.06
Piperacillin-tazobactam	80.7	9.3	67.4	19.3	8 / 64
Klebsiella spp. (13,418)					
Ceftolozane-tazobactam	84.3	13.4	81.0	19.0	0.25 / 32
Ceftazidime	74.0	23.7	71.6	26.0	0.25 / >16
Colistin			95.8	4.2	≤0.5 / 1
Meropenem	91.1	8.1	91.9	6.2	≤0.06 / 0.5
Piperacillin-tazobactam	78.2	17.0	72.8	21.8	4 / >64
CRE *Klebsiella* spp. (1,134)					
Ceftolozane-tazobactam	2.0	97.3	1.1	98.9	>32 / >32
Ceftazidime	1.9	97.0	1.4	98.1	>16 / >16
Colistin			70.4	29.6	≤0.5 / >4
Meropenem	0.9	96.0	4.0	73.6	>8 / >8
Piperacillin-tazobactam	0.4	98.2	0.2	99.6	>64 / >64
ESBL, nonCRE *Klebsiella* spp. (2,980)					
Ceftolozane-tazobactam	66.8	23.1	53.3	46.7	1 / >32
Ceftazidime	20.3	69.5	9.8	79.7	>16 / >16
Colistin			95.7	4.3	≤0.5 / 1
Meropenem	97.7	0.0	100.0	0.0	≤0.06 / 0.12
Piperacillin-tazobactam	46.9	35.7	33.1	53.1	32 / >64

Criteria as published by CLSI [2017] and EUCAST [2017]

Conclusions

- Ceftolozane-tazobactam activity was assessed against 51,315 isolates of *P. aeruginosa*, *E. coli*, and *Klebsiella* spp. collected from 88 PACTS hospitals in APAC, ANZ, EU, LA, and NA from 2011 through 2016
- Ceftolozane-tazobactam demonstrated good activity overall against *E. coli*, *Klebsiella* spp., and ESBL, non-CRE *E. coli*, but lacked activity against CR *E. coli* and *Klebsiella* spp.
- For *P. aeruginosa*, C-T demonstrated potent activity in all regions and maintained activity against most isolates resistant to CAZ, MER, TZP, or COL
- Among the antimicrobials tested, C-T was the most active β-lactam against *P. aeruginosa* and, except for MER, was also the most active β-lactam against *E. coli* and *Klebsiella* spp.
- Ceftolozane-tazobactam may represent a valuable treatment option for serious gram-negative infections in hospitalized patients worldwide

Table 3 Susceptibility summary of antimicrobials tested against isolates stratified by continent

Organism/ organism group	% susceptible[†]				
	Ceftolozane-tazobactam	Ceftazidime	Meropenem	Colistin	Piperacillin-tazobactam
P. aeruginosa (14,440)	92.2	78	75.3	99.3	74.1
Australia / New Zealand (596)	96.5	86.4	93	99.8	83.4
North America (including USA) (5,708)	96.9	84.4	80.7	99.4	79.5
Europe (6,741)	88.6	72.6	70.4	99.3	68.8
Latin America (770)	88.1	74.2	67.5	99.2	72.3
APAC without Australia, New Zealand, or China (625)	90.6	75.4	72.4	98.4	74.5
Ceftazidime-nonsusceptible *P. aeruginosa* (3,172)	65.9	0	35.7	98.9	7.5
Australia / New Zealand (81)	74.1	0	72.8	98.8	12.3
North America (including USA) (891)	80.2	0	43.7	99.3	6.7
Europe (1,847)	60	0	31.6	98.9	6.8
Latin America (199)	55.3	0	26.6	99	14.1
APAC without Australia, New Zealand, or China (154)	63	0	29.9	96.8	9.7
Meropenem-nonsusceptible *P. aeruginosa* (3,559)	72.1	42.7	0	98.9	32.8
Australia / New Zealand (42)	76.2	47.6	0	100	33.3
North America (including USA) (1,100)	87.5	54.5	0	99.1	41.4
Europe (1,995)	64.6	36.7	0	99	27.2
Latin America (250)	66.4	41.6	0	99.2	37.2
APAC without Australia, New Zealand, or China (172)	68.6	37.2	0	96.5	36
Colistin-nonsusceptible *P. aeruginosa* (101)	84.2	65.3	62.4	0	64.4
Australia / New Zealand (1)	0	0	100	0	0
North America (including USA) (35)	91.4	82.9	71.4	0	80
Europe (49)	85.7	57.1	59.2	0	55.1
Latin America (6)	66.7	66.7	66.7	0	83.3
APAC without Australia, New Zealand, or China (10)	70	50	40	0	50
Piperacillin-tazobactam-nonsusceptible *P. aeruginosa* (3,741)	71.8	21.6	36	99	0
Australia / New Zealand (99)	79.8	28.3	71.7	99	0
North America (including USA) (1,170)	86.1	29	44.8	99.4	0
Europe (2,100)	64.5	18	30.9	99	0
Latin America (213)	65.3	19.7	26.3	99.5	0
APAC without Australia, New Zealand, or China (159)	66.7	12.6	30.8	96.9	0
E. coli (23,457)	98.3	87	99.8	99.5[‡]	93.2
Australia / New Zealand (653)	99.7	94	100	99.7[‡]	96.3
North America (including USA) (8,972)	98.6	89.5	99.7	99.7[‡]	95.2
Europe (12,054)	98.4	87.1	99.9	99.5[‡]	91.7
Latin America (1,046)	97.2	70.6	99.7	99.2[‡]	91.5
APAC without Australia, New Zealand, or China (732)	95.2	73.2	98.8	98.8[‡]	92.9
CRE *E. coli* (43)	0	2.3	2.3	97.7[‡]	2.3
Australia / New Zealand (0)					
North America (including USA) (22)	0	4.5	4.5	95.5[‡]	0
Europe (9)	0	0	0	100.0[‡]	0
Latin America (3)	0	0	0	100.0[‡]	0
APAC without Australia, New Zealand, or China (9)	0	0	0	100.0[‡]	11.1
ESBL, nonCRE *E. coli* (4,390)	92.1	31.8	99.9	99.3[‡]	80.7
Australia / New Zealand (76)	97.4	48.7	100	100.0[‡]	86.8
North America (including USA) (1,286)	91.8	28.5	99.8	99.7[‡]	83.2
Europe (2,384)	92.2	35.3	99.9	99.2[‡]	77.9
Latin America (377)	93.1	19.1	100	99.2[‡]	83.2
APAC without Australia, New Zealand, or China (267)	90.3	30	100	98.5[‡]	87.6
Klebsiella spp. (13,418)	84.3	74	91.1	95.8[‡]	78.2
Australia / New Zealand (343)	98.5	94.5	99.1	98.8[‡]	93.6
North America (including USA) (5,339)	90.9	85.7	94.1	97.6[‡]	87.4
Europe (6,046)	79.5	66.5	89.1	94.3[‡]	71.3
Latin America (934)	72.3	52.1	82.9	92.3[‡]	64.3
APAC without Australia, New Zealand, or China (756)	84.7	68.3	92.7	97.3[‡]	78.2
CRE *Klebsiella* spp. (1,134)	2	1.9	0.9	70.4[‡]	0.4
Australia / New Zealand (3)	0	0	0	100.0[‡]	0
North America (including USA) (303)	1	0	0.7	79.9[‡]	0.3
Europe (632)	2.7	3	1.3	66.5[‡]	0.5
Latin America (144)	1.4	1.4	0	63.2[‡]	0
APAC without Australia, New Zealand, or China (52)	1.9	0	0	82.4[‡]	1.9
ESBL, nonCRE *Klebsiella* spp. (2,980)	66.8	20.3	97.7	95.7[‡]	46.9
Australia / New Zealand (30)	93.3	46.7	100	100.0[‡]	43.3
North America (including USA) (626)	70.3	26.7	97.4	95.3[‡]	49.7
Europe (1,758)	64.7	20	98.1	95.5[‡]	44.9
Latin America (350)	66.6	12.9	95.4	95.9[‡]	50.1
APAC without Australia, New Zealand, or China (216)	69.9	13	98.6	97.2[‡]	49.8

[†] CLSI [2017]
[‡] EUCAST [2017]

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