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Antimicrobial Activity of Ceftolozane-Tazobactam Tested against Contemporary (2014-2016) Gram-Negative Organisms Collected from European Medical Centres

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Revised Abstract

Background: Ceftolozane-tazobactam (C-T) is an antibacterial combination consisting of a novel antipseudomonal cephalosporin and a β-lactamase inhibitor. C-T was approved by the US Food and Drug Administration in 2014 and by the European Medicine Agency in 2015 to treat complicated urinary tract infections, acute pyelonephritis, and complicated intra-abdominal infections. The Program to Assess Ceftolozane-Tazobactam Susceptibility (PACTS) monitors C-T resistance among gram-negative isolates worldwide.

Methods and Materials: A total of 18,285 gram-negative bacilli (GNB), including 13,289 *Enterobacteriaceae* (ENT) and 3,284 *Pseudomonas aeruginosa* (PSA), were collected in 2014 through 2016 from 42 European hospitals and tested for susceptibility by CLSI broth microdilution method in a central monitoring laboratory (JMI Laboratories). Other antibiotics tested were amikacin (AMK), cefepime (FEP), ceftazidime (CAZ), colistin (COL), levofloxacin (LVX), meropenem (MER), and piperacillin-tazobactam (TZP). The laboratory identified carbapenem-resistant ENT (CRE; resistant to doripenem, imipenem, or meropenem); extended-spectrum beta-lactamase (ESBL, non-CRE); ceftazidime-nonsusceptible (CAZ-NS) PSA; meropenem-nonsusceptible (MER-NS) PSA; multidrug-resistant (MDR); and extensively drug-resistant (XDR) phenotypes. EUCAST 2017 clinical breakpoints were applied.

Results: C-T inhibited 88.4% of ENT at the susceptible (S) breakpoint of ≤1 mg/L. ENT isolates were 95.8%S to AMK, 79.4%S to FEP, 76.1%S to CAZ, 82.1%S to COL, 72.9%S to LVX, 97.1%S to MER, and 81.6%S to TZP. A total of 2,308 ENT isolates had an ESBL (non-CRE) phenotype: 71.8%S to C-T, 89.6%S to AMK, 13.6%S to FEP, 10.0%S to CAZ, 93.4%S to COL, 27.6%S to LVX, 99.4%S to MER, and 53.5%S to TZP. A total of 389 (2.9%) ENT isolates were CRE; <5% were S to any beta-lactam tested, 37.3% were S to AMK, and 66.0% were S to COL. Of the 2,467 (18.6%) MDR ENT isolates, AMK (78.5%S), COL (73.1%S), and MER (84.4%S) were the most active, 51.1% were S to C-T, and the remaining comparators were ≤30.6%S.

For PSA, C-T inhibited 90.1% at the S breakpoint of ≤4 mg/L. PSA isolates were 83.4%S to AMK, 79.7%S to FEP, 75.1%S to CAZ, 99.2%S to COL, 61.9%S to LVX, 72.3%S to MER, and 72.5%S to TZP. A total of 1,040 PSA were MDR (31.7%). The most active drugs against MDR PSA were COL (98.8% S) and C-T (69.6%S), 51.3% were S to AMK, and the remaining drugs were ≤40.3%S.

Conclusions: C-T demonstrated potent activity against a large collection of contemporary GNB European isolates. For ENT, AMK and MER were the most active followed by C-T. AMK, COL, and MER were more active against non-CRE ESBL and CRE. For PSA, including MDR isolates, C-T was the most potent antimicrobial agent tested except COL.

Organism antibacterial agent	Number of isolates	% susceptible[a]							
		C-T	FEP	CAZ	MER	TZP	LVX	AMK	COL
ENT	13,289	88.4	79.4	76.1	97.1	81.6	72.9	95.8	82.1
ESBL (non-CRE)	2,308	71.8	13.6	10.0	99.4	53.5	27.6	89.6	93.4
CRE	389	3.1	3.3	5.4	4.6	1.8	8.8	37.3	66.0
MDR	2,467	51.1	22.6	17.7	84.4	30.6	15.2	78.5	73.1
XDR	478	10.5	4.2	4.4	31.6	8.8	2.1	40.4	56.3
PSA	3,284	90.1	79.7	75.1	72.3	72.5	61.9	83.4	99.2
MDR	1,040	69.6	40.3	33.3	22.6	23.8	9.9	51.3	98.8
XDR	639	52.1	18.2	13.1	8.3	4.5	1.9	31.8	98.1
CAZ-NS	817	62.2	28.8	0.0	31.8	9.2	22.3	52.0	98.9
MER-NS	909	66.2	42.5	38.7	0.0	29.6	18.9	50.8	98.9

[a] EUCAST (2017)

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 β-lactam agent spectrum
- Ceftolozane-tazobactam (C-T) was approved by the US Food and Drug Administration in 2014 and by the European Medicine Agency in 2015 to treat complicated urinary tract infections, acute pyelonephritis, and complicated intra-abdominal infections when combined with metronidazole
  - Currently a phase 3 study for treatment of hospital-associated/ventilator-associated pneumonia is underway
- The Program to Assess Ceftolozane-Tazobactam Susceptibility (PACTS) monitors C-T resistance among gram-negative (GN) isolates worldwide

Materials and Methods

- A total of 18,285 gram-negative bacilli (GNB), including 13,289 *Enterobacteriaceae* (ENT) and 3,284 *Pseudomonas aeruginosa* (PSA), were collected from 2014 through 2016 from 42 European hospitals and tested for susceptibility against ceftolozane-tazobactam (C-T) by CLSI broth microdilution method in a central monitoring laboratory (JMI Laboratories)
- Other antibiotics tested were amikacin (AMK), cefepime (FEP), ceftazidime (CAZ), colistin (COL), levofloxacin (LVX), meropenem (MER), and piperacillin-tazobactam (TZP)
- The laboratory identified resistance phenotypes that included carbapenem-resistant ENT (CRE), which were resistant to doripenem, imipenem, and/or meropenem; extended-spectrum beta-lactamase (ESBL, non-CRE); ceftazidime-nonsusceptible (CAZ-NS) PSA; meropenem-nonsusceptible (MER-NS) PSA; multidrug-resistant (MDR); and extensively drug-resistant (XDR)
- Classifications were based on the following recommended parameters:
  - MDR = nonsusceptible (NS) to at least 3 antimicrobial classes[1]
  - XDR = susceptible (S) to 2 or fewer antimicrobial classes[1]
  - ESBL isolates analyzed were non-carbapenem resistant (non-CRE ESBL), because ESBL phenotype may also include carbapenemase-producing ENT
    - ESBL criteria used were according to CLSI M100[2]
- EUCAST (2017)[3] clinical breakpoints were applied
  - For C-T, ENT breakpoints are ≤1.0 S / >1.0 resistant (R), and *Pseudomonas* spp. breakpoints are ≤4.0 S / >4.0 R
- CLSI (2017)[2] C-T breakpoints for ENT are ≤2.0 mg/L S, 4.0 mg/L intermediate (I), and ≥8.0 mg/L R, and *Pseudomonas* spp. C-T breakpoints are ≤4.0 mg/L S, 8.0 mg/L I, and ≥16.0 mg/L R

Results

- The 10 most frequently isolated GN species in this study are shown in Figure 1
  - The top 4 species, *Escherichia coli* (EC), PSA, *Klebsiella pneumoniae* (KP), and *Enterobacter cloacae* complex accounted for 79% of the isolates
- The infection types included in this study and the most common GN species isolated from each are shown in Table 1
  - EC was the most frequent isolate from bloodstream infections, intra-abdominal infections, and urinary tract infections, and PSA was the most common isolate from pneumonia in hospitalized patients and skin and soft tissue infections
- The % susceptible[2,3] MIC_{50} and MIC_{90} for C-T and antimicrobial comparators are shown in Table 2 for all organism groups and resistant phenotypes examined in this study
  - The C-T MIC distributions for the 4 most common ENT are shown in Figure 2

Table 1 Most common infection types in PACTS (2014-2016) and top 4 GN species isolated from each

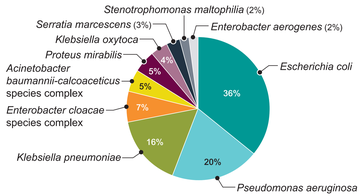
Infection type/species	Number of isolates
Bloodstream infection	3,986
Enterobacter cloacae complex	257
Escherichia coli	2,292
Klebsiella pneumoniae	894
Pseudomonas aeruginosa	543
Intra-abdominal infection	1,065
Enterobacter cloacae complex	89
Escherichia coli	644
Klebsiella pneumoniae	197
Pseudomonas aeruginosa	135
Pneumonia in hospitalized patients	3,235
Acinetobacter baumannii-calcoaceticus species complex	453
Escherichia coli	619
Klebsiella pneumoniae	705
Pseudomonas aeruginosa	1,458
Skin and skin structure infection	2,286
Enterobacter cloacae	303
Escherichia coli	772
Klebsiella pneumoniae	358
Pseudomonas aeruginosa	853
Urinary tract infection	2,596
Escherichia coli	1,680
Klebsiella pneumoniae	478
Proteus mirabilis	188
Pseudomonas aeruginosa	250

Table 2 Activity of C-T and comparators against organism groups and resistant phenotypes in PACTS (2014-2016)

Antimicrobial agent	MIC_{50} (mg/L)	MIC_{90} (mg/L)	CLSI[a] %S	CLSI[a] %R	EUCAST[a] %S	EUCAST[a] %R
Enterobacteriaceae[b] (n=13,289)						
Ceftolozane-tazobactam	0.25	2	91.5	6.6	88.4	11.6
Amikacin	2	4	97.6	1.3	95.8	2.4
Cefepime	≤0.5	>16	81.4	15.4	79.4	16.9
Ceftazidime	0.25	32	80.3	17.3	76.1	19.7
Colistin	≤0.5	>8			82.1	17.9
Levofloxacin	≤0.12	>4	77.4	19.9	72.9	24.3
Meropenem	0.03	0.06	96.7	2.9	97.1	2
Piperacillin-tazobactam	2	64	85.8	8.8	81.6	14.2
CRE (n=389)						
Enterobacter cloacae complex	>32	>32	4.9	93.3	3.1	96.9
Amikacin	16	>32	51.9	20.1	37.3	48.1
Cefepime	>16	>16	4.9	91.5	3.3	92.8
Ceftazidime	>32	>32	5.9	93.8	5.4	94.1
Colistin	≤0.5	>8			66	34
Levofloxacin	>4	>4	13.9	84.3	8.8	88.4
Meropenem	32	>32	1.3	95.4	4.6	69.4
Piperacillin-tazobactam	>64	>64	2.3	95.4	1.8	97.7
E. coli (n=6,027)						
Ceftolozane-tazobactam	0.25	0.5	98.4	1.2	97.3	2.7
Amikacin	2	4	99.5	0.1	98	0.5
Cefepime	≤0.5	>16	82.4	14.0	80.5	15.8
Ceftazidime	0.25	16	86.2	11.1	80.7	13.8
Colistin	≤0.5	≤0.5			99.5	0.5
Levofloxacin	≤0.12	>4	70.8	26	69.1	29.7
Meropenem	≤0.015	0.03	99.9	0.1	99.9	0.1
Piperacillin-tazobactam	2	16	92.1	4.3	88.5	7.9
EC non-CRE ESBL (n=1,268)						
Ceftolozane-tazobactam	0.5	2	93.1	5.2	87.8	12.2
Amikacin	4	8	98	0.4	92	2
Cefepime	>16	>16	18.4	66.0	12.2	74.2
Ceftazidime	16	>32	34.7	52.5	8.9	65.3
Colistin	≤0.5	≤0.5			98.9	1.1
Levofloxacin	>4	>4	24.5	71.3	22.3	76.2
Meropenem	≤0.015	0.03	99.8	0.1	99.9	0
Piperacillin-tazobactam	4	>64	79.9	10.9	67.3	20.1
EC MDR (n=686)						
Ceftolozane-tazobactam	0.5	4	87.9	9.5	80.5	19.5
Amikacin	4	16	95.9	1.2	84.3	4.1
Cefepime	>16	>16	19.3	70.9	9.9	75.1
Ceftazidime	16	>32	31.2	60.8	16	68.8
Colistin	≤0.5	≤0.5			97.4	2.6
Levofloxacin	>4	>4	6.3	90.4	4.2	94.2
Meropenem	0.03	0.06	98.8	0.9	99.1	0.6
Piperacillin-tazobactam	16	>64	58.6	20.3	35.6	41.4
K. pneumoniae (n=2,648)						
Ceftolozane-tazobactam	0.5	>32	75.3	20.7	71.4	28.6
Amikacin	1	16	91	4.5	86.7	9
Cefepime	≤0.5	>16	59	38.3	58	40
Ceftazidime	0.5	>32	58.8	37.7	56.7	41.2
Colistin	≤0.5	1			93.1	6.9
Levofloxacin	≤0.12	>4	68.5	28.2	61.9	33.5
Meropenem	0.03	8	85.6	12.8	87.2	9.6
Piperacillin-tazobactam	4	>64	68.3	24.1	62	31.7
KP CRE (n=335)						
Ceftolozane-tazobactam	>32	>32	2.4	96.7	1.8	98.2
Amikacin	32	>32	47.2	20.3	32.8	52.8
Cefepime	>16	>16	2.1	95.8	0.9	97
Ceftazidime	>32	>32	2.4	97.1	2.1	97.6
Ceftriaxone	>8	>8	0.3	98.4	0.3	98.4
Colistin	≤0.5	>8			65.9	34.1
Levofloxacin	>4	>4	6	92.2	2.1	95.8
Meropenem	32	>32	0	97	3	75.5
Piperacillin-tazobactam	>64	>64	0.3	98.8	0	99.7
KP non-CRE ESBL (n=840)						
Ceftolozane-tazobactam	1	>32	61.3	26.5	50.1	49.9
Amikacin	2	16	93	6	85.5	7
Cefepime	>16	>16	10	82.5	7.7	87.4
Ceftazidime	32	>32	9	80.1	2.5	91
Colistin	≤0.5	1			94	6
Levofloxacin	4	>4	44.5	47.1	31.8	59.2
Meropenem	0.03	0.5	94.8	1.7	98.3	0
Piperacillin-tazobactam	32	>64	47.2	32.7	33.8	52.8
KP MDR (n=1,004)						
Ceftolozane-tazobactam	8	>32	36.2	54.3	27.3	72.7
Amikacin	4	>32	76.6	11.7	65.6	23.4
Cefepime	>16	>16	5.6	89.1	3.9	92.6
Ceftazidime	>32	>32	5.7	88.1	3.4	94.3
Colistin	≤0.5	>8			83.6	16.4
Levofloxacin	>4	>4	23.7	69.1	13.6	79.4
Meropenem	0.12	>32	62.2	33.9	66.1	25.2
Piperacillin-tazobactam	>64	>64	24.2	58.6	12.6	75.8
KP XDR (n=379)						
Ceftolozane-tazobactam	>32	>32	7.4	90.2	3.7	96.3
Amikacin	16	>32	51.2	19.8	35.9	48.8
Cefepime	>16	>16	1.3	96.6	0.8	97.9
Ceftazidime	>32	>32	2.1	97.6	1.1	98.1
Ceftriaxone	>8	>8	0.3	98.4	0.3	98.4
Colistin	≤0.5	>8			86	14
Levofloxacin	≤0.12	4	88.6	9.5	83.4	13.4
Meropenem	0.03	0.12	97.3	2.4	97.6	0.8
Piperacillin-tazobactam	2	64	76	10	69.7	24
P. aeruginosa (n=3,284)						
Ceftolozane-tazobactam	0.5	4	90.1	8.3	90.1	9.9
Amikacin	4	32	88.5	8.3	83.4	11.5
Ceftazidime	2	16	79.7	7.8	79.7	20.3
Cefepime	2	32	75.1	18.9	75.1	24.9
Colistin	1	2	99.2	0.8	99.2	0.8
Levofloxacin	0.5	>4	69.8	24.4	61.9	38.1
Meropenem	0.5	16	72.3	20.5	72.3	14.1
Piperacillin-tazobactam	4	>64	72.5	12.9	72.5	27.5
PSA MER-NS (n=909)						
Ceftolozane-tazobactam	2	>32	66.2	29	66.2	33.8
Amikacin	8	>32	63.3	27	50.8	36.7
Cefepime	16	>16	42.5	24.8	42.5	57.5
Ceftazidime	32	>32	38.7	50.3	38.7	61.3
Colistin	1	2	98.9	1.1	98.9	1.1
Levofloxacin	>4	>4	29.6	61.7	18.9	81.1
Meropenem	16	>32	8.3	79.7	8.3	62.4
Piperacillin-tazobactam	64	>64	4.5	48.5	4.5	95.5
Colistin	≤0.5	>8			52.7	37.3
Levofloxacin	>4	>4	5.3	90.2	1.3	96
Meropenem	32	>32	13.2	79.9	20.1	61.7
Piperacillin-tazobactam	>64	>64	1.6	93.4	0	98.4
Enterobacter cloacae species complex[c] (n=1,118)						
Ceftolozane-tazobactam	0.25	8	80.3	13.9	73.7	26.3
Amikacin	1	2	97.8	2.1	96.4	2.2
Cefepime	≤0.5	16	83.5	11.3	77.8	12.8
Ceftazidime	0.5	>32	67.9	30.5	64.6	32.1
Colistin	≤0.5	>8			86	14
Levofloxacin	≤0.12	4	88.6	9.5	83.4	13.4
Meropenem	0.03	0.12	97.3	2.4	97.6	0.8
Piperacillin-tazobactam	2	64	76	10	69.7	24
P. aeruginosa (n=3,284)						
Ceftolozane-tazobactam	0.5	4	90.1	8.3	90.1	9.9
Amikacin	4	32	88.5	8.3	83.4	11.5
Cefepime	2	16	79.7	7.8	79.7	20.3
Ceftazidime	2	32	75.1	18.9	75.1	24.9
Colistin	1	2	99.2	0.8	99.2	0.8
Levofloxacin	0.5	>4	69.8	24.4	61.9	38.1
Meropenem	0.5	16	72.3	20.5	72.3	14.1
Piperacillin-tazobactam	4	>64	72.5	12.9	72.5	27.5
PSA MER-NS (n=909)						
Ceftolozane-tazobactam	2	>32	66.2	29	66.2	33.8
Amikacin	8	>32	63.3	27	50.8	36.7
Cefepime	16	>16	42.5	24.8	42.5	57.5
Ceftazidime	32	>32	38.7	50.3	38.7	61.3
Colistin	1	2	98.9	1.1	98.9	1.1
Levofloxacin	>4	>4	29.6	61.7	18.9	81.1
Meropenem	16	>32	8.3	79.7	8.3	62.4
Piperacillin-tazobactam	64	>64	4.5	48.5	4.5	95.5
Colistin	≤0.5	>8			52.7	37.3
Levofloxacin	>4	>4	5.3	90.2	1.3	96
Meropenem	32	>32	13.2	79.9	20.1	61.7
Piperacillin-tazobactam	>64	>64	1.6	93.4	0	98.4
PSA CAZ-NS (n=817)						
Ceftolozane-tazobactam	2	>32	62.2	32.9	62.2	37.8
Amikacin	8	>32	63.7	28.1	52	36.3
Cefepime	16	>16	28.8	28.9	28.8	71.2
Ceftazidime	32	>32	0	76.1	0	100
Colistin	1	2	98.9	1.1	98.9	1.1
Levofloxacin	>4	>4	29.7	62.5	22.3	77.7
Meropenem	8	>32	31.8	58	31.8	44.9
Piperacillin-tazobactam	64	>64	9.2	47.7	9.2	90.8
PSA MDR (n=1,040)						
Ceftolozane-tazobactam	2	>32	69.6	26.1	69.6	30.4
Amikacin	8	>32	64.8	25.7	51.3	35.2
Cefepime	16	>16	40.3	23.7	40.3	59.7
Ceftazidime	32	>32	33.3	52.9	33.3	66.7
Colistin	1	2	98.8	1.2	98.8	1.2
Levofloxacin	>4	>4	24.4	65.1	9.9	90.1
Meropenem	8	>32	22.6	62.3	22.6	44
Piperacillin-tazobactam	64	>64	23.8	36.8	23.8	76.2
PSA XDR (n=639)						
Ceftolozane-tazobactam	4	>32	52.1	41.3	52.1	47.9
Amikacin	32	>32	48.4	38.2	31.8	51.6
Cefepime	16	>16	18.2	35.4	18.2	81.8
Ceftazidime	32	>32	13.1	70.9	13.1	86.9
Colistin	1	2	98.1	1.9	98.1	1.9
Levofloxacin	>4	>4	8.9	81.4	1.9	98.1
Meropenem	16	>32	8.3	79.7	8.3	62.4
Piperacillin-tazobactam	64	>64	4.5	48.5	4.5	95.5

[a] Criteria as published by CLSI [2017][2] and EUCAST [2017][3]
[b] Organisms include: *Citrobacter amalonaticus / farmeri* (2), *C. braakii* (30), *C. freundii* (166), *C. freundii* species complex (75), *C. koseri* (217), *C. werkmanii* (1), *C. youngae* (2), *Cronobacter sakazakii* (1), *Enterobacter aerogenes* (315), *E. amnigenus* (4), *E. asburiae* (24), *E. cancerogenus* (3), *E. cloacae* (821), *E. cloacae* species complex (273), *E. kobei* (5), *Escherichia coli* (6,027), *E. hermannii* (1), *E. vulneris* (1), gram-negative rods in the family *Enterobacteriaceae* (1), *Hafnia alvei* (37), *Klebsiella oxytoca* (621), *K. pneumoniae* (2,648), *K. variicola* (10), *Leclercia adecarboxylata* (2), *Morganella morganii* (304), *Pantoea agglomerans* (7), *Pluralibacter gergoviae* (3), *Proteus mirabilis* (808), *P. penneri* (5), *P. vulgaris* (105), *P. vulgaris* group (28), *Providencia rettgeri* (30), *P. stuartii* (55), *Raoultella ornithinolytica* (5), *R. planticola* (5), *Serratia fonticola* (1), *S. liquefaciens* (36), *S. marcescens* (586), *S. odorifera* (2), *S. plymuthica* (1), *S. rubidaea* (1), unspeciated *Cedecea* (1), unspeciated *Raoultella* (7), unspeciated *Serratia* (1), *Yersinia enterocolitica* (1)
[c] *Enterobacter cloacae* complex includes *E. asburiae* (24), *E. cloacae* (821), *E. cloacae* species complex (273)

Figure 1 Top 10 species isolated from 42 European hospitals in PACTS (2014-2016)



- For ENT, C-T inhibited 88.4% at the S breakpoint of ≤1 mg/L
  - ENT isolates were 95.8%S to AMK, 79.4%S to FEP, 76.1%S to CAZ, 82.1%S to COL, 72.9%S to LVX, 97.1%S to MER, and 81.6%S to TZP
  - A total of 2,308 isolates had an ESBL (non-CRE) phenotype: 71.8%S to C-T, 89.6%S to AMK, 13.6%S to FEP, 10.0%S to CAZ, 93.4%S to COL, 27.6%S to LVX, 99.4%S to MER, and 53.5%S to TZP
  - A total of 389 (2.9%) ENT isolates were CRE. For CRE <5.4% were S to any beta-lactam tested, 37.3% were S to AMK, and 66.0% were S to COL
  - In 2,467 (18.6%) MDR isolates, AMK (78.5%S), COL (73.1%S), and MER (84.4%S) were the most active; 51.1% were S to C-T; and the remaining comparators were ≤31%S
- For PSA, C-T inhibited 90.1% at the S breakpoint of ≤4 mg/L
  - PSA isolates were 83.4%S to AMK, 79.7%S to FEP, 75.1%S to CAZ, 99.2%S to COL, 61.9%S to LVX, 72.3%S to MER, and 72.5%S to TZP
- A total of 1,040 PSA were MDR (31.7%), and the most active drugs against MDR PSA were COL (98.8% S) and C-T (69.6%S) while 51.3% were S to AMK and the remaining drugs were ≤40%S
- The MIC distributions of C-T, MER, and TZP for PSA are shown in Figure 3

Conclusions

- C-T demonstrated potent activity against a large collection of contemporary GNB European isolates (PACTS 2014-2016)
- For ENT, AMK and MER were the most active followed by C-T
  - Against non-CRE ESBL, MER was the most active followed by COL, AMK, and C-T
- For PSA, including MDR isolates, C-T was the most active beta-lactam; only COL was more active
- These data indicate that C-T is an important antimicrobial therapy for hospitalized patients with GN infections

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References

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2. Clinical and Laboratory Standards Institute (2017). *M100-S27. Performance standards for antimicrobial susceptibility testing: 27th informational supplement*. Wayne, PA: CLSI.
3. EUCAST (2017). Breakpoint tables for interpretation of MICs and zone diameters. Version 7.0, January 2017. Available at http://www.eucast.org/clinical_breakpoints/. Accessed January 2017.

Figure 2 C-T MIC distribution for the 4 most common enteric pathogens (PACTS 2014-2016)

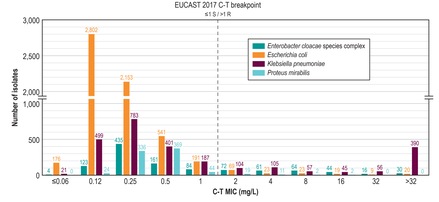
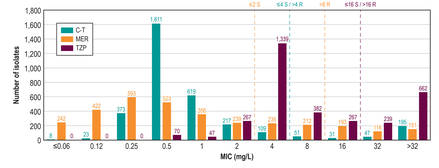


Figure 3 MIC distribution of C-T, MER, and TZP for PSA (PACTS 2014-2016)



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