Poster # 245

Ceftolozane/Tazobactam Activity Tested Against Aerobic Gram-negative Organisms Isolated From Intra-abdominal Infections in United States Hospitals (2013)

D.J. Farrell, H.S. Sader, R.K. Flamm, R.N. Jones

JMI Laboratories, North Liberty, IA, USA

David J. Farrell, Ph.D., D (ABMM)
JMI Laboratories
345 Beaver Kreek Ctr, Ste A
North Liberty, Iowa, 52317, USA
Tel: 319-665-3370
E-mail: david-farrell@jmilabs.com

AMENDED ABSTRACT

BACKGROUND: Timely and appropriate antimicrobial therapy is important for the management of intra-abdominal infection (IAI). Ceftolozane/tazobactam (TOL/TAZ) is a novel antibacterial with activity against *Pseudomonas aeruginosa* (PSA), including drug-resistant strains, and Enterobacteriaceae, including many ESBL-producing and MDR strains. TOL/TAZ is currently under clinical development for treatment of complicated IAI.
METHODS: 425 isolates (1 per patient) were collected in 27 hospitals in the USA from patients with IAI by the Program to Assess TOL/TAZ Susceptibility (PACTS) in 2013. Susceptibility (S) testing was performed by CLSI broth microdilution methods.
RESULTS: TOL/TAZ was potent ($MIC_{50/90}$, 0.25/1 µg/mL) against 364 Enterobacteriaceae inhibiting 95.6% of isolates at ≤8 µg/mL. *Escherichia coli* was the most common organism (43.5% of total) and had overall ESBL-/MDR-phenotype rates of 12.4/4.9%. All *E. coli* strains were S to meropenem (MEM) and 98.9% were inhibited at TOL/TAZ of ≤8 µg/mL ($MIC_{50/90}$, 0.25/0.5 µg/mL). *E. coli* S rates for gentamicin (GEN) and levofloxacin (LVX) were 85.9 and 72.3%, respectively. Among *Klebsiella* spp. (KSP; 2nd most common pathogen, 20.7%), ESBL/MDR rates were 18.2/13.6%. TOL/TAZ was active ($MIC_{50/90}$, 0.25/32 µg/mL; inhibited 89.8% at ≤8 µg/mL) against most KSP, but was less active against ESBL and MDR strains inhibiting only 43.8 and 25.0% at ≤8 µg/mL, respectively. TOL/TAZ was more active against MEM-S-ESBL phenotype KSP (Table). S rates to GEN and LVX were 92.0 and 88.6%, respectively. TOL/TAZ ($MIC_{50/90}$, 0.25/4 µg/mL) showed greater activity than ceftazidime (CAZ; $MIC_{50/90}$, 0.5/>32 µg/mL) and piperacillin/TAZ (PIP/TAZ; $MIC_{50/90}$, 4/32 µg/mL) against *Enterobacter* spp. PSA was the 3rd most common pathogen (13.6%); TOL/TAZ ($MIC_{50/90}$, 0.5/2 µg/mL) and amikacin ($MIC_{50/90}$, 2/8 µg/mL; 100.0% S) were the most active compounds tested. TOL/TAZ was 4- to 16-fold more active than CAZ ($MIC_{50/90}$, 2/32 µg/mL) when tested against PSA.

	% Susceptible (CLSI criteria)			
Organism (No. Tested)	TOL/TAZ*	PIP/TAZ	CAZ	MEM
All Enterobacteriaceae (364)	(95.6)ª	89.0	87.9	97.5
E. coli (185)	(98.9)ª	94.1	91.9	100.0
ESBL-phenotype (23)	(91.3)ª	78.3	34.8	100.0
MDR (9)	(77.8)ª	44.4	11.1	100.0
Klebsiella spp. (88)	(89.8)ª	83.0	86.4	89.8
ESBL-phenotype (16)	(43.8)ª	6.3	25.0	43.8
MEM-S-ESBL phenotype (7)	(71.4)	14.3	57.1	100.0
MDR (12)	(25.0)ª	0.0	8.3	25.0
Enterobacter spp. (41)	(95.1)ª	75.0	73.2	100.0
P. aeruginosa (58)	(98.3)ª	82.8	87.9	73.7
MDR (9)	(88.9)ª	22.2	55.5	0.0

ªInhibited at ≤8 µg/mL.

CONCLUSIONS: TOL/TAZ was very active against aerobic Gram-negative organisms isolated from IAIs in USA hospitals in 2013. TOL/TAZ coverage against Enterobacteriaceae was comparable to MEM and greater than PIP/TAZ and CAZ. TOL/TAZ activity against PSA was greater than MEM, PIP/TAZ, and CAZ.

INTRODUCTION

- Intra-abdominal infections (IAIs) can either be mono- or poly-microbial and often include anaerobes as well as aerobes. Gram-negative bacilli (increasingly drug-resistant strains) play a prominent role in IAIs.
- Among aerobic Gram-negative bacilli, *Escherichia coli* is the species isolated most frequently (in ~50% of cases) followed by other Enterobacteriaceae and *Pseudomonas aeruginosa*.
- Ceftolozane/tazobactam is a novel antibacterial with activity against *P. aeruginosa*, including multidrug-resistant (MDR) strains, and other common Gram-negative pathogens including most extended-spectrum β-lactamases (ESBL)–producing Enterobacteriaceae.
- In the Assessment of the Safety Profile and Efficacy of Ceftolozane/Tazobactam in Complicated Intra-abdominal Infection (ASPECT-cIAI) trial, ceftolozane/tazobactam plus metronidazole met its primary endpoint of noninferior efficacy to meropenem for clinical cure in patients with cIAI.
- In this study, we evaluated the activity of ceftolozane/tazobactam and comparator agents tested against Gram-negative organisms causing IAI in United States (USA) hospitals during 2013.

MATERIALS AND METHODS

Organism collection: The organism collection included only aerobic Gram-negative bacilli collected from hospitalized patients with a diagnosis of IAI. In 2013, a total of 425 unique patient organisms were consecutively collected from USA (27 hospitals) medical centers by the Program to Assess Ceftolozane/Tazobactam Susceptibility (PACTS). Species identification was performed at the participant medical center and confirmed at the monitoring laboratory (JMI Laboratories, North Liberty, IA, USA) using the VITEK 2 System (bioMerieux, Hazelwood, MO, USA) or MALDI-TOF (Bruker, Billerica, MA, USA), when necessary. Only 1 strain per patient infection episode was included in this surveillance study.

Susceptibility testing: Isolates were tested for susceptibility to multiple antimicrobial agents at a reference laboratory (JMI Laboratories) by standardized broth microdilution methods as described by the Clinical and Laboratory Standards Institute (CLSI) M07-A9 document. Minimum inhibitory concentration (MIC) results were interpreted according to CLSI criteria in M100-S24 (2014), as well as European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint tables (version 4.0, January 2014). *E. coli* and *Klebsiella* spp. isolates with a MIC of ≥2 µg/mL for ceftazidime or ceftriaxone or aztreonam were categorized as an ESBL-phenotype. Strains were stratified by susceptibility pattern to ceftazidime and meropenem. MDR, extensively drug-resistant (XDR), and pandrug-resistant (PDR) bacteria were classified as such as per recently recommended guidelines by Magiorakos et al (2012), using antimicrobial class representative agents and CLSI susceptibility MIC breakpoints. Classifications were based on the following recommended parameters: MDR = non-susceptible to ≥3 antimicrobial classes; XDR = susceptible to ≤2 antimicrobial classes; PDR = non-susceptible to all antimicrobial classes.

RESULTS

- Ceftolozane/tazobactam was very active (MIC required to inhibit the growth of 50%/90% of organisms [$MIC_{50/90}$], 0.25/1 µg/mL; 94.2/95.6% inhibited at ≤4/≤8 µg/mL) against 364 Enterobacteriaceae (**Table 1**). The MDR, XDR, and PDR rates in Enterobacteriaceae were 8.5%, 1.9%, and 0.0%, respectively.
- Against all 185 *E. coli* isolates, ceftolozane/tazobactam was very active ($MIC_{50/90}$, 0.25/0.5 µg/mL).
  - Ceftolozane/tazobactam retained activity against many of the MDR isolates, inhibiting 77.8% (7/9) at a MIC of ≤8 µg/mL (**Table 1**).
  - 91.3% (21/23) of ESBL-phenotype isolates were inhibited at a MIC of ≤8 µg/mL (**Table 1**).
  - Meropenem was the most potent ($MIC_{50/90}$, ≤0.06/≤0.06 µg/mL) agent overall against *E. coli* (**Table 2**).
  - Susceptibility rates (CLSI) ranged from 72.3% for levofloxacin to 100.0% for meropenem and tigecycline (**Table 2**).
- Ceftolozane/tazobactam demonstrated good activity ($MIC_{50/90}$, 0.25/8 µg/mL) against 88 isolates of *Klebsiella* spp., inhibiting 89.8% at a MIC ≤8 µg/mL (**Table 1**).
  - Ceftolozane/tazobactam potency was very high against all 72 non-ESBL-phenotype *Klebsiella* spp. ($MIC_{50/90}$, 0.25/0.5 µg/mL).
  - However, activity was much lower against the 16 ESBL-phenotype isolates (MIC_{50}, 32 µg/mL), 12 MDR (MIC_{50}, >32 µg/mL), and 6 XDR (MIC_{50}, >32 µg/mL), likely due to the co-carriage of carbapenemases in some of these strains as evidenced by an overall meropenem resistance rate for *Klebsiella* spp. of 9.1% (**Tables 1** and **2**).
  - For the 7 meropenem-susceptible, ESBL-phenotype *Klebsiella* spp., 71.4% (5/7) of isolates were inhibited at a MIC of ≤8 µg/mL (**Table 1**).
- Ceftolozane/tazobactam also demonstrated good activity against other Enterobacteriaceae; Enterobacter spp. ($MIC_{50/90}$, 0.25/4 µg/mL), *Citrobacter* spp. ($MIC_{50/90}$, 0.25/16 µg/mL; 3/19 isolates were 16 µg/mL), *Proteus mirabilis* ($MIC_{50/90}$, 0.5/0.5 µg/mL), and *Serratia marcescens* ($MIC_{50/90}$, 0.5/1 µg/mL; **Table 2**).
- Overall, ceftolozane/tazobactam was the most active agent ($MIC_{50/90}$, 0.5/2 µg/mL; **Table 2**) tested against the 58 *P. aeruginosa*, demonstrating at least 4-fold greater activity than ceftazidime ($MIC_{50/90}$, 2/32 µg/mL) and cefepime ($MIC_{50/90}$, 2/16 µg/mL), at least 8- to 16-fold greater activity than aztreonam ($MIC_{50/90}$, 8/>16 µg/mL) and piperacillin/tazobactam ($MIC_{50/90}$, 4/>64 µg/mL), and up to 4-fold greater activity than meropenem ($MIC_{50/90}$, 0.5/8 µg/mL; **Table 2**). Susceptibility rates (CLSI criteria) for β-lactam agents tested ranged from 72.4% for aztreonam to 87.9% for ceftazidime and cefepime (**Table 2**). All isolates were susceptible to colistin and amikacin (by CLSI criteria), whereas levofloxacin susceptibility was only 72.4% (**Table 2**).
- Importantly, ceftolozane/tazobactam retained potency against most (8/9) of 9 MDR strains (MIC_{50}, 2 µg/mL; 88.9% inhibited at ≤4 µg/mL) and 2/3 XDR strains of *P. aeruginosa* (**Table 1**).
- Ceftolozane/tazobactam had variable activity against the limited number of *Acinetobacter* spp. (only 3 isolates; **Table 1**).

Table 1. Cumulative MIC Distributions of Ceftolozane/Tazobactam Tested Against Gram-negative Pathogens by Resistance Phenotype

		Number of Isolates (Cumulative %) Inhibited at Ceftolozane/Tazobactam MIC (µg/mL)											
Organismª	No. of Isolates	≤0.12	0.25	0.5	1	2	4	8	16	32	>32	MIC_{50}	MIC_{90}
Enterobacteriaceae (all)	364	86 (23.6)	167 (69.5)	58 (85.4)	19 (90.7)	8 (92.9)	5 (94.2)	5 (95.6)	3 (96.4)	2 (97.0)	11 (100.0)	0.25	1
E. coli	185	67 (36.2)	86 (82.7)	19 (93.0)	7 (96.8)	3 (98.4)	1 (98.9)	0 (98.9)	0 (98.9)	0 (98.9)	2 (100.0)	0.25	0.5
MDR	9	0 (0.12)	1 (11.1)	2 (33.3)	3 (66.7)	0 (66.7)	1 (77.8)	0 (77.8)	0 (77.8)	0 (77.8)	2 (100.0)	1	-
non-ESBL-phenotype	162	67 (41.4)	82 (92.0)	11 (98.8)	1 (99.4)	1 (100.0)	-	-	-	-	-	0.25	0.25
ESBL-phenotype	23	0 (0.0)	4 (17.4)	8 (52.2)	6 (78.3)	2 (87.0)	1 (91.3)	0 (91.3)	0 (91.3)	0 (91.3)	2 (100.0)	0.5	4
Klebsiella spp.	88	14 (15.9)	42 (63.6)	13 (78.4)	4 (83.0)	3 (86.4)	0 (86.4)	3 (89.8)	0 (89.8)	1 (90.9)	8 (100.0)	0.25	32
MDR	12	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	0 (8.3)	2 (25.0)	0 (25.0)	1 (33.3)	8 (100.0)	>32	>32
XDR	6	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (16.7)	1 (33.3)	4 (100.0)	>32	-
non-ESBL-phenotype	72	13 (18.1)	42 (76.4)	13 (94.4)	3 (98.6)	1 (100.0)	-	-	-	-	-	0.25	0.5
ESBL-phenotype	16	1 (6.3)	0 (6.3)	0 (6.3)	1 (12.5)	2 (25.0)	0 (25.0)	3 (43.8)	0 (43.8)	1 (50.0)	8 (100.0)	32	>32
MEM-S-ESBL phenotype	7	1 (14.3)	0 (14.3)	0 (14.3)	1 (28.6)	2 (57.1)	0 (57.1)	1 (71.4)	0 (71.4)	0 (71.4)	2 (100.0)	2	-
MEM-S	79	1 (1.3)	42 (70.9)	13 (87.3)	4 (92.4)	3 (96.2)	0 (96.2)	1 (97.5)	0 (97.5)	0 (97.5)	2 (100.0)	0.25	1
Enterobacter spp.	41	3 (7.3)	19 (53.7)	7 (70.7)	3 (78.1)	2 (82.9)	4 (92.7)	1 (95.1)	0 (95.1)	1 (97.6)	1 (100.0)	0.25	4
CAZ-S	30	3 (10.0)	19 (73.3)	6 (93.3)	2 (100.0)	-	-	-	-	-	-	0.25	0.5
CAZ-NS	11	0 (0.0)	0 (0.0)	1 (9.1)	1 (18.2)	2 (36.4)	4 (72.3)	1 (81.8)	0 (81.8)	1 (90.9)	1 (100.0)	4	32
Citrobacter spp.	19	1 (5.3)	13 (73.7)	1 (79.0)	0 (79.0)	0 (79.0)	0 (79.0)	1 (84.2)	3 (100.0)	-	-	0.25	16
P. mirabilis	17	0 (0.0)	6 (35.3)	10 (94.1)	1 (100.0)	-	-	-	-	-	-	0.5	0.5
S. marcescens	10	0 (0.0)	0 (0.0)	6 (60.0)	4 (100.0)	-	-	-	-	-	-	0.5	1
Indole-positive *Proteus* spp.	4	1 (25.0)	1 (50.0)	2 (100.0)	-	-	-	-	-	-	-	0.25	-
P. aeruginosa	58	0 (0.0)	4 (6.9)	35 (67.2)	9 (82.8)	8 (96.6)	1 (98.3)	0 (98.3)	0 (98.3)	0 (98.3)	1 (100.0)	0.5	2
MDR	9	0 (0.0)	0 (0.0)	1 (11.1)	1 (22.2)	5 (77.8)	1 (88.9)	0 (88.9)	0 (88.9)	0 (88.9)	1 (100.0)	2	-
XDR	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (66.7)	0 (66.7)	0 (66.7)	0 (66.7)	0 (66.7)	1 (100.0)	2	-
Acinetobacter spp.	3	1 (33.3)	0 (33.3)	0 (33.3)	0 (33.3)	0 (33.3)	0 (33.3)	1 (66.7)	0 (66.7)	0 (66.7)	1 (100.0)	8	-

CAZ = ceftazidime; MEM = meropenem; NS = non-susceptible; S = susceptible.

Table 2. Antimicrobial Activity of Ceftolozane/Tazobactam and Various Comparator Agents Tested Against Gram-negative Pathogens Isolated From Intra-abdominal Infections Collected in the USA during 2013

	MIC (µg/mL)		%S/%I/%R[a]	
Organisms (No. Tested)/Antimicrobial Agent	50%	90%	CLSI[b]	EUCAST[c]
E. coli (185)				
Ceftolozane/tazobactam	0.25	0.5	(98.9)[h]	
Ceftriaxone	≤0.06	>8	89.1/0.6/10.3	89.1/10.6/0.3
Ceftazidime	0.25	4	91.9/1.1/7.0	88.6/3.3/8.1
Cefepime	≤0.5	≤0.5	92.4/1.7/5.9	91.4/1.6/7.0
Meropenem	≤0.06	≤0.06	100.0/0.0/0.0	100.0/0.0/0.0
Aztreonam	≤0.12	4	90.8/3.3/5.9	88.1/2.7/9.2
Piperacillin/tazobactam	2	8	94.1/1.6/4.3	94.1/0.0/5.9
Levofloxacin	≤0.12	>4	72.3/0.0/27.7	71.2/1.1/27.7
Gentamicin	≤1	>8	85.9/0.0/14.1	84.3/1.6/14.1
Tigecycline[e]	0.12	0.12	100.0/0.0/0.0	100.0/0.0/0.0
Colistin	0.5	0.5	-/-/-[d]	100.0/0.0/0.0
Klebsiella spp. (88)[e]				
Ceftolozane/tazobactam	0.25	32	(89.8)[h]	
Ceftriaxone	≤0.06	>8	83.0/1.1/15.9	83.0/1.1/15.9
Ceftazidime	0.12	>32	86.4/0.0/13.6	84.1/2.3/13.6
Cefepime	≤0.5	16	87.5/2.3/10.2	85.2/3.4/11.4
Meropenem	≤0.06	2	89.8/1.1/9.1	90.9/3.4/5.7
Aztreonam	≤0.12	>16	84.1/1.1/14.8	83.0/1.1/15.9
Piperacillin/tazobactam	4	>64	83.0/1.1/15.9	79.5/3.5/17.0
Levofloxacin	≤0.12	>4	88.6/0.0/11.4	85.2/3.4/11.4
Gentamicin	≤1	4	92.0/2.3/5.7	89.8/2.2/8.0
Tigecycline[e]	0.25	1	98.9/1.1/0.0	95.4/3.5/1.1
Colistin	0.5	0.5	-/-/-	100.0/0.0/0.0
Enterobacter spp. (41)[f]				
Ceftolozane/tazobactam	0.25	4	(95.1)[h]	
Ceftriaxone	0.25	>8	68.3/0.0/31.7	68.3/0.0/31.7
Ceftazidime	0.5	>32	73.2/4.8/22.0	70.7/2.5/26.8
Cefepime	≤0.5	2	97.6/0.0/2.4	87.8/9.8/2.4
Meropenem	≤0.06	0.12	100.0/0.0/0.0	100.0/0.0/0.0
Aztreonam	≤0.12	16	73.2/4.8/22.0	73.2/0.0/26.8
Piperacillin/tazobactam	4	32	75.0/17.5/7.5	70.0/5.0/25.0
Levofloxacin	≤0.12	0.25	95.1/0.0/4.9	95.1/0.0/4.9
Gentamicin	≤1	≤1	100.0/0.0/0.0	100.0/0.0/0.0
Tigecycline[e]	0.25	0.5	100.0/0.0/0.0	97.6/2.4/0.0
Colistin	0.5	>8	-/-/-	70.7/0.0/29.3
Citrobacter spp. (19)[g]				
Ceftolozane/tazobactam	0.25	16	(84.2)[h]	
Ceftriaxone	0.25	>8	73.7/0.0/26.3	73.7/0.0/26.3
Ceftazidime	0.5	>32	73.7/0.0/26.3	73.7/0.0/26.3
Cefepime	≤0.5	2	100.0/0.0/0.0	89.5/10.5/0.0
Meropenem	≤0.06	≤0.06	100.0/0.0/0.0	100.0/0.0/0.0
Aztreonam	≤0.12	>16	73.7/0.0/26.3	73.7/0.0/26.3
Piperacillin/tazobactam	4	>64	78.9/5.3/15.8	78.9/0.0/21.1
Levofloxacin	≤0.12	4	89.5/5.2/5.3	89.5/0.0/10.5
Gentamicin	≤1	>8	84.2/0.0/15.8	84.2/0.0/15.8
Tigecycline[e]	0.12	1	100.0/0.0/0.0	94.7/5.3/0.0
Colistin	0.5	1	-/-/-	100.0/0.0/0.0
P. mirabilis (17)				
Ceftolozane/tazobactam	0.5	0.5	100.0)[h]	
Ceftriaxone	≤0.06	≤0.06	100.0/0.0/0.0	100.0/0.0/0.0
Ceftazidime	0.06	0.06	100.0/0.0/0.0	100.0/0.0/0.0
Cefepime	≤0.5	≤0.5	100.0/0.0/0.0	100.0/0.0/0.0
Meropenem	≤0.06	≤0.06	100.0/0.0/0.0	100.0/0.0/0.0
Aztreonam	≤0.12	≤0.12	100.0/0.0/0.0	100.0/0.0/0.0
Piperacillin/tazobactam	≤0.5	≤0.5	100.0/0.0/0.0	100.0/0.0/0.0
Levofloxacin	≤0.12	>4	70.6/0.0/29.4	64.7/5.9/29.4
Gentamicin	≤1	>8	82.4/5.8/11.8	76.5/5.9/17.6
Tigecycline[e]	1	4	88.2/5.9/5.9	58.8/29.4/11.8
Colistin	>8	>8	-/-/-	0.0/0.0/100.0
S. marcescens (10)				
Ceftolozane/tazobactam	0.5	1	(100.0)[h]	
Ceftriaxone	0.25	0.5	90.0/0.0/10.0	90.0/0.0/10.0
Ceftazidime	0.12	0.25	100.0/0.0/0.0	100.0/0.0/0.0
Cefepime	≤0.5	≤0.5	100.0/0.0/0.0	100.0/0.0/0.0
Meropenem	≤0.06	≤0.06	100.0/0.0/0.0	100.0/0.0/0.0
Aztreonam	≤0.12	0.5	100.0/0.0/0.0	100.0/0.0/0.0
Piperacillin/tazobactam	2	4	100.0/0.0/0.0	100.0/0.0/0.0
Levofloxacin	≤0.12	0.5	100.0/0.0/0.0	90.0/10.0/0.0
Gentamicin	≤1	2	100.0/0.0/0.0	100.0/0.0/0.0
Tigecycline[e]	0.5	1	100.0/0.0/0.0	90.0/10.0/0.0
Colistin	>8	>8	-/-/-	0.0/0.0/100.0
P. aeruginosa (58)				
Ceftolozane/tazobactam	0.5	2	(98.3)[h]	
Ceftazidime	2	32	87.9/0.0/12.1	87.9/0.0/12.1
Cefepime	2	16	87.9/6.9/5.2	87.9/0.0/12.1
Meropenem	0.5	8	73.7/8.8/17.5	73.7/26.3/0.0
Aztreonam	8	>16	72.4/6.9/20.7	0.0/79.3/20.7
Piperacillin/tazobactam	4	>64	82.8/6.9/10.3	82.8/0.0/17.2
Levofloxacin	0.5	>4	72.4/3.5/24.1	70.7/1.7/27.6
Gentamicin	≤1	4	96.6/0.0/3.4	99.6/0.0/3.4
Amikacin	2	8	100.0/0.0/0.0	98.3/1.7/0.0
Colistin	1	2	100.0/0.0/0.0	100.0/0.0/0.0

I = intermediate; R = resistant; S = susceptible.
[a]Criteria as published by the CLSI [2014] and EUCAST [2014].
[b]Percentage inhibited at ceftolozane/tazobactam MICs of ≤8 µg/mL; for comparison purpose only.
[c]In the absence of CLSI breakpoints, USA-FDA breakpoints were applied when available [Tygacil Product Insert, 2012].
[d]Breakpoints not available.
[e]Includes: *K. oxytoca* (20 strains), and *K. pneumoniae* (68 strains).
[f]Includes: *E. aerogenes* (6 strains), and *E. cloacae* (35 strains).
[g]Includes: *C. braakii* (2 strains), *C. freundii* (15 strains), *C. koseri* (2 strains), and *Citrobacter youngae* (1 strain).

CONCLUSIONS

- Ceftolozane/tazobactam demonstrated potent activity against contemporary aerobic Gram-negative pathogens causing IAIs in the USA.
- Ceftolozane/tazobactam was very active against most Enterobacteriaceae, including many ESBL-phenotype and MDR strains; and also showed potent activity against contemporary *P. aeruginosa* including a number of MDR and XDR strains.
- Ceftolozane/tazobactam could represent a potential alternative treatment for IAI in the USA, including infections with MDR Gram-negative pathogens.

REFERENCES

Clinical and Laboratory Standards Institute. 2012. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard: ninth edition. CLSI document M07-A9. CLSI, Wayne, PA.
Clinical and Laboratory Standards Institute. 2014. Performance standards for antimicrobial susceptibility testing: 24th informational supplement. CLSI document M100-S24. CLSI, Wayne, PA.
Eckmann C, et al. Presented at: European Congress of Clinical Microbiology and Infectious Diseases (ECCMID); Barcelona, Spain; May 10-13, 2014. Poster P0266a.
European Committee on Antimicrobial Susceptibility Testing (2014). Breakpoint tables for interpretation of MICs and zone diameters. Version 4.0, January 2014. Available at: http://www.eucast.org/clinical_breakpoints/. Accessed January 1, 2014.
Farrell DJ, et al. *Antimicrob Agents Chemother* 2013;57:6305-6310.
Magiorakos AP, et al. *Clin Microbiol Infect*. 2012;18:268-281.
Mazuski JE, Solomkin JS. *Surg Clin North Am*. 2009;89:421-437.
Sader HS, et al. *Antimicrob Agents Chemother* 2011;55:2390-2394.

ACKNOWLEDGMENTS

This study was funded by research grants from Cubist Pharmaceuticals (Lexington, MA, USA). Editorial and layout support for this poster was provided by PAREXEL and funded by Cubist Pharmaceuticals.