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Antimicrobial Activity of Ceftaroline Tested against 10,956 Organisms Causing Acute Bacterial Skin and Skin Structure Infections in United States Medical Centers (2012)

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Amended Abstract

Background: We evaluated the spectrum and potency of ceftaroline (CPT) and comparators tested against contemporary pathogens causing acute bacterial skin and skin structure infections (ABSSSI) in USA hospitals.

Methods: 10,956 organisms from the 2012 AWARE CPT surveillance program were isolated from ABSSSI. Pathogens were collected from patients in 163 medical centers and tested for susceptibility (S) against CPT and commonly used antimicrobials by the CLSI broth microdilution method. S interpretations and ESBL-phenotype were determined per CLSI guidelines.

Results: CPT MIC results are summarized in Table 1. 51.3% of *S. aureus* isolates were resistant (R) to oxacillin (MRSA). CPT was very active against methicillin-S *S. aureus* (MSSA; MIC_{90}, 0.25 µg/mL; 100.0% S) and MRSA (MIC_{90}, 1 µg/mL; 98.6% S). Against MSSA, CPT was 16-, 4- and 4-fold more active than ceftriaxone, linezolid, and vancomycin, respectively. β-hemolytic streptococci were highly CPT-S (MIC_{90}, ≤0.015 µg/mL; highest MIC only 0.03 µg/mL). CPT exhibited good activity against non-ESBL-phenotype strains of *E. coli* and *Klebsiella* spp. (MIC_{90}, 0.5 µg/mL), but limited activity against ESBL-producing strains. 46.2% of ESBL-phenotype *K. pneumoniae* showed decreased S (MIC, ≥2 µg/mL) to meropenem. CPT was very active against coagulase-negative staphylococci ($MIC_{50/90}$, 0.25/0.5 µg/mL), viridans group streptococci ($MIC_{50/90}$, 0.03/0.06 µg/mL), *P. mirabilis* ($MIC_{50/90}$, 0.12/0.5 µg/mL), and ceftazidime-S *E. cloacae* ($MIC_{50/90}$, 0.25/0.5 µg/mL), but showed moderate activity against *M. morganii* ($MIC_{50/90}$, 0.12/>32 µg/mL), *S. marcescens* ($MIC_{50/90}$, 1/2 µg/mL) and *E. faecalis* ($MIC_{50/90}$, 2/8 µg/mL). *P. aeruginosa* and *Acinetobacter* spp. strains were generally CPT-R.

Conclusions: CPT demonstrated potent in vitro activity against gram-positive organisms, including MRSA strains, and non-ESBL-phenotype Enterobacteriaceae recently isolated from patients with documented ABSSSI.

Introduction

Ceftaroline, the active metabolite of the prodrug ceftaroline fosamil, is a broad-spectrum cephalosporin with in vitro bactericidal activity against resistant gram-positive organisms, including methicillin (oxacillin)-resistant *Staphylococcus aureus* (MRSA), multidrug-resistant (MDR) strains of *Streptococcus pneumoniae*, and common gram-negative organisms, including non-ESBL-phenotype Enterobacteriaceae.

Ceftaroline fosamil is approved by the United States Food and Drug Administration (USA-FDA) for the treatment of acute bacterial skin and skin structure infections (ABSSSIs) and community-acquired bacterial pneumonia (CABP), and similar indications in Europe and other countries. As part of the Assessing Worldwide Antimicrobial Resistance Evaluation (AWARE) Program, a global ceftaroline surveillance study, we evaluated the activity of ceftaroline tested against a large collection of bacterial isolates collected from patients hospitalized with ABSSSI in USA medical centers.

Methods

Organism collection: A total of 10,956 clinically significant, nonduplicate isolates were collected from patients hospitalized with ABSSSI in 163 USA medical centers during 2012, and the antimicrobial susceptibility testing results for the most frequently isolated species/groups (10,795 strains) are presented here. *Escherichia coli* and *Klebsiella* spp. isolates were grouped as "extended-spectrum β-lactamase (ESBL)-phenotype" based on the Clinical and Laboratory Standards Institute (CLSI) screening criteria for ESBL production, ie. MIC of ≥2 µg/mL for ceftazidime or ceftriaxone or aztreonam [CLSI, 2013 - M100-S23]. Species identification was confirmed when necessary by Matrix-Assisted Laser Desorption Ionization-Time Of Flight Mass Spectrometry (MALDI-TOF MS) using the Bruker Daltonics MALDI Biotyper (Billerica, Massachusetts, USA) by following manufacturer instructions.

Susceptibility testing methods: Broth microdilution tests conducted according to CLSI methods were performed to determine antimicrobial susceptibility of ceftaroline and comparator antimicrobials used to treat ABSSSI. Validated MIC panels were manufactured by ThermoFisher Scientific (Cleveland, Ohio, USA). ABSSSI pathogens were tested in cation-adjusted Mueller-Hinton broth (CA-MHB). β-hemolytic streptococci were tested in CA-MHB supplemented with 2.5-5% lysed horse blood (M07-A9, 2012).

Quality control: Concurrent quality control (QC) testing was performed to assure proper test conditions and procedures. Susceptibility percentages and validation of QC results were based on CLSI guidelines and susceptibility breakpoints established by the CLSI (M100-S23; 2013) were used to determine susceptibility/resistance rates when available.

Results

- Ceftaroline exhibited activity against methicillin-susceptible *S. aureus* (MSSA) isolates (MIC_{50} and MIC_{90}, 0.25 µg/mL) and MRSA isolates ($MIC_{50/90}$, 0.5/1 µg/mL). Ceftaroline was 16-fold more active than ceftriaxone when tested against MSSA based on MIC_{50} and MIC_{90} values (Tables 1 and 2)
- Ceftaroline was one of the most active agents tested against MRSA ($MIC_{50/90}$, 0.5/1 µg/mL; 98.6% susceptible [S]), with potency and spectrum similar to that of vancomycin ($MIC_{50/90}$, 1/1; 100% S), linezolid ($MIC_{50/90}$, 1/1 µg/mL; >99.9% S) and daptomycin ($MIC_{50/90}$, 0.25/0.5 µg/mL; >99.9% S). The highest resistance rate for MRSA was observed with erythromycin (88.1%), followed by levofloxacin (58.3%) and clindamycin (17.2%; Table 2)
- Ceftaroline was slightly more active (two-fold) against CoNS ($MIC_{50/90}$, 0.25/0.5 µg/mL) compared to *S. aureus* ($MIC_{50/90}$, 0.5/1 µg/mL; Table 2). The highest ceftaroline MIC value was 1 µg/mL among CoNS (Table 1); the *S. aureus* susceptible breakpoint
- Against β-hemolytic streptococci, ceftaroline demonstrated activity (MIC_{50} and MIC_{90}, ≤0.015 µg/mL) comparable to that of penicillin (MIC_{50} and MIC_{90}, ≤0.06 µg/mL). Decreased susceptibility was observed with erythromycin (MIC_{90}, >16 µg/mL; 66.1% S) and clindamycin (MIC_{90}, >2 µg/mL; 80.6% S; Table 2). Group A β-hemolytic streptococci (100.0% inhibited at ≤0.015 µg/mL) had slightly lower ceftaroline MIC values when compared than to Group B (93.3% inhibited at ≤0.015 µg/mL) and Group C isolates (74.3% inhibited at ≤0.015 µg/mL; Tables 1 and 2)
- Viridans group streptococci, including strains resistant to penicillin and ceftriaxone, were susceptible to ceftaroline (MIC_{90}, 0.06 µg/mL; Tables 1 and 2)
- Ceftaroline exhibited low to moderate in vitro activity against *Enterococcus faecalis,* although MIC values were elevated compared with those noted against other gram-positive species tested ($MIC_{50/90}$, 2/8 µg/mL; Table 1). All *E. faecalis* strains were susceptible to ampicillin ($MIC_{50/90}$, 1/2 µg/mL), linezolid ($MIC_{50/90}$, 1/2 µg/mL), and daptomycin ($MIC_{50/90}$, 1/2 µg/mL); 3.3% of strains were vancomycin-resistant (data not shown)
- Overall, 79.1 and 84.3% of Enterobacteriaceae strains were inhibited at ceftaroline MIC of ≤0.5 and ≤1 µg/mL respectively (Table 1). Ceftaroline and ceftriaxone exhibited similar in vitro activities against *E. coli* and *Klebsiella* spp. Non-ESBL-phenotype strains were generally susceptible to ceftaroline while strains with an ESBL-phenotype exhibited compromised susceptibility rates to ceftaroline and all cephalosporins tested (Table 2)
- When tested against *Enterobacter cloacae*, ceftaroline ($MIC_{50/90}$, 0.25/>32 µg/mL) demonstrated similar activity compared to those of ceftriaxone ($MIC_{50/90}$, 0.25/>8 µg/mL) and ceftazidime ($MIC_{50/90}$, 0.25/32 µg/mL). Overall, 79.7 and 83.3% of *E. cloacae* strains were susceptible to ceftriaxone and ceftazidime, respectively, and 78.1% were susceptible to ceftaroline (Table 2)
- Ceftaroline showed variable activity against *Morganella morganii* ($MIC_{50/90}$, 0.12/>32 µg/mL). Overall, 73.7% of strains were inhibited at ≤0.5 µg/mL of ceftaroline and 88.1% of strains were susceptible to ceftazidime (Tables 1 and 2)
- Ceftaroline was slightly more active against *Citrobacter koseri* ($MIC_{50/90}$, 0.12/0.5 µg/mL; 96.8% S) compared to *C. freundii* ($MIC_{50/90}$, 0.25/16 µg/mL; 81.8% S; Table 2)
- Ceftaroline exhibited modest activity against *Serratia marcescens* ($MIC_{50/90}$, 1/2 µg/mL; 37.7% S), *Proteus vulgaris* ($MIC_{50/90}$, 2/32 µg/mL; 36.4% S) and *Providencia* spp. ($MIC_{50/90}$, 0.5/8 µg/mL; 54.5% S; Table 1), and very limited activity against *Pseudomonas aeruginosa* ($MIC_{50/90}$, 16/>32 µg/mL) and *Acinetobacter* spp. (MIC_{50} and MIC_{90} of >32 µg/mL; Tables 1 and 2).

Table 1. Summary of ceftaroline activity tested against the main USA pathogen groups isolated from ABSSSI in USA medical centers (2012)

Organism/subgroup	No. of Isolates	No. of isolates (cumulative %) inhibited at ceftaroline MIC (µg/mL) of:												MIC_{50}	MIC_{90}
		≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	>16		
Staphylococcus aureus	6,085	1 (<0.1)	2 (<0.1)	22 (0.4)	279 (5.0)	2,549 (46.9)	1,757 (75.8)	1,432 (99.3)	43 (100.0)	--	--	--	--	0.5	1
MSSA	2,961	1 (<0.1)	2 (0.1)	22 (0.8)	279 (10.3)	2,508 (95.0)	149 (100.0)	--	--	--	--	--	--	0.25	0.25
MRSA	3,124	--	--	--	--	41 (1.3)	1,608 (52.8)	1,432 (98.6)	43 (100.0)	--	--	--	--	0.5	1
Coagulase-negative staphylococci	328	2 (0.6)	15 (5.2)	77 (28.7)	53 (44.8)	134 (85.7)	44 (99.1)	3 (100.0)	--	--	--	--	--	0.25	0.5
β-hemolytic streptococci	604	575 (95.2)	29 (100.0)	--	--	--	--	--	--	--	--	--	--	≤0.015	≤0.015
Group A Streptococcus	272	272 (100.0)	--	--	--	--	--	--	--	--	--	--	--	≤0.015	≤0.015
Group B Streptococcus	297	277 (93.3)	20 (100.0)	--	--	--	--	--	--	--	--	--	--	≤0.015	≤0.015
Group C Streptococcus	35	26 (74.3)	9 (100.0)	--	--	--	--	--	--	--	--	--	--	≤0.015	0.03
Viridans group streptococci	179	77 (43.0)	82 (88.8)	15 (97.2)	0 (97.2)	3 (98.9)	1 (99.4)	1 (100.0)	--	--	--	--	--	0.03	0.06
Enterococcus faecalis	395	--	--	--	--	--	6 (1.5)	83 (22.5)	209 (75.4)	42 (86.1)	44 (97.2)	7 (99.0)	4 (100.0)	2	8
Enterobacteriaceae	2,543	11 (0.4)	120 (5.2)	607 (29.0)	641 (54.2)	397 (69.8)	235 (79.1)	132 (84.3)	62 (86.7)	33 (88.0)	29 (89.1)	42 (90.8)	234 (100.0)	0.12	16
Escherichia coli	645	2 (0.3)	68 (10.9)	212 (43.7)	150 (67.0)	74 (78.4)	32 (83.4)	19 (86.4)	7 (87.4)	3 (87.9)	5 (88.7)	10 (90.2)	63 (100.0)	0.12	16
non-ESBL-phenotype	561	2 (0.4)	68 (12.5)	212 (50.3)	148 (76.6)	73 (89.7)	31 (95.2)	19 (98.6)	6 (99.6)	1 (99.8)	1 (100.0)	--	--	0.06	0.5
ESBL-phenotype	84	--	--	--	2 (2.4)	1 (3.6)	1 (4.8)	0 (4.8)	1 (6.0)	2 (8.3)	4 (13.1)	10 (25.0)	63 (100.0)	>32	>32
Klebsiella pneumoniae	444	3 (0.7)	16 (4.3)	138 (35.4)	141 (67.1)	42 (76.6)	28 (82.9)	8 (84.7)	5 (85.8)	2 (86.3)	3 (86.9)	2 (87.4)	56 (100.0)	0.12	>32
non-ESBL-phenotype	379	3 (0.8)	16 (5.0)	138 (41.4)	141 (78.6)	42 (89.7)	28 (97.1)	8 (99.2)	2 (99.7)	0 (99.7)	1 (100.0)	--	--	0.12	0.5
ESBL-phenotype	65	--	--	--	--	--	--	--	3 (4.6)	2 (7.7)	2 (10.8)	2 (13.8)	56 (100.0)	>32	>32
Klebsiella oxytoca	157	--	5 (3.2)	19 (15.3)	39 (40.1)	56 (75.8)	21 (89.2)	4 (91.7)	1 (92.4)	0 (92.4)	1 (93.0)	2 (94.3)	9 (100.0)	0.25	1
non-ESBL-phenotype	144	--	5 (3.5)	19 (16.7)	39 (43.8)	56 (82.6)	21 (97.2)	4 (100.0)	--	--	--	--	--	0.25	0.5
ESBL-phenotype	13	--	--	--	--	--	--	--	1 (7.7)	0 (7.7)	1 (15.4)	2 (30.8)	9 (100.0)	>32	>32
Proteus mirabilis	319	--	6 (1.9)	122 (40.1)	125 (79.3)	30 (88.7)	12 (92.5)	7 (94.7)	4 (95.9)	1 (96.2)	1 (96.6)	2 (97.2)	9 (100.0)	0.12	0.5
Enterobacter cloacae	360	5 (1.4)	1 (1.7)	19 (6.9)	84 (30.3)	128 (65.8)	44 (78.1)	13 (81.7)	2 (82.2)	3 (83.1)	4 (84.2)	4 (85.3)	53 (100.0)	0.25	>32
Enterobacter aerogenes	92	--	--	31 (33.7)	28 (64.1)	8 (72.8)	5 (78.3)	2 (80.4)	1 (81.5)	2 (83.7)	1 (84.8)	2 (87.0)	12 (100.0)	0.12	32
Morganella morganii	118	1 (0.8)	10 (9.3)	33 (37.3)	24 (57.6)	12 (67.8)	7 (73.7)	3 (76.3)	1 (77.1)	4 (80.5)	3 (83.1)	6 (88.1)	14 (100.0)	0.12	>32
Citrobacter koseri	62	--	3 (4.8)	20 (37.1)	29 (83.9)	2 (87.1)	6 (96.8)	1 (98.4)	1 (100.0)	--	--	--	--	0.12	0.5
Citrobacter freundii	66	--	--	2 (3.0)	17 (28.8)	27 (69.7)	8 (81.8)	0 (81.8)	1 (83.3)	2 (86.4)	2 (89.4)	3 (93.9)	4 (100.0)	0.25	16
Serratia marcescens	159	--	--	1 (0.6)	1 (1.3)	9 (6.9)	49 (37.7)	64 (78.0)	23 (92.5)	3 (94.3)	4 (96.9)	1 (97.5)	4 (100.0)	1	2
Proteus vulgaris	55	--	--	2 (3.6)	1 (5.5)	7 (18.2)	10 (36.4)	6 (47.3)	9 (63.6)	4 (70.9)	1 (72.7)	7 (85.5)	8 (100.0)	2	32
Providencia spp.	66	--	11 (16.7)	8 (28.8)	2 (31.8)	2 (34.8)	13 (54.5)	5 (62.1)	7 (72.7)	9 (86.4)	4 (92.4)	3 (97.0)	2 (100.0)	0.5	8
Pseudomonas aeruginosa	541	--	--	--	--	--	1 (0.2)	3 (0.7)	7 (2.0)	31 (7.8)	101 (26.4)	168 (57.5)	230 (100.0)	16	>32
Acinetobacter baumannii	120	--	--	--	--	--	--	5 (4.2)	16 (17.5)	17 (31.7)	16 (45.0)	2 (46.7)	64 (100.0)	>32	>32

Table 2. Activity of ceftaroline and comparator antimicrobial agents when tested against bacterial isolates collected from patients hospitalized with ABSSSI (USA, 2012)

Organism (no. tested) / antimicrobial agent	MIC (µg/mL) 50%	90%	%S / %I / %R[a]
Staphylococcus aureus (6,085)			
Ceftaroline	0.5	1	99.3 / 0.7 / 0.0
Oxacillin	>2	>2	48.7 / 0.0 / 51.3
Ceftriaxone	>8	>8	48.7 / 0.0 / 51.3
Erythromycin	>16	>16	35.6 / 2.3 / 62.1
Clindamycin	≤0.25	>2	88.8 / 0.2 / 11.0
Levofloxacin	0.25	>4	63.0 / 1.4 / 35.6
Tigecycline[b]	0.06	0.06	100.0 / - / -
Linezolid	1	1	>99.9 / 0.0 / <0.1
Vancomycin	1	1	100.0 / 0.0 / 0.0
Daptomycin	0.25	0.5	>99.9 / - / -
MSSA (2,961)			
Ceftaroline	0.25	0.25	100.0 / 0.0 / 0.0
Ceftriaxone	4	4	100.0 / - / -
Erythromycin	0.25	>16	62.1 / 3.3 / 34.6
Clindamycin	≤0.25	≤0.25	95.4 / 0.1 / 4.5
Levofloxacin	0.25	4	87.3 / 1.2 / 11.6
Tigecycline[b]	0.06	0.06	100.0 / - / -
Linezolid	1	1	100.0 / 0.0 / 0.0
Vancomycin	1	1	100.0 / 0.0 / 0.0
Daptomycin	0.25	0.5	100.0 / - / -
MRSA (3,124)			
Ceftaroline	0.5	1	98.6 / 1.4 / 0.0
Ceftriaxone	>8	>8	0.0 / 0.0 / 100.0
Erythromycin	>16	>16	10.5 / 1.4 / 88.1
Clindamycin	≤0.25	>2	82.5 / 0.3 / 17.2
Levofloxacin	4	>4	39.9 / 1.8 / 58.3
Tigecycline[b]	0.06	0.06	100.0 / - / -
Linezolid	1	1	>99.9 / 0.0 / <0.1
Vancomycin	1	1	100.0 / 0.0 / 0.0
Daptomycin	0.25	0.5	>99.9 / - / -
CoNS (328)			
Ceftaroline	0.25	0.5	- / - / -
Oxacillin	0.5	>2	38.4 / 0.0 / 61.6
Ceftriaxone	4	>8	38.4 / 0.0 / 61.6
Erythromycin	8	>16	47.0 / 2.4 / 50.6
Clindamycin	≤0.25	>2	79.8 / 0.9 / 19.3
Levofloxacin	0.25	>4	73.2 / 0.9 / 25.9
Linezolid	0.5	1	99.7 / 0.0 / 0.3
Vancomycin	1	2	100.0 / 0.0 / 0.0
Daptomycin	0.25	0.5	100.0 / - / -
β-hemolytic streptococci[c] (604)			
Ceftaroline	≤0.015	≤0.015	100.0 / - / -
Penicillin	≤0.06	≤0.06	100.0 / - / -
Ceftriaxone	≤0.06	0.12	100.0 / - / -
Erythromycin	≤0.12	>16	66.1 / 1.2 / 32.7
Clindamycin	≤0.25	>2	80.6 / 0.8 / 18.6
Levofloxacin	0.5	1	99.3 / 0.0 / 0.7
Linezolid	1	1	100.0 / - / -
Tetracycline	8	>32	48.5 / 0.7 / 50.8
Tigecycline[b]	0.03	0.03	100.0 / - / -
Vancomycin	0.5	0.5	100.0 / - / -
Daptomycin	0.12	0.25	100.0 / - / -
Viridans group streptococci[d] (179)			
Ceftaroline	0.03	0.06	- / - / -
Penicillin	≤0.06	0.25	85.5 / 13.9 / 0.6
Ceftriaxone	0.25	0.5	98.9 / 1.1 / 0.0
Erythromycin	≤0.12	8	65.9 / 3.3 / 30.7
Clindamycin	≤0.25	>2	88.8 / 0.0 / 11.2
Levofloxacin	0.5	2	98.3 / 0.0 / 1.7
Linezolid	1	1	100.0 / - / -
Tigecycline[b]	≤0.015	0.06	100.0 / - / -
Vancomycin	0.5	1	100.0 / - / -
Daptomycin	0.25	0.5	100.0 / - / -
Enterobacteriaceae (2,543)			
Ceftaroline	0.12	16	79.1 / 5.2 / 15.7
Ceftriaxone	≤0.06	4	87.8 / 1.3 / 10.9
Ceftazidime	0.12	4	90.8 / 1.1 / 8.1
Ampicillin/sulbactam	8	>32	55.6 / 17.2 / 27.2
Piperacillin/tazobactam	2	16	93.1 / 2.4 / 4.5
Meropenem	≤0.06	≤0.06	98.5 / 0.1 / 1.4
Levofloxacin	≤0.12	>4	82.6 / 2.2 / 15.2
Gentamicin	≤1	2	91.6 / 1.5 / 6.9
Tigecycline[b]	0.25	2	97.1 / 2.9 / <0.1
Escherichia coli (645)			
Ceftaroline	0.12	16	83.4 / 3.0 / 13.6
Ceftriaxone	≤0.06	>8	87.8 / 0.1 / 12.1
Ceftazidime	0.25	4	91.0 / 1.9 / 7.1
Ampicillin/sulbactam	8	>32	52.7 / 18.8 / 28.5
Piperacillin/tazobactam	2	8	95.8 / 2.0 / 2.2
Meropenem	≤0.06	≤0.06	99.8 / 0.0 / 0.2
Levofloxacin	≤0.12	>4	68.4 / 0.5 / 31.1
Gentamicin	≤1	>8	89.5 / 0.1 / 10.4
Tigecycline[b]	0.12	0.12	100.0 / 0.0 / 0.0
ESBL-phenotype (84)			
Ceftaroline	>32	>32	4.8 / 0.0 / 95.2
Ceftriaxone	>8	>8	6.0 / 1.1 / 92.9
Ceftazidime	16	>32	31.0 / 14.2 / 54.8
Ampicillin/sulbactam	32	>32	13.1 / 16.7 / 70.2
Piperacillin/tazobactam	8	64	79.8 / 11.9 / 8.3
Meropenem	≤0.06	≤0.06	98.8 / 0.0 / 1.2
Levofloxacin	>4	>4	31.0 / 2.3 / 66.7
Gentamicin	2	>8	71.4 / 0.0 / 28.6
Tigecycline[b]	0.12	0.25	100.0 / 0.0 / 0.0
Klebsiella spp.[e] (601)			
Ceftaroline	0.12	>32	84.5 / 2.0 / 13.5
Ceftriaxone	≤0.06	8	88.4 / 0.5 / 11.1
Ceftazidime	0.12	8	89.4 / 1.3 / 9.3
Ampicillin/sulbactam	8	>32	71.9 / 12.3 / 15.8
Piperacillin/tazobactam	2	>64	88.3 / 1.3 / 10.4
Meropenem	≤0.06	≤0.06	94.8 / 0.4 / 4.8
Levofloxacin	≤0.12	4	90.0 / 1.2 / 8.8
Gentamicin	≤1	≤1	93.5 / 2.0 / 4.5
Tigecycline[b]	0.25	0.5	99.3 / 0.7 / 0.0
ESBL-phenotype[f] (78)			
Ceftaroline	>32	>32	0.0 / 0.0 / 100.0
Ceftriaxone	>8	>8	10.3 / 3.8 / 85.9
Ceftazidime	>32	>32	17.9 / 10.3 / 71.8
Ampicillin/sulbactam	>32	>32	2.6 / 6.4 / 91.0
Piperacillin/tazobactam	>64	>64	19.2 / 7.7 / 73.1
Meropenem	≤0.06	>8	60.3 / 2.5 / 37.2
Levofloxacin	>4	>4	33.3 / 3.9 / 62.8
Gentamicin	4	>8	53.8 / 14.1 / 32.1
Tigecycline[b]	0.5	1	98.7 / 1.3 / 0.0
Proteus mirabilis (319)			
Ceftaroline	0.12	0.5	92.5 / 2.2 / 5.3
Ceftriaxone	≤0.06	≤0.06	96.2 / 1.0 / 2.8
Ceftazidime	0.06	0.06	99.7 / 0.3 / 0.0
Ampicillin/sulbactam	1	16	88.4 / 7.1 / 4.4
Piperacillin/tazobactam	≤0.5	1	99.7 / 0.0 / 0.3
Meropenem	≤0.06	0.12	100.0 / 0.0 / 0.0
Levofloxacin	≤0.12	>4	78.9 / 3.8 / 17.3
Gentamicin	≤1	8	88.4 / 1.8 / 9.7
Tigecycline[b]	2	4	83.4 / 16.3 / 0.3
Enterobacter cloacae (360)			
Ceftaroline	0.25	>32	78.1 / 3.7 / 18.3
Ceftriaxone	0.25	>8	79.7 / 1.7 / 18.6
Ceftazidime	0.25	32	83.3 / 0.3 / 16.4
Ampicillin/sulbactam	16	>32	34.8 / 22.0 / 43.2
Piperacillin/tazobactam	2	64	87.4 / 5.3 / 7.3
Meropenem	≤0.06	≤0.06	99.4 / 0.0 / 0.6
Levofloxacin	≤0.12	0.5	95.5 / 1.7 / 2.8
Gentamicin	≤1	≤1	95.3 / 0.5 / 4.2
Tigecycline[b]	0.25	0.5	98.6 / 1.4 / 0.0
E. aerogenes (92)			
Ceftaroline	0.12	32	78.3 / 2.1 / 19.6
Ceftriaxone	0.12	8	78.3 / 3.2 / 18.5
Ceftazidime	0.25	32	82.6 / 1.2 / 16.3
Ampicillin/sulbactam	16	>32	37.0 / 26.0 / 37.0
Piperacillin/tazobactam	4	32	83.7 / 9.8 / 6.5
Meropenem	≤0.06	≤0.06	98.9 / 0.0 / 1.1
Levofloxacin	≤0.12	0.25	97.8 / 1.2 / 1.1
Gentamicin	≤1	≤1	97.8 / 0.0 / 2.2
Tigecycline[b]	0.25	0.5	100.0 / 0.0 / 0.0
Morganella morganii (118)			
Ceftaroline	0.12	>32	73.7 / 2.6 / 23.7
Ceftriaxone	≤0.06	1	90.5 / 1.7 / 7.8
Ceftazidime	0.12	8	88.1 / 4.4 / 7.6
Ampicillin/sulbactam	16	32	22.2 / 38.5 / 39.3
Piperacillin/tazobactam	≤0.5	2	98.3 / 0.8 / 0.9
Meropenem	≤0.06	0.12	100.0 / 0.0 / 0.0
Levofloxacin	≤0.12	>4	70.1 / 8.5 / 21.4
Gentamicin	≤1	>8	86.3 / 1.7 / 12.0
Tigecycline[b]	0.5	2	95.8 / 4.2 / 0.0
Citrobacter koseri (62)			
Ceftaroline	0.12	0.5	96.8 / 1.7 / 1.6
Ceftriaxone	≤0.06	0.12	98.4 / 0.0 / 1.6
Ceftazidime	0.12	0.5	98.4 / 1.6 / 0.0
Ampicillin/sulbactam	2	8	96.8 / 1.7 / 1.6
Piperacillin/tazobactam	2	8	100.0 / 0.0 / 0.0
Meropenem	≤0.06	≤0.06	100.0 / 0.0 / 0.0
Levofloxacin	≤0.12	≤0.12	98.4 / 0.0 / 1.6
Gentamicin	≤1	≤1	100.0 / 0.0 / 0.0
Tigecycline[b]	0.12	0.25	100.0 / 0.0 / 0.0
C. freundii (66)			
Ceftaroline	0.25	16	81.8 / 0.0 / 18.2
Ceftriaxone	0.25	>8	81.5 / 3.1 / 15.4
Ceftazidime	0.5	16	84.8 / 1.7 / 13.6
Ampicillin/sulbactam	8	>32	66.2 / 9.2 / 24.6
Piperacillin/tazobactam	4	32	87.9 / 10.6 / 1.5
Meropenem	≤0.06	≤0.06	100.0 / 0.0 / 0.0
Levofloxacin	≤0.12	>4	87.9 / 1.5 / 10.6
Gentamicin	≤1	>8	84.8 / 1.7 / 13.6
Tigecycline[b]	0.25	1	100.0 / 0.0 / 0.0
Serratia marcescens (159)			
Ceftaroline	1	2	37.7 / 40.3 / 22.0
Ceftriaxone	0.25	1	92.3 / 1.9 / 5.8
Ceftazidime	0.12	0.5	96.2 / 0.0 / 3.8
Ampicillin/sulbactam	32	>32	8.8 / 15.7 / 75.5
Piperacillin/tazobactam	2	4	96.9 / 2.5 / 0.6
Meropenem	≤0.06	≤0.06	98.1 / 0.7 / 1.3
Levofloxacin	≤0.12	2	92.5 / 3.1 / 4.4
Gentamicin	≤1	2	96.9 / 0.6 / 2.5
Tigecycline[b]	0.5	1	98.1 / 1.9 / 0.0
Proteus vulgaris (55)			
Ceftaroline	2	32	36.4 / 10.9 / 52.7
Ceftriaxone	0.12	4	71.7 / 13.2 / 15.1
Ceftazidime	0.06	0.12	100.0 / 0.0 / 0.0
Ampicillin/sulbactam	8	16	60.0 / 38.2 / 1.8
Piperacillin/tazobactam	≤0.5	1	100.0 / 0.0 / 0.0
Meropenem	≤0.06	0.12	100.0 / 0.0 / 0.0
Levofloxacin	≤0.12	≤0.12	96.4 / 1.8 / 1.8
Gentamicin	≤1	2	98.1 / 1.9 / 0.0
Tigecycline[b]	0.5	1	100.0 / 0.0 / 0.0
Providencia spp.[g] (66)			
Ceftaroline	0.5	8	54.5 / 7.6 / 37.9
Ceftriaxone	≤0.06	0.5	93.9 / 4.6 / 1.5
Ceftazidime	0.12	2	92.4 / 0.0 / 7.6
Ampicillin/sulbactam	16	32	33.8 / 27.7 / 38.5
Piperacillin/tazobactam	2	8	97.0 / 0.0 / 3.0
Meropenem	≤0.06	0.12	100.0 / 0.0 / 0.0
Levofloxacin	4	>4	47.0 / 15.1 / 37.9
Gentamicin	2	8	73.4 / 17.1 / 9.4
Tigecycline[b]	1	2	93.9 / 6.1 / 0.0
Pseudomonas aeruginosa (541)			
Ceftaroline	16	>32	- / - / -
Ceftazidime	2	32	86.9 / 2.8 / 10.2
Cefepime	2	16	88.2 / 6.3 / 5.4
Piperacillin/tazobactam	4	>64	83.4 / 5.5 / 11.1
Meropenem	0.5	4	88.2 / 3.8 / 8.0
Levofloxacin	0.5	>4	79.5 / 5.0 / 15.5
Gentamicin	≤1	4	94.6 / 0.7 / 4.8
Amikacin	2	4	98.7 / 0.7 / 0.6
Colistin	2	2	98.9 / 1.1 / 0.0
Acinetobacter spp. (120)			
Ceftaroline	>32	>32	- / - / -
Ceftazidime	16	>32	45.8 / 6.7 / 47.5
Cefepime	>16	>16	42.5 / 2.5 / 55.0
Piperacillin/tazobactam	>64	>64	43.3 / 0.0 / 56.7
Ampicillin/sulbactam	16	>32	49.2 / 13.3 / 37.5
Meropenem	4	>8	50.8 / 3.4 / 45.8
Levofloxacin	4	>4	46.7 / 5.0 / 48.3
Gentamicin	4	>8	56.7 / 5.0 / 38.3
Amikacin	4	>32	76.7 / 4.1 / 19.2
Colistin	1	2	98.3 / 0.0 / 1.7

a. Criteria as published by the CLSI [2013].
b. US-FDA breakpoints were applied when available [Tygacil Product Insert, 2012].
c. Includes: Group A *Streptococcus* (272 strains), Group B *Streptococcus* (297 strains), and Group C *Streptococcus* (35 strains).
d. Includes: *Streptococcus anginosus* (74 strains), *S. bovis* group (one strain), *S. canis* (one strain), *S. constellatus* (21 strains), *S. gallolyticus* (three strains), *S. gordonii* (three strains), *S. halichoeri* (one strain), *S. infantarius* (one strain), *S. intermedius* (eight strains), *S. massiliensis* (two strains), *S. milleri* (nine strains), *S. mitis* (19 strains), *S. oralis* (12 strains), *S. parasanguinis* (eight strains), *S. pasteurianus* (one strain), *S. salivarius* (five strains), *S. sanguinis* (four strains), *S. vestibularis* (two strains), unspeciated alpha-hemolytic streptococci (three strains), and unspeciated viridans group streptococci (one strain).
e. Includes: *Klebsiella oxytoca* (157 strains) and *K. pneumoniae* (444 strains).
f. Includes: *Klebsiella oxytoca* (13 strains) and *K. pneumoniae* (65 strains).
g. Includes: *Providencia rettgeri* (24 strains) and *P. stuartii* (42 strains).

Conclusions

- Ceftaroline demonstrated potent in vitro activity against gram-positive organisms, including MRSA strains, and non-ESBL-phenotype Enterobacteriaceae recently isolated from USA patients with documented ABSSSI collected in 2012
- Activity of ceftaroline tested against staphylococci causing ABSSSI was similar to that of vancomycin, daptomycin and linezolid. Activity against streptococci was most similar to that of ceftriaxone but ≥eight-fold more potent
- The broad-spectrum in vitro activity of ceftaroline suggests that ceftaroline fosamil represents a valuable option for the treatment of ABSSSI, including those caused by MRSA.

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