IDSA 2011
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Antimicrobial Activity and Spectrum of the Novel Cephalosporin Ceftaroline Tested Against Bacterial Isolates Causing Skin and Skin Structure Infections in USA Medical Centers

H.S. SADER, D.J. FARRELL, R.N. JONES

JMI Laboratories, North Liberty, Iowa, USA

Helio S. Sader, MD, PhD
JMI Laboratories
North Liberty, IA, USA
www.jmilabs.com
ph. 319.665.3370
fax 319.665.3371
helio-sader@jmilabs.com

Abstract

Background: Ceftaroline (CPT), the active form of CPT fosamil, is a broad-spectrum cephalosporin with bactericidal activity against resistant (R) Gram-positive (GP) organisms, including MRSA, and common Gram-negative organisms, including wild-type Enterobacteriaceae (ENT). CPT fosamil is FDA-approved for acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia.

Methods: 1917 isolates were consecutively collected from patients with ABSSSI in 65 USA medical centers (2010). Strains were tested for susceptibility (S) by CLSI broth microdilution against CPT and comparators.

Results: 51.5% of *S. aureus* isolates were MRSA. CPT was very active against methicillin-S *S. aureus* (MSSA; MIC_{90}, 0.25 µg/mL) and MRSA (MIC_{90}, 1 µg/mL). Against MSSA, CPT was 16-, 4- and 4-fold more active than ceftriaxone (CRO), linezolid (LZD) and vancomycin (VAN), respectively. MRSA showed high R rates to levofloxacin (LEV; 58.0%) and clindamycin (21.2%). Against β-haemolytic streptococci (βHS), CPT was 64-, 32- and 4-fold more active than LZD, VAN and penicillin (PEN), respectively, and all strains were inhibited at CPT MIC of ≤0.06 µg/mL. CPT was slightly more active against group A (MIC_{90}, ≤0.008 µg/mL) compared to other βHS groups. Viridans group streptococci (VGS) were very S to CPT ($MIC_{50/90}$, 0.03/0.06 µg/mL), while 88.6 and 95.5% of strains were PEN- and CRO-S, respectively. CPT exhibited good activity against non-ESBL-phenotype strains of *Klebsiella* spp. and *E. coli* (MIC_{90}, 0.25 µg/mL for both), but limited activity against ESBL-producing and/or CRO-R strains.

Conclusion: CPT was highly active against GP and ENT pathogens recently isolated from ABSSSI in USA medical centers, including MRSA. CPT spectrum against GP was similar to that of LZD and VAN; against ENT, CPT had a spectrum comparable to CRO. CPT appears to be a promising agent for ABSSSI, including those caused by MRSA.

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 wild-type Enterobacteriaceae.

Ceftaroline fosamil was recently 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). As part of the Assessing Worldwide Antimicrobial Resistance Evaluation (AWARE) Program, a global ceftaroline surveillance study, we evaluated the activity of ceftaroline tested against bacterial isolates collected from patients hospitalized with ABSSSI in USA medical centers.

Methods

Organism collection: Clinically significant, consecutively collected, nonduplicate isolates from patients hospitalized with ABSSSI in 65 USA medical centers during 2010 were utilized for this study. A total of 1917 isolates were collected, including: *S. aureus* (n = 1114; 51.5% MRSA), β-haemolytic streptococci (n = 433), *Klebsiella* spp. (n = 90), viridans group streptococci (n = 88), coagulase-negative staphylococci (CoNS; n = 72), *Escherichia coli* (n = 66), *Morganella morganii* (n = 36), and *Enterococcus faecalis* (n = 18).

Susceptibility testing methods: Broth microdilution tests conducted according to the Clinical and Laboratory Standards Institute (CLSI) methods were performed to determine antimicrobial susceptibility of ceftaroline and comparator antimicrobials used to treat ABSSSI. Validated MIC panels were manufactured by TREK Diagnostics (Cleveland, Ohio, USA). *S. aureus* strains were tested in cation-adjusted Mueller-Hinton broth (CA-MHB). β-haemolytic streptococci were tested in CA-MHB supplemented with 2.5-5% lysed horse blood (M07-A8, 2009).

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 (M100-S21), and susceptibility breakpoints were used to determine susceptibility/resistance rates (CLSI and EUCAST, 2011). USA-FDA interpretive criteria for ceftaroline susceptibility were used 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}, 0.5 µg/mL and MIC_{90} 1 µg/mL). Ceftaroline was 16-fold more active than ceftriaxone when tested against MSSA based on MIC_{50} values (Tables 1 and 2)
- Ceftaroline was one of the most active agents tested against MRSA (MIC_{90}, 1 µg/mL; 99.3% susceptible [S]), with potency and spectrum similar to that of vancomycin (MIC_{90}, 1 µg/mL; 100% S), linezolid (MIC_{90}, 1 µg/mL; 100% S), and daptomycin (MIC_{90}, 0.5 µg/mL; 100% S). The highest resistance (R) rate for MRSA was observed with erythromycin (86.6% R by CLSI criteria), followed by levofloxacin (55.4% R) and clindamycin (20.2% R; Table 2)
- Ceftaroline activity against CoNS (MIC_{50}, 0.25 µg/mL and MIC_{90}, 0.5 µg/mL) was similar to that observed against *S. aureus*. The highest ceftaroline MIC value was 1 µg/mL among CoNS (Tables 1 and 2)
- Against β-haemolytic streptococci, ceftaroline demonstrated activity (MIC_{50}, ≤0.008 µg/mL and MIC_{90}, 0.015 µg/mL) comparable to that of penicillin (MIC_{50}, ≤0.003 µg/mL and MIC_{90}, 0.06 µg/mL). Decreased susceptibility was observed with erythromycin (MIC_{90}, >4 µg/mL; 69.7% S) and clindamycin (MIC_{90}, >2 µg/mL; 83.4% S by CLSI criteria; Table 2)
- Group A β-haemolytic streptococci (MIC_{50} and MIC_{90}, ≤0.008 µg/mL) had lower ceftaroline MIC values than Group B isolates (MIC_{50} and MIC_{90}, 0.015 µg/mL), although the percentages susceptible were similar (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 *E. faecalis*, although MIC values were elevated compared with those noted against other Gram-positive species tested (MIC_{50}, 2 µg/mL and MIC_{90}, 8 µg/mL; Tables 1 and 2). All *E. faecalis* strains were susceptible to ampicillin (MIC_{90}, 2 µg/mL), linezolid (MIC_{90}, 1 µg/mL), and daptomycin (MIC_{90}, 1 µg/mL); 5.6% of strains were vancomycin-resistant (Table 2)
- Ceftaroline and ceftriaxone exhibited similar in vitro activities against *E. coli* and *Klebsiella* spp. (Table 2). Non-extended-spectrum β-lactamase (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).

Table 1. Antimicrobial Activity of Ceftaroline Against Organisms Causing Skin and Skin Structure Infections in USA Medical Centers (2010)

	No. of isolates (cumulative %) inhibited at ceftaroline MIC (µg/mL)								
Organism (n)	≤0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8
S. aureus (1114)	-	-	1(0.1)	2(0.3)	66(6.2)	465(47.9)	463(89.5)	113(99.6)	4(100.0)	-	-
MSSA (540)	-	-	1(0.2)	2(0.6)	66(12.8)	457(97.4)	13(99.8)	1(100.0)	-	-	-
MRSA (574)	-	-	-	-	-	8(1.4)	450(79.8)	112(99.3)	4(100.0)	-	-
βHS (433)	234(54.0)	161(91.2)	33(98.9)	5(100.0)	-	-	-	-	-	-	-
Group A (183)	175(95.6)	7(99.5)	1(100.0)	-	-	-	-	-	-	-	-
Group B (174)	7(4.0)	150(90.2)	16(99.4)	1(100.0)	-	-	-	-	-	-	-
Others (76)	52(68.4)	4(73.7)	16(94.7)	4(100.0)	-	-	-	-	-	-	-
VGS (88)	17(19.3)	24(46.6)	29(79.6)	12(93.2)	2(95.5)	0(95.5)	3(98.9)	1(100.0)	-	-	-
CoNS (72)	-	-	-	17(23.6)	12(40.3)	30(81.9)	12(98.6)	1(100.0)	-	-	-
E. faecalis (18)	-	-	-	-	-	-	-	6(33.3)	9(83.3)	1(88.9)	2(100.0)
Klebsiella spp. (90)	-	-	7(7.8)	31(42.2)	23(67.8)	14(83.3)	4(87.8)	0(87.8)	0(87.8)	0(87.8)	4(92.2)
non-ESBL phenotype[a] (79)	-	-	7(8.9)	31(48.1)	23(77.2)	14(94.9)	3(98.7)	0(98.7)	0(98.7)	0(98.7)	1(100.0)
ESBL phenotype[a] (11)	-	-	-	-	-	-	1(9.1)	0(9.1)	0(9.1)	0(9.1)	3(36.4)
E. coli (66)	-	-	8(12.1)	19(40.9)	17(66.7)	7(77.3)	2(80.3)	1(81.8)	0(81.8)	0(81.8)	4(87.9)
non-ESBL phenotype[a] (55)	-	-	8(14.6)	19(49.1)	17(80.0)	7(92.7)	2(96.4)	1(98.2)	0(98.2)	0(98.2)	0(98.2)
ESBL phenotype[a] (11)	-	-	-	-	-	-	-	-	-	-	4(36.4)
M. morganii (36)	-	-	6(16.7)	11(47.2)	7(66.7)	3(75.0)	2(80.6)	1(83.3)	0(83.3)	0(83.3)	2(88.9)

a. ESBL phenotype defined as an MIC≥2 µg/mL for ceftazidime or ceftriaxone or aztreonam. [CLSI, 2011].
βHS = β-haemolytic streptococci; CoNS = coagulase-negative staphylococci; ESBL = extended-spectrum β-lactamase; MIC = minimum inhibitory concentration; MSSA = methicillin-susceptible *Staphylococcus aureus*; MRSA = methicillin-resistant *S. aureus*; VGS = viridans group streptococci.

Table 2. Activity of Ceftaroline and Comparator Antimicrobial Agents When Tested Against Isolates Causing Skin and Skin Structure Infections in USA Medical Centers (2010)

Antimicrobial agent	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	Range (µg/mL)	CLSI[a] %S / %R	EUCAST[a] %S / %R
S. aureus (1114)					
Ceftaroline[b]	0.5	1	0.03 – 2	99.6 / -	- / -
Ceftriaxone[c]	8	>8	≤0.06 – >8	47.3 / 51.5	48.5 / 51.5
Erythromycin	>4	>4	≤0.25 – >4	38.5 / 60.1	38.5 / 61.0
Clindamycin	≤0.25	>2	≤0.25 – >2	87.2 / 12.7	86.9 / 12.8
Levofloxacin	≤0.5	>4	≤0.5 – >4	64.7 / 33.5	64.7 / 33.5
Linezolid	1	1	≤0.12 – 2	100.0 / 0.0	100.0 / 0.0
Tetracycline	≤0.25	0.5	≤0.25 – >8	95.3 / 4.4	93.7 / 5.3
TMP/SMX	≤0.5	≤0.5	≤0.5 – >4	99.0 / 1.0	99.0 / 0.9
Vancomycin	1	1	0.25 – 2	100.0 / 0.0	100.0 / 0.0
Daptomycin	0.25	0.5	0.12 – 1	100.0 / -	100.0 / 0.0
Oxacillin	>2	>2	≤0.25 – >2	48.5 / 51.5	48.5 / 51.5
MSSA (540)					
Ceftaroline[b]	0.25	0.25	0.03 – 1	100.0 / -	- / -
Ceftriaxone[c]	4	4	≤0.06 – >8	97.2 / 0.2	100.0 / 0.0
Erythromycin	≤0.25	>4	≤0.25 – >4	65.7 / 32.0	65.7 / 33.5
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	95.0 / 4.8	94.6 / 5.0
Levofloxacin	≤0.5	4	≤0.5 – >4	88.9 / 10.2	88.9 / 10.2
Linezolid	1	1	≤0.12 – 2	100.0 / 0.0	100.0 / 0.0
Tetracycline	≤0.25	0.5	≤0.25 – >8	95.4 / 4.1	94.3 / 5.4
TMP/SMX	≤0.5	≤0.5	≤0.5 – >4	99.6 / 0.4	99.6 / 0.4
Vancomycin	1	1	0.25 – 2	100.0 / 0.0	100.0 / 0.0
Daptomycin	0.25	0.5	0.12 – 1	100.0 / -	100.0 / 0.0
MRSA (574)					
Ceftaroline[b]	0.5	1	0.25 – 2	99.3 / -	- / -
Ceftriaxone[c]	>8	>8	4 – >8	0.0 / 100.0	0.0 / 100.0
Erythromycin	>4	>4	≤0.25 – >4	12.9 / 86.6	12.9 / 86.8
Clindamycin	≤0.25	>2	≤0.25 – >2	79.8 / 20.2	79.6 / 20.2
Levofloxacin	4	>4	≤0.5 – >4	42.0 / 55.4	42.0 / 55.4
Linezolid	1	1	≤0.12 – 2	100.0 / 0.0	100.0 / 0.0
Tetracycline	≤0.25	0.5	≤0.25 – >8	95.3 / 4.7	93.2 / 6.2
TMP/SMX	≤0.5	≤0.5	≤0.5 – >4	98.4 / 1.6	98.4 / 1.4
Vancomycin	1	1	0.25 – 2	100.0 / 0.0	100.0 / 0.0
Daptomycin	0.25	0.5	0.12 – 1	100.0 / -	100.0 / 0.0
β-haemolytic streptococci[d] (433)					
Ceftaroline[b]	≤0.008	0.015	≤0.008 – 0.06	- / -	- / -
Penicillin	≤0.03	0.06	≤0.03 – 0.06	100.0 / -	100.0 / 0.0
Ceftriaxone	≤0.06	0.12	≤0.06 – 0.5	100.0 / -	100.0 / 0.0
Erythromycin	≤0.25	>4	≤0.25 – >4	69.7 / 29.8	69.7 / 29.8
Clindamycin	≤0.25	>2	≤0.25 – >2	83.4 / 16.4	83.6 / 16.4
Levofloxacin	≤0.5	1	≤0.5 – >4	99.3 / 0.5	96.5 / 0.7
Linezolid	1	1	≤0.12 – 1	100.0 / -	100.0 / 0.0
Tetracycline	1	>8	≤0.25 – >8	50.6 / 48.0	50.3 / 49.4
Vancomycin	0.25	0.5	0.25 – 1	100.0 / -	100.0 / 0.0
Daptomycin	≤0.06	0.25	≤0.06 – 0.5	100.0 / -	100.0 / 0.0
Group A (183)					
Ceftaroline[b]	≤0.008	≤0.008	≤0.008 – 0.03	99.5 / -	- / -
Penicillin	≤0.03	≤0.03	≤0.03 – 0.06	100.0 / -	100.0 / 0.0
Ceftriaxone	≤0.06	≤0.06	≤0.06 – 0.25	100.0 / -	100.0 / 0.0
Erythromycin	≤0.25	2	≤0.25 – >4	86.9 / 12.6	86.9 / 12.6
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	92.9 / 7.1	92.9 / 7.1
Levofloxacin	≤0.5	1	≤0.5 – >4	99.5 / 0.5	95.1 / 0.5
Linezolid	1	1	0.25 – 1	100.0 / -	100.0 / 0.0
Tetracycline	≤0.25	>8	≤0.25 – >8	83.6 / 16.4	83.1 / 16.4
Vancomycin	0.25	0.5	0.25 – 1	100.0 / -	100.0 / 0.0
Daptomycin	≤0.06	≤0.06	≤0.06 – 0.25	100.0 / -	100.0 / 0.0
Group B (174)					
Ceftaroline[b]	0.015	0.015	≤0.008 – 0.06	99.4 / -	- / -
Penicillin	≤0.03	0.06	≤0.03 – 0.06	100.0 / -	100.0 / 0.0
Ceftriaxone	≤0.06	0.12	≤0.06 – 0.25	100.0 / -	100.0 / 0.0
Erythromycin	≤0.25	>4	≤0.25 – >4	50.0 / 50.0	50.0 / 50.0
Clindamycin	≤0.25	>2	≤0.25 – >2	68.4 / 31.0	69.0 / 31.0
Levofloxacin	≤0.5	1	≤0.5 – >4	99.4 / 0.6	97.1 / 0.6
Linezolid	1	1	0.5 – 1	100.0 / -	100.0 / 0.0
Tetracycline	>8	>8	≤0.25 – >8	12.1 / 86.8	12.1 / 87.9
Daptomycin	0.25	0.25	≤0.06 – 0.5	100.0 / -	100.0 / 0.0
Other groups (76)					
Ceftaroline[b]	≤0.008	0.03	≤0.008 – 0.06	- / -	- / -
Penicillin	≤0.03	0.06	≤0.03 – 0.06	100.0 / -	100.0 / 0.0
Ceftriaxone	≤0.06	0.25	≤0.06 – 0.5	100.0 / -	100.0 / 0.0
Erythromycin	≤0.25	4	≤0.25 – >4	73.7 / 25.0	73.7 / 25.0
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	94.7 / 5.3	94.7 / 5.3
Levofloxacin	≤0.5	1	≤0.5 – 4	98.7 / 0.0	98.7 / 1.3
Linezolid	1	1	≤0.12 – 1	100.0 / -	100.0 / 0.0
Tetracycline	0.5	>8	≤0.25 – >8	59.2 / 35.5	59.2 / 40.8
Vancomycin	0.25	0.5	0.25 – 1	100.0 / -	100.0 / 0.0
Daptomycin	≤0.06	0.25	≤0.06 – 0.5	100.0 / -	100.0 / 0.0
Viridans group streptococci[e] (88)					
Ceftaroline[b]	0.03	0.06	≤0.008 – 1	- / -	- / -
Penicillin	≤0.03	0.25	≤0.03 – >4	88.6 / 3.4	92.0 / 3.4
Ceftriaxone	0.25	0.5	≤0.06 – 8	95.5 / 3.4	93.2 / 6.8
Erythromycin	≤0.25	>4	≤0.25 – >4	52.3 / 38.6	- / -
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	90.9 / 9.1	93.2 / 6.8
Levofloxacin	≤0.5	1	≤0.5 – >4	96.6 / 2.3	- / -
Linezolid	1	1	≤0.12 – 1	100.0 / -	- / -
Tetracycline	0.5	>8	≤0.25 – >8	73.9 / 22.7	- / -
Vancomycin	0.5	1	≤0.12 – 1	100.0 / -	100.0 / 0.0
Daptomycin	0.25	0.5	≤0.06 – 4	98.9 / -	- / -
CoNS[f] (72)					
Ceftaroline[b]	0.25	0.5	0.06 – 1	- / -	- / -
Oxacillin	1	>2	≤0.25 – >2	36.1 / 63.9	36.1 / 63.9
Ceftriaxone[c]	4	>8	0.5 – >8	36.1 / 63.9	36.1 / 63.9
Erythromycin	>4	>4	≤0.25 – >4	38.9 / 59.7	38.9 / 61.1
Clindamycin	≤0.25	>2	≤0.25 – >2	72.2 / 26.4	69.4 / 27.8
Levofloxacin	≤0.5	>4	≤0.5 – >4	65.3 / 31.9	65.3 / 31.9
Linezolid	0.5	1	0.25 – 1	100.0 / 0.0	100.0 / 0.0
Tetracycline	≤0.25	>8	≤0.25 – >8	83.3 / 15.3	76.4 / 16.7
TMP/SMX	≤0.5	>4	≤0.5 – >4	72.2 / 27.8	72.2 / 19.4
Vancomycin	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Daptomycin	0.25	0.5	≤0.06 – 1	100.0 / -	100.0 / 0.0
E. faecalis (18)					
Ceftaroline[b]	2	8	1 – 8	- / -	- / -
Ampicillin	≤1	2	≤1 – 2	100.0 / 0.0	100.0 / 0.0
Erythromycin	2	>4	≤0.25 – >4	11.1 / 44.4	- / -
Levofloxacin	1	>4	≤0.5 – >4	77.8 / 22.2	- / -
Linezolid	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Tetracycline	>8	>8	≤0.25 – >8	16.7 / 83.3	- / -
Vancomycin	1	2	1 – >16	94.4 / 5.6	94.4 / 5.6
Daptomycin	1	1	0.5 – 2	100.0 / -	- / -
Klebsiella spp.[g] (90)					
Ceftaroline[b]	0.12	8	0.03 – >32	87.8 / 12.2	- / -
Ceftriaxone	≤0.06	4	≤0.06 – >8	88.9 / 11.1	88.9 / 11.1
Ceftazidime	0.12	1	0.03 – >32	93.3 / 6.7	91.1 / 6.7
P/T	2	32	≤0.5 – >64	88.9 / 10.0	86.7 / 11.1
Meropenem	≤0.12	≤0.12	≤0.12 – >8	97.8 / 2.2	97.8 / 2.2
Levofloxacin	≤0.5	≤0.5	≤0.5 – >4	92.2 / 4.4	91.1 / 7.8
Gentamicin	≤1	≤1	≤1 – >8	95.6 / 3.3	94.4 / 4.4
Non-ESBL phenotype[a] (79)					
Ceftaroline[b]	0.12	0.25	0.03 – 8	98.7 / 1.3	- / -
Ceftriaxone	≤0.06	0.12	≤0.06 – 1	100.0 / 0.0	100.0 / 0.0
Ceftazidime	0.12	0.25	0.03 – 1	100.0 / 0.0	100.0 / 0.0
P/T	2	4	≤0.5 – >64	97.5 / 1.3	97.5 / 2.5
Meropenem	≤0.12	≤0.12	≤0.12	100.0 / 0.0	100.0 / 0.0
Levofloxacin	≤0.5	≤0.5	≤0.5 – 4	98.7 / 0.0	97.5 / 1.3
Gentamicin	≤1	≤1	≤1 – >8	98.7 / 1.3	98.7 / 1.3
ESBL phenotype[a] (11)					
Ceftaroline[b]	>32	>32	0.5 – >32	9.1 / 90.9	- / -
Ceftriaxone	>8	>8	0.25 – >8	9.1 / 90.9	9.1 / 90.9
Ceftazidime	16	>32	0.12 – >32	45.5 / 54.5	27.3 / 54.5
P/T	>64	>64	4 – >64	27.3 / 72.7	9.1 / 72.7
Meropenem	≤0.12	>8	≤0.12 – >8	81.8 / 18.2	81.8 / 18.2
Levofloxacin	4	>4	≤0.5 – >4	45.5 / 36.4	45.5 / 54.5
Gentamicin	≤1	>8	≤1 – >8	72.7 / 18.2	63.6 / 27.3
E. coli (66)					
Ceftaroline[b]	0.12	32	0.03 – >32	80.3 / 18.2	- / -
Ceftriaxone	≤0.06	>8	≤0.06 – >8	83.3 / 16.7	83.3 / 16.7
Ceftazidime	0.25	16	0.06 – >32	84.8 / 12.1	83.3 / 15.2
P/T	2	4	1 – >64	95.5 / 1.5	90.9 / 4.5
Meropenem	≤0.12	≤0.12	≤0.12 – 0.25	100.0 / 0.0	100.0 / 0.0
Levofloxacin	≤0.5	>4	≤0.5 – >4	66.7 / 31.8	66.7 / 33.3
Gentamicin	≤1	>8	≤1 – >8	84.8 / 15.2	84.8 / 15.2
Non-ESBL phenotype[a] (55)					
Ceftaroline[b]	0.12	0.25	0.03 – 16	96.4 / 1.8	- / -
Ceftriaxone	≤0.06	0.12	≤0.06 – 0.25	100.0 / 0.0	100.0 / 0.0
Ceftazidime	0.12	0.25	0.06 – 1	100.0 / 0.0	100.0 / 0.0
P/T	2	4	1 – >64	98.2 / 1.8	92.7 / 1.8
Meropenem	≤0.12	≤0.12	≤0.12 – 0.25	100.0 / 0.0	100.0 / 0.0
Levofloxacin	≤0.5	>4	≤0.5 – >4	72.7 / 27.3	72.7 / 27.3
Gentamicin	≤1	>8	≤1 – >8	89.1 / 10.9	89.1 / 10.9
ESBL-phenotype[a] (11)					
Ceftaroline[b]	>32	>32	8 – >32	0.0 / 100.0	- / -
Ceftriaxone	>8	>8	8 – >8	0.0 / 100.0	0.0 / 100.0
Ceftazidime	16	32	4 – >32	9.1 / 72.7	0.0 / 90.9
P/T	2	64	1 – 64	81.8 / 0.0	81.8 / 18.2
Meropenem	≤0.12	≤0.12	≤0.12	100.0 / 0.0	100.0 / 0.0
Levofloxacin	>4	>4	≤0.5 – >4	36.4 / 54.5	36.4 / 63.6
Gentamicin	≤1	>8	≤1 – >8	63.6 / 36.4	63.6 / 36.4
M. morganii (36)					
Ceftaroline[b]	0.12	>32	0.03 – >32	80.6 / 16.7	- / -
Ceftriaxone	≤0.06	2	≤0.06 – 4	88.9 / 2.8	88.9 / 2.8
Ceftazidime	0.12	8	0.03 – 16	88.9 / 8.3	86.1 / 11.1
P/T	≤0.5	1	≤0.5 – 4	100.0 / 0.0	100.0 / 0.0
Meropenem	≤0.12	≤0.12	≤0.12	100.0 / 0.0	100.0 / 0.0
Levofloxacin	≤0.5	2	≤0.5 – 4	97.2 / 0.0	88.9 / 2.8
Gentamicin	≤1	>8	≤1 – >8	86.1 / 11.1	86.1 / 13.9

a. Criteria as published by the CLSI [2011] and EUCAST [2011].
b. USA-FDA breakpoints were applied when available [Teflaro® Product Insert, 2010].
c. USA-FDA breakpoints were applied when available [Rocephin® Product Insert, 2010].
d. Includes: *Streptococcus dysgalactiae* (6 strains), Group A *Streptococcus* (183 strains), Group B *Streptococcus* (174 strains), Group C *Streptococcus* (27 strains), Group F *Streptococcus* (8 strains), and Group G *Streptococcus* (35 strains).
e. Includes: *Streptococcus anginosus* (14 strains), *S. constellatus* (7 strains), *S. intermedius* (5 strains), *S. milleri* (1 strain), *S. mitis* (8 strains), *S. oralis* (1 strain), *S. parasanguinis* (1 strain), *S. sanguinis* (1 strain), unspeciated α-haemolytic streptococci (2 strains), and unspeciated viridans group streptococci (48 strains).
f. Includes: *Staphylococcus epidermidis* (8 strains), *S. haemolyticus* (2 strains), *S. hominis* (1 strain), *S. lugdunensis* (7 strains), *S. saprophyticus* (1 strain), *S. sciuri* (1 strain), and unspeciated coagulase-negative staphylococci (51 strains).
g. Includes: *Klebsiella oxytoca* (43 strains) and *K. pneumoniae* (47 strains).
h. ESBL phenotype was defined as MIC ≥2 µg/mL for ceftazidime or ceftriaxone or aztreonam.
CLSI = Clinical and Laboratory Standards Institute; CoNS = coagulase-negative staphylococci; ESBL = extended-spectrum β-lactamase; EUCAST = European Committee on Antimicrobial Susceptibility Testing; MIC = minimum inhibitory concentration; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-susceptible *S. aureus*; R = resistant; S = susceptible; TMP/SMX=trimethoprim/sulfamethoxazole; P/T=piperacillin/tazobactam.

Conclusions

- Ceftaroline was highly active in vitro against Gram-positive pathogens, including MRSA and β-hemolytic streptococci, and Enterobacteriaceae recently isolated from ABSSSI in USA medical centers
- The ceftaroline spectrum for Gram-positive organisms (with the exception of *E. faecalis*) was similar to that of linezolid and vancomycin. When tested in vitro against Enterobacteriaceae, ceftaroline had a spectrum comparable to ceftriaxone
- Ceftaroline fosamil appears to be a promising agent for treatment of ABSSSIs, including those caused by oxacillin-resistant staphylococci.

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Acknowledgments

This study was supported by Forest Laboratories, Inc.

Forest Laboratories, Inc., was involved in the study design and in the decision to present these results. Forest Laboratories, Inc., had no involvement in the analysis, collection, and interpretation of data.

Scientific Therapeutics Information, Inc, provided editorial coordination, which was funded by Forest Research Institute, Inc.