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Antimicrobial Activity of Ceftaroline Tested Against Bacteria Collected from Patients with Respiratory Tract Infections in the United States (2010)

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 Gram-positive pathogens causing respiratory tract infections (RTI), including MRSA, penicillin (PEN)-resistant (R) *S. pneumoniae* (SPN), and common Gram-negative organisms. CPT fosamil is USA-FDA-approved for the treatment of community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections.

Methods:
Isolates were consecutively collected in 62 United States (USA) medical centers from patients with RTI in 2010. CPT and comparator antimicrobials used to treat RTI were evaluated by CLSI broth microdilution methods. A total of 2,263 strains were tested, including 863 SPN (23.8% PEN-R [MIC, ≥2 μg/mL]; 10.8% ceftriaxone [CRO]-non-susceptible [S]), 670 *H. influenzae* (HI; 27.9% β-lactamase [BL]-producers), 190 *S. aureus* (47.8% MRSA), 178 *M. catarrhalis* (MC), 110 β-haemolytic streptococci (BHS), 178 enteric bacilli (EB), 40 viridans group streptococci and 34 *H. parainfluenzae*.

Results:
Against PEN-R SPN, CPT ($MIC_{50/90}$, 0.12/0.25 μg/mL; highest MIC, 0.5 μg/mL) was 8- to 32-fold more active than CRO ($MIC_{50/90}$, 1/2 μg/mL; 55.1% S), amoxicillin/clavulanate ($MIC_{50/90}$, 8/8 μg/mL; 20.5% S) and cefuroxime ($MIC_{50/90}$, 8/16 μg/mL; 0.0% S). CPT was also very active against CRO-non-S SPN ($MIC_{50/90}$, 0.25/0.5 μg/mL). The highest CPT MIC among HI was 0.25 μg/mL (1 isolate) and activity against HI was not adversely affected by BL production. CPT was very active against MRSA ($MIC_{50/90}$, 0.5/1 μg/mL) and 16-fold more active than CRO ($MIC_{50/90}$, 4/4 μg/mL) when tested against MSSA. MC ($MIC_{50/90}$, 0.06/0.12 μg/mL), BHS ($MIC_{50/90}$, ≤0.008/0.015 μg/mL) and VGS ($MIC_{50/90}$, 0.03/0.5 μg/mL) were also very S to CPT. Non-ESBL-producing EB were CPT-S while ESBL-phenotype EB exhibited decreased S to CPT and all cephalosporins tested.

Conclusion:
CPT exhibited potent activity against pathogens recently collected from RTI patients in USA centers, including multidrug-R SPN and MRSA. Based on these results, CPT appears to be a valuable agent for contemporary treatment of RTI.

Introduction

Ceftaroline is the active metabolite of the prodrug ceftaroline fosamil, an N-phosphonoamino water-soluble cephalosporin. Ceftaroline fosamil was approved in 2010 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).

Ceftaroline fosamil has demonstrated broad-spectrum activity against pathogens frequently encountered in CABP, including *Streptococcus pneumoniae*, methicillin-susceptible *Staphylococcus aureus* (MSSA), and Enterobacteriaceae. In vitro, and in animal models, ceftaroline has demonstrated potent activity against resistant isolates, including multi-drug-resistant *S. pneumoniae* and methicillin-resistant *S. aureus* (MRSA).

As part of the Assessing Worldwide Antimicrobial Resistance Evaluation (AWARE) Program, a global ceftaroline surveillance study, we evaluated the spectrum and antimicrobial activity of ceftaroline and comparator agents tested against bacterial pathogens recovered from respiratory tract infections (RTI), including commonly encountered resistance phenotypes, recently collected from United States (USA) medical centers.

Methods

Organism collection: Isolates were consecutively collected in 62 USA medical centers from patients with RTI in 2010. A total of 2263 strains were tested, including 863 *S. pneumoniae* (23.8% penicillin-resistant [MIC, ≥2 μg/mL]; 10.8% ceftriaxone-nonsusceptible), 670 *Haemophilus influenzae* (27.9% β-lactamase-producers), 190 *S. aureus* (47.8% MRSA), 178 *Moraxella catarrhalis*, 110 β-haemolytic streptococci, 178 Enterobacteriaceae, 40 viridans group streptococci, and 34 *Haemophilus parainfluenzae*.

Susceptibility 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 RTI. 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).

Extended-spectrum β-lactamase (ESBL) phenotype was defined as an MIC value of ≥2 μg/mL for ceftazidime or ceftriaxone or aztreonam. Concurrent quality control (QC) testing was performed to assure proper test conditions and procedures. QC strains included: *S. aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, and *S. pneumoniae* ATCC 49619. Susceptibility percentages and validation of QC results were based on the 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 was active against *S. pneumoniae* and maintained low MIC values (≤0.5 μg/mL) for isolates with decreased susceptibility to penicillin or ceftriaxone (Table 1)
- When tested against *S. pneumoniae,* ceftaroline (MIC_{90}, 0.12 μg/mL) was 16-, 32-, 64-, and 64-fold more active than ceftriaxone (MIC_{90}, 2 μg/mL), penicillin (MIC_{90}, 4 μg/mL), amoxicillin/clavulanate (MIC_{90}, 8 μg/mL), and cefuroxime (MIC_{90}, 8 μg/mL; Table 2), respectively. Only ceftaroline (98.6%) and levofloxacin (98.7%) showed >90% susceptibility rates (Table 2)
- For the penicillin-resistant *S. pneumoniae*, ceftaroline ($MIC_{50/90}$, 0.12/0.25 μg/mL) was 8-fold more active than ceftriaxone ($MIC_{50/90}$, 1/2 μg/mL; 55.1% susceptible [S]; data not shown). Furthermore, ceftaroline exhibited good activity against ceftriaxone-nonsusceptible strains (MIC_{50}, 0.25 μg/mL, 87.1% S, highest MIC, 0.5 μg/mL; Table 1)
- Ceftaroline was active against *H. influenzae* (MIC_{90}, 0.015 μg/mL and 0.03 μg/mL for β-lactamase-negative and -positive isolates, respectively; Table 1), with 99.9% of isolates being categorized as ceftaroline-susceptible according to the breakpoints established by the USA-FDA (Table 2)
- Ceftaroline activity against *M. catarrhalis* isolates (MIC_{90}, 0.12 μg/mL) was 4- and 16-fold greater than ceftriaxone (MIC_{90}, 0.5 μg/mL) and cefuroxime (MIC_{90}, 2 μg/mL), respectively. All comparators tested demonstrated susceptibility rates of ≥99.4%, except for trimethoprim/sulfamethoxazole (96.1%; Table 2)
- Ceftaroline was active against MRSA ($MIC_{50/90}$, 0.5/1 μg/mL; Table 1) and 16-fold more active than ceftriaxone ($MIC_{50/90}$, 4/4 μg/mL) when tested against methicillin-S *S. aureus* ($MIC_{50/90}$, 0.25/0.25 μg/mL, data not shown) from RTI. Overall, 97.9% of *S. aureus* isolates were inhibited by ceftaroline at ≤1 μg/mL (Table 2)
- Against β-haemolytic streptococci, ceftaroline demonstrated activity ($MIC_{50/90}$, ≤0.008/0.015 μg/mL) comparable to that of penicillin ($MIC_{50/90}$, ≤0.03/0.06 μg/mL). Decreased susceptibility was observed with erythromycin (MIC_{90}, >4 μg/mL; 74.5% S), tetracycline (MIC_{90}, >8 μg/mL; 72.7% S by CLSI criteria) and clindamycin (MIC_{90}, >2 μg/mL; 90.9% S by CLSI criteria; Table 2)
- Ceftaroline and ceftriaxone exhibited similar in vitro activities against commonly isolated RTI Enterobacteriaceae species (Table 2). Non-ESBL-producing Enterobacteriaceae strains were generally susceptible to ceftaroline while strains with an ESBL phenotype exhibited greatly reduced susceptibility rates to ceftaroline and all cephalosporins tested (Table 1)
- The highest ceftaroline MIC value among *H. parainfluenzae* was 0.5 μg/mL (1 strain), and 97.1% of strains were inhibited at a ceftaroline MIC of ≤0.12 μg/mL (MIC_{50}, ≤0.008 μg/mL and MIC_{90}, 0.03 μg/mL; Tables 1 and 2).

Table 1. Antimicrobial Activity of Ceftaroline Against Organisms Causing Respiratory Tract 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. pneumoniae (863)	411(47.6)	88(57.8)	64(65.2)	84(75.0)	149(92.2)	55(98.6)	12(100.0)	-	-	-	-
Penicillin-susceptible (458)[a]	405(88.4)	40(97.2)	9(99.1)	4(100.0)	-	-	-	-	-	-	-
Penicillin-intermediate (200)[a]	6(3.0)	48(27.0)	55(54.5)	75(92.0)	15(99.5)	1(100.0)	-	-	-	-	-
Penicillin-resistant (205)[a]	-	-	-	5(2.4)	134(67.8)	54(94.2)	12(100.0)	-	-	-	-
Ceftriaxone-nonsusceptible (93)	-	-	-	-	34(36.6)	47(87.1)	12(100.0)	-	-	-	-
H. influenzae (670)	447(66.7)	147(88.7)	56(97.0)	15(99.3)	4(99.9)	1(100.0)	-	-	-	-	-
β-lactamase-negative (482)	373(77.4)	89(95.9)	18(99.6)	2(100.0)	-	-	-	-	-	-	-
β-lactamase-positive (188)	74(39.6)	58(70.2)	38(90.4)	13(97.3)	4(99.5)	1(100.0)	-	-	-	-	-
M. catarrhalis (178)	9(5.1)	6(8.4)	46(34.3)	56(65.7)	52(94.9)	9(100.0)	-	-	-	-	-
S. aureus (190)	-	-	-	1(0.5)	7(4.2)	92(52.6)	53(80.5)	33(97.9)	4(100.0)	-	-
MSSA (99)	-	-	-	1(1.0)	7(8.1)	89(98.0)	2(100.0)	-	-	-	-
MRSA (91)	-	-	-	-	-	3(3.3)	51(59.3)	33(95.6)	4(100.0)	-	-
β-haemolytic streptococci (110)	78(70.9)	24(92.7)	5(97.3)	3(100.0)	-	-	-	-	-	-	-
S. pyogenes (Group A; 66)	63(95.5)	1(97.0)	1(98.5)	1(100.0)	-	-	-	-	-	-	-
S. agalactiae (Group B; 23)	1(4.4)	20(91.3)	2(100.0)	-	-	-	-	-	-	-	-
Others (21)	14(66.7)	3(81.0)	2(90.5)	2(100.0)	-	-	-	-	-	-	-
K. pneumoniae (106)	-	-	5(4.7)	44(46.2)	24(68.9)	10(78.3)	9(86.8)	2(88.7)	1(89.6)	1(90.6)	1(91.5)
Non-ESBL-phenotype (95)	-	-	5(5.3)	44(51.6)	24(76.8)	10(87.4)	9(96.8)	2(99.0)	1(100.0)	-	-
ESBL-phenotype (11)	-	-	-	-	-	-	-	-	-	1(9.1)	1(18.2)
K. oxytoca (37)	-	-	2(5.4)	8(27.0)	6(43.2)	7(62.2)	6(78.4)	0(78.4)	0(78.4)	1(81.1)	0(81.1)
Non-ESBL-phenotype (29)	-	-	2(6.9)	8(34.5)	6(55.2)	7(79.3)	6(100.0)	-	-	-	-
ESBL-phenotype (8)	-	-	-	-	-	-	-	-	-	1(12.5)	0(12.5)
E. coli (35)	1(2.9)	0(2.9)	6(20.0)	6(37.1)	4(48.6)	3(57.1)	3(65.7)	2(71.4)	0(71.4)	0(71.4)	1(74.3)
Non-ESBL-phenotype (24)	1(4.2)	0(4.2)	6(29.2)	6(54.2)	4(70.8)	3(83.3)	2(91.7)	2(100.0)	-	-	-
ESBL-phenotype (11)	-	-	-	-	-	-	1(9.1)	0(9.1)	0(9.1)	0(9.1)	1(18.2)
H. parainfluenzae (34)	25(75.5)	4(85.3)	2(91.2)	1(94.1)	1(97.1)	0(97.1)	1(100.0)	-	-	-	-
Viridans gr. streptococci (40)	4(10.0)	6(25.0)	13(57.5)	6(72.5)	2(77.5)	3(85.0)	4(95.0)	1(100.0)	-	-	-

a. Criteria as published by the CLSI [2011] for 'Penicillin (oral penicillin V)': susceptible at ≤0.06μg/mL, intermediate at 0.12 – 1 μg/mL, and resistant at ≥2 μg/mL.
ESBL = extended-spectrum β-lactamase; MIC = minimum inhibitory concentration; MRSA = methicillin (oxacillin)-resistant *Staphylococcus aureus*; MSSA = methicillin (oxacillin)-susceptible *S. aureus*.

Table 2. Activity of Ceftaroline and Comparator Antimicrobial Agents When Tested Against Isolates of Respiratory Tract Infection Collected in USA Medical Centers in 2010

Antimicrobial agent	MIC_{50} (μg/mL)	MIC_{90} (μg/mL)	Range (μg/mL)	CLSI[a] %S / %R	EUCAST[a] %S / %R
Streptococcus pneumoniae (863)					
Ceftaroline[b]	0.015	0.12	≤0.008 – 0.5	98.6 / -	- / -
Ceftriaxone	≤0.06	2	≤0.06 – 8	89.2 / 2.0	76.6 / 2.0
Cefuroxime	≤0.12	8	≤0.12 – >16	69.6 / 26.2	68.0 / 30.4
Amoxicillin/clavulanate	≤1	8	≤1 – >8	81.1 / 15.4	- / -
Penicillin[c]	0.06	4	≤0.03 – >4	83.9 / 0.8	- / -
Penicillin[d]	0.06	4	≤0.03 – >4	53.1 / 23.8	53.1 / 16.1
Erythromycin	≤0.06	>8	≤0.06 – >8	56.0 / 43.3	56.0 / 43.3
Clindamycin	≤0.25	>1	≤0.25 – >1	75.7 / 23.8	76.2 / 23.8
Levofloxacin	1	1	≤0.5 – >4	98.7 / 1.2	98.7 / 1.3
Tetracycline	0.5	>8	≤0.25 – >8	72.6 / 27.3	72.6 / 27.4
Trimethoprim/sulfamethoxazole	≤0.5	>4	≤0.5 – >4	65.2 / 26.5	70.2 / 26.5
Haemophilus influenzae (670)					
Ceftaroline[b]	≤0.008	0.03	≤0.008 – 0.25	99.9 / -	- / -
Ceftriaxone	≤0.06	≤0.06	≤0.06 – 0.5	100.0 / -	99.4 / 0.6
Cefuroxime	0.5	2	≤0.12 – 8	99.4 / 0.0	80.0 / 3.4
Ampicillin[e]	≤1	>8	≤1 – >8	71.9 / 28.1	71.9 / 28.1
Amoxicillin/clavulanate	≤1	≤1	≤1 – 4	100.0 / 0.0	90.3 / 9.7
Piperacillin/tazobactam	≤0.5	≤0.5	≤0.5 – 1	100.0 / 0.0	- / -
Meropenem	≤0.12	≤0.12	≤0.12 – 0.5	100.0 / -	100.0 / 0.0
Azithromycin	1	2	≤0.25 – >4	98.4 / -	0.3 / 1.6
Levofloxacin	≤0.5	≤0.5	≤0.5	100.0 / -	100.0 / 0.0
Tetracycline	0.5	1	≤0.25 – >8	98.7 / 1.2	98.4 / 1.3
Trimethoprim/sulfamethoxazole	≤0.5	>4	≤0.5 – >4	76.0 / 21.3	76.0 / 23.4
Moraxella catarrhalis (178)					
Ceftaroline[b]	0.06	0.12	≤0.008 – 0.25	- / -	- / -
Ceftriaxone	0.25	0.5	≤0.06 – 2	100.0 / -	99.4 / 0.0
Cefuroxime	1	2	≤0.12 – 8	99.4 / 0.0	75.3 / 2.2
Amoxicillin/clavulanate	≤1	≤1	≤1	100.0 / 0.0	100.0 / 0.0
Meropenem	0.12	0.12	≤0.12 – 0.12	- / -	100.0 / 0.0
Erythromycin	0.12	0.25	≤0.06 – 4	99.4 / -	91.6 / 0.6
Levofloxacin	≤0.5	≤0.5	≤0.5 – 1	100.0 / -	100.0 / 0.0
Tetracycline	≤0.25	0.5	≤0.25 – 1	100.0 / 0.0	100.0 / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	≤0.5 – >4	96.1 / 2.2	96.1 / 3.4
Staphylococcus aureus (190)					
Ceftaroline[b]	0.25	1	0.06 – 2	97.9 / -	- / -
Ceftriaxone[f]	4	>8	0.5 – >8	52.1 / 47.9	52.1 / 47.9
Erythromycin	>4	>4	≤0.25 – >4	34.2 / 65.8	34.2 / 65.8
Clindamycin	≤0.25	>2	≤0.25 – >2	76.8 / 22.1	75.3 / 23.2
Levofloxacin	≤0.5	>4	≤0.5 – >4	53.2 / 45.3	53.2 / 45.3
Tetracycline	≤0.25	0.5	≤0.25 – >8	95.8 / 4.2	94.7 / 4.7
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	≤0.5 – >4	97.4 / 2.6	97.4 / 1.6
Linezolid	1	2	0.5 – 4	100.0 / 0.0	100.0 / 0.0
Daptomycin	≤0.25	0.5	≤0.06 – 0.5	100.0 / -	100.0 / 0.0
Vancomycin	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Oxacillin	1	>2	≤0.25 – >2	52.1 / 47.9	52.1 / 47.9
β-haemolytic streptococci (110)[g]					
Ceftaroline[b]	≤0.008	0.015	≤0.008 – 0.06	- / -	- / -
Ceftriaxone	≤0.06	0.12	≤0.06 – 0.5	100.0 / -	100.0 / 0.0
Penicillin	≤0.03	0.06	≤0.03 – 0.12	100.0 / -	100.0 / 0.0
Erythromycin	≤0.25	>4	≤0.25 – >4	74.5 / 24.5	74.5 / 24.5
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	90.9 / 8.2	91.8 / 8.2
Levofloxacin	≤0.5	1	≤0.5 – 2	100.0 / 0.0	92.7 / 0.0
Tetracycline	≤0.25	>8	≤0.25 – >8	72.7 / 24.5	71.8 / 27.3
Linezolid	1	1	≤0.12 – 1	100.0 / -	100.0 / 0.0
Daptomycin	≤0.06	0.25	≤0.06 – 0.25	100.0 / -	100.0 / 0.0
Klebsiella pneumoniae (106)					
Ceftaroline[b]	0.12	4	0.03 – >32	86.8 / 11.3	- / -
Ceftriaxone	≤0.06	4	≤0.06 – >8	89.6 / 10.4	89.6 / 10.4
Cefuroxime	0.12	4	0.03 – >32	91.5 / 8.5	89.6 / 8.5
Ampicillin/sulbactam	8	32	0.5 – >32	74.5 / 15.1	- / 25.5
Piperacillin/tazobactam	4	16	≤0.5 – >64	93.4 / 2.8	86.8 / 6.6
Levofloxacin	≤0.5	4	≤0.5 – >4	89.6 / 9.4	86.8 / 10.4
Gentamicin	≤1	≤1	≤1 – >8	91.5 / 3.8	91.5 / 8.5
Meropenem	≤0.12	≤0.12	≤0.12 – >8	96.2 / 2.8	97.2 / 2.8
Klebsiella group streptococci (40)[h]					
Ceftaroline[b]	0.03	0.5	≤0.008 – 1	- / -	- / -
Ceftriaxone	0.25	2	≤0.06 – 8	82.5 / 7.5	75.0 / 25.0
Cefuroxime	0.5	8	≤0.12 – >16	- / -	57.5 / 42.5
Penicillin	0.12	2	≤0.03 – >4	57.5 / 10.0	65.0 / 10.0
Clindamycin	≤0.25	>2	≤0.25 – >2	82.5 / 17.5	82.5 / 17.5
Levofloxacin	1	4	≤0.5 – >4	87.5 / 10.0	- / -
Tetracycline	1	>8	≤0.25 – >8	60.0 / 32.5	- / -
Linezolid	1	1	≤0.12 – 1	100.0 / -	- / -
Daptomycin	0.25	0.5	0.12 – 1	100.0 / -	- / -
Klebsiella oxytoca (37)					
Ceftaroline[b]	0.25	>32	0.03 – >32	78.4 / 21.6	- / -
Ceftriaxone	0.12	>8	≤0.06 – >8	78.4 / 21.6	78.4 / 21.6
Ceftazidime	0.12	1	0.03 – 16	97.3 / 2.7	97.3 / 2.7
Ampicillin/sulbactam	8	>32	4 – >32	64.9 / 21.6	- / 35.1
Piperacillin/tazobactam	2	>64	1 – >64	81.1 / 18.9	81.1 / 18.9
Levofloxacin	≤0.5	≤0.5	≤0.5 – >4	97.3 / 2.7	94.6 / 2.7
Gentamicin	≤1	≤1	≤1 – 8	97.3 / 0.0	97.3 / 2.7
Meropenem	≤0.12	≤0.12	≤0.12	100.0 / 0.0	100.0 / 0.0
Escherichia coli (35)					
Ceftaroline[b]	0.25	>32	≤0.008 – >32	65.7 / 28.6	- / -
Ceftriaxone	≤0.06	>8	≤0.06 – >8	74.3 / 25.7	74.3 / 25.7
Ceftazidime	0.25	8	0.03 – 16	88.6 / 8.6	71.4 / 11.4
Ampicillin/sulbactam	16	>32	0.5 – >32	45.7 / 34.3	- / 54.3
Piperacillin/tazobactam	2	16	≤0.5 – >64	91.4 / 5.7	85.7 / 8.6
Levofloxacin	≤0.5	>4	≤0.5 – >4	54.3 / 45.7	54.3 / 45.7
Gentamicin	≤1	>8	≤1 – >8	82.9 / 17.1	80.0 / 17.1
Meropenem	≤0.12	≤0.12	≤0.12	100.0 / 0.0	100.0 / 0.0
Haemophilus parainfluenzae (34)					
Ceftaroline[b]	≤0.008	0.03	≤0.008 – 0.5	- / -	- / -
Ceftriaxone	≤0.06	≤0.06	≤0.06 – 0.12	100.0 / -	- / -
Cefuroxime	≤0.12	1	≤0.12 – 2	100.0 / 0.0	- / -
Ampicillin	≤1	2	≤1 – >8	88.2 / 8.8	- / -
Amoxicillin/clavulanate	≤1	≤1	≤1 – 2	100.0 / 0.0	- / -
Piperacillin/tazobactam	≤0.5	≤0.5	≤0.5	100.0 / 0.0	- / -
Meropenem	≤0.12	≤0.12	≤0.12	100.0 / -	- / -
Azithromycin	0.5	2	≤0.25 – >8	97.1 / -	- / -
Levofloxacin	≤0.5	≤0.5	≤0.5 – >4	97.1 / -	- / -
Tetracycline	0.5	1	≤0.25 – >8	94.1 / 2.9	- / -
Trimethoprim/sulfamethoxazole	≤0.5	4	≤0.5 – >4	85.3 / 14.7	- / -

a. Criteria as published by the CLSI [2011] and EUCAST [2011]. β-lactam susceptibility should be directed by the oxacillin test results.
b. USA-FDA breakpoints were applied when available [Teflaro® Product Insert, 2010].
c. Criteria as published by the CLSI [2011] for 'Penicillin parenteral (non-meningitis)'.
d. Criteria as published by the CLSI [2011] for 'Penicillin (oral penicillin V)'.
e. Percentages of susceptible/resistant based on β-lactamase production [CLSI, 2011].
f. USA-FDA breakpoints were applied when available [Rocephin® Product Insert, 2010].
g. Includes: Group A *Streptococcus* (66 strains), Group B *Streptococcus* (23 strains), Group C *Streptococcus* (9 strains), Group F *Streptococcus* (6 strains), and Group G *Streptococcus* (6 strains).
h. Includes: *Streptococcus anginosus* (2 strains), *S. constellatus* (4 strains), *S. intermedius* (3 strains), *S. mitis* (1 strain), and unspeciated viridans group streptococci (30 strains).
CLSI = Clinical and Laboratory Standards Institute; EUCAST = European Committee on Antimicrobial Susceptibility Testing; MIC = minimum inhibitory concentration; R = resistant; S = susceptible.

Conclusions

- Ceftaroline exhibited potent in vitro activity against the frequently observed respiratory tract bacterial pathogens, including multidrug-resistant *S. pneumoniae* (MIC_{90}, 0.12 μg/mL)
- Ceftaroline was highly active in vitro against *S. aureus* (MIC_{90}, 1 μg/mL), including MRSA strains (highest MIC, 2 μg/mL). Furthermore, ceftaroline activity against Enterobacteriaceae was most similar to that of ceftriaxone
- Based on these in vitro results that demonstrate potent activity of ceftaroline against resistant respiratory pathogens, additional clinical studies of ceftaroline fosamil in treating infections by resistant CABP pathogens (including MRSA) are warranted.

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