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Ceftaroline Activity When Tested Against Respiratory Tract Infection Pathogens Isolated From USA Medical Centers in 2009

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Abstract

Background: Ceftaroline (CPT) is a novel broad-spectrum cephalosporin with potent activity against pathogens causing RTI including MRSA and multidrug-resistant (MDR) *S. pneumoniae* (SPN).

Methods: 1,557 RTI and 128 blood culture (BC; all SPN) isolates were collected in 2009 from 26 hospitals in the USA. Bacterial isolates tabulated included: SPN (748), *H. influenzae* (HI; 274), *S. aureus* (SA; 288 [50% MRSA]), *M. catarrhalis* (MCAT; 188), *Klebsiella* spp. (KSP; 95), *E. coli* (EC; 52) and *Enterobacter* spp. (EBS; 37). Susceptibility (S) testing was performed by CLSI broth microdilution methods against CPT and candidate agents for RTI treatment.

Results: Rank order of CPT activity ($MIC_{50/90}$ in µg/mL) was HI (≤0.008/0.015) > MCAT (0.06/0.12) > SPN (0.015/0.25) > SA (0.5/1) > KSP (0.12/>8) = EC (0.25/>8) = EBS (0.25/>8). Against SPN, the CPT potency ($MIC_{50/90}$, 0.015/0.25 µg/mL) was eight-, 32- and 32-fold greater than ceftriaxone (CRO; $MIC_{50/90}$, ≤0.25/2 µg/mL), amoxicillin/clavulanate (A/C; $MIC_{50/90}$, ≤1/8 µg/mL), and cefuroxime ($MIC_{50/90}$, ≤1/8 µg/mL), respectively. SPN non-S to penicillin (PEN; MIC, ≥ 4 µg/mL; 112 strains) exhibited very low S to CRO (26.8%) and A/C (3.6%). SPN strains isolated from BC were two-fold more S to CPT than RTI strains and showed higher S for comparator agents. CPT was very active against HI (MIC_{90}, 0.015 µg/mL) independent of β-lactamase production. CPT ($MIC_{50/90}$, 0.25 µg/mL) was eight- to 16-fold more potent than CRO ($MIC_{50/90}$, 4 µg/mL) and cefepime (CPM; $MIC_{50/90}$, 2/4 µg/mL) against oxacillin-S SA. Highest CPT MIC among MRSA was only 2 µg/mL and 98.7% of isolates were inhibited at ≤1 µg/mL. CPT activity against KSP, EC, and EBS ($MIC_{50/90}$, 0.12-0.25/>32 µg/mL) was similar to CRO (70.3-82.7% S) and CPM (88.5-94.6% S). ESBL phenotype was observed in 17.3% of EC and 17.9% of KSP; all cephalosporins showed limited activity against these ESBL-producing strains.

Conclusion: RTI organisms from USA hospitals were very CPT-S, including MRSA and MDR-SPN. These results indicate that CPT could be a valuable agent for RTI therapy.

Introduction

Ceftaroline, the active component of the prodrug ceftaroline fosamil, is a novel, broad-spectrum cephalosporin exhibiting bactericidal activity against Gram-positive organisms, including methicillin (oxacillin)-resistant *Staphylococcus aureus* (MRSA) and multidrug-resistant *Streptococcus pneumoniae* (MDRSP), as well as many Enterobacteriaceae. Ceftaroline is currently under review for the treatment of complicated skin and skin structure infections and community-acquired bacterial pneumonia.

This study evaluated the spectrum and antimicrobial activity of ceftaroline and comparator agents against bacterial pathogens recovered from respiratory tract infections, including commonly encountered resistance phenotypes, recently collected from United States (USA) medical centers.

Methods

Organism Collection: 1557 isolates recovered from respiratory tract infections and 128 blood culture isolates (all *S. pneumoniae*) were collected from patients in 26 USA medical centers in 2009. Rank order of pathogen frequency was *S. pneumoniae* (n=748), *Haemophilus influenzae* (n=274), *S. aureus* (n=228), *Moraxella catarrhalis* (n=188), *Klebsiella* spp. (n=95), *Escherichia coli* (n=52), *Enterobacter* spp. (n=37), *Serratia* spp. (n=27), *Proteus mirabilis* (n=12), and *Citrobacter* spp. (n=8).

Susceptibility Testing: Isolates were tested for susceptibility to ceftaroline and multiple comparator agents by reference broth microdilution methods as described by Clinical and Laboratory Standards Institute (CLSI) M07-A8 (2009) and CLSI interpretations were based on M100-S20-U and M45-A breakpoints. *S. pneumoniae* were tested in Mueller-Hinton broth supplemented with 3-5% lysed horse blood, and *H. influenzae* were tested in Haemophilus Test Media, while *S. aureus* and Enterobacteriaceae isolates were tested in cation-adjusted Mueller-Hinton broth.

Concurrent testing of quality control (QC) strains assured proper test conditions were applied. These QC strains included *S. aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, *E coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *S. pneumoniae* ATCC 49619, and *H. influenzae* ATCC 49247 and 49766.

Results

- Ceftaroline activity against common respiratory tract bacterial pathogens is summarized in Table 1. Rank order of ceftaroline activity (MIC_{90} in µg/mL) was *H. influenzae* (≤0.015) > *M. catarrhalis* (0.12) > *S. pneumoniae* (0.25) > *S. aureus* (1) > Enterobacteriaceae (>8)

- Against *S. pneumoniae,* ceftaroline (MIC_{90}, 0.25 µg/mL) was 8-, 16-, 32-, and 32-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. Among non-β-lactam comparator agents, only levofloxacin (MIC_{90}, 1 µg/mL; 99.1% susceptible [S]) showed >80% susceptibility rate

- Ceftaroline maintained low MIC values for isolates of *S. pneumoniae,* regardless of susceptibility or resistance to penicillin. In contrast, very low susceptibility rates were observed for cefuroxime (0.8%; MIC_{90}, >8 µg/mL), amoxicillin/clavulanate (18.1%; MIC_{90}, 8 µg/mL), and ceftriaxone (42.3%; MIC_{90}, 2 µg/mL; Table 2)

- Ceftaroline was highly active against *H. influenzae* (MIC_{90}, 0.015 µg/mL and 0.03 µg/mL for β-lactamase-negative and -positive isolates, respectively). Comparators with the highest susceptibility rates were ceftriaxone, levofloxacin, amoxicillin/clavulanate, cefuroxime, and azithromycin (≥98.5% S; 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 excellent susceptibility rates ≥99.5%, except for trimethoprim/sulfamethoxazole (92.6%; Table 2)

- Ceftaroline was active against MRSA ($MIC_{50/90}$, 0.5/1 µg/mL) and methicillin-susceptible *S. aureus* (MSSA; $MIC_{50/90}$, 0.25/0.25 µg/mL) from respiratory tract infections. 98.7% of *S. aureus* isolates were inhibited by ceftaroline at ≤1 µg/mL (Tables 1 and 3)

- Ceftaroline (MIC_{50} and MIC_{90}, 0.25 µg/mL) was 8-fold more active than ceftriaxone (MIC_{50} and MIC_{90}, 2 µg/mL) when tested against penicillin-resistant *S. pneumoniae*. The highest ceftaroline MIC value was only 0.5 µg/mL (Tables 1 and 3)

- Ceftaroline and ceftriaxone exhibited similar in vitro activities against commonly isolated respiratory tract infection Enterobacteriaceae species (Table 3).

Table 1. Ceftaroline MIC Distributions of Respiratory Tract Pathogens Collected in USA Medical Centers (2009)

	Cumulative % inhibited at ceftaroline MIC (µg/mL) of:											
Organism (no. tested)	**≤0.008**	**0.015**	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**>8**
Streptococcus pneumoniae (748)	49.7	61.1	69.9	78.6	88.0	98.7	100.0	-	-	-	-	-
Penicillin MIC, ≤2 µg/mL (636)	58.5	71.9	82.2	92.3	99.2	100.0	-	-	-	-	-	-
Penicillin MIC, ≥4 µg/mL (112)	0.0	0.0	0.0	0.9	22.3	91.1	100.0	-	-	-	-	-
Haemophilus influenzae (274)	67.2	92.3	97.8	100.0	-	-	-	-	-	-	-	-
β-lactamase-negative (206)	77.2	97.6	100.0	-	-	-	-	-	-	-	-	-
β-lactamase-positive (68)	36.8	76.5	91.2	100.0	-	-	-	-	-	-	-	-
Moraxella catarrhalis (188)	10.6	20.7	47.3	77.7	97.9	100.0	-	-	-	-	-	-
Staphylococcus aureus (228)	0.0	0.0	0.4	0.9	6.1	48.3	79.0	98.7	100.0	-	-	-
Methicillin-susceptible (114)	0.0	0.0	0.9	1.8	12.3	95.6	100.0	-	-	-	-	-
Methicillin-resistant (114)	0.0	0.0	0.0	0.0	0.0	0.9	57.9	97.4	100.0	-	-	-
Klebsiella spp. (95)	0.0	0.0	1.1	20.0	52.6	64.2	70.5	80.0	81.1	82.1	83.2	100.0
Escherichia coli (52)	0.0	0.0	0.0	21.2	42.3	67.3	78.9	82.7	84.6	84.6	84.6	100.0
Enterobacter spp. (37)	0.0	0.0	0.0	8.1	37.8	54.1	70.3	73.0	73.0	78.4	100.0	
Serratia spp. (27)	0.0	0.0	0.0	0.0	0.0	14.8	40.7	77.8	92.6	92.6	92.6	100.0
Proteus mirabilis (12)	0.0	0.0	0.0	33.3	91.7	91.7	100.0	-	-	-	-	-
Citrobacter spp. (8)	0.0	0.0	0.0	12.5	62.5	75.0	87.5	87.5	87.5	87.5	87.5	100.0

Table 2. Comparison of In Vitro Activity of Ceftaroline and Selected Antimicrobial Agents Tested Against *Streptococcus pneumoniae, Haemophilus influenzae* and *Moraxella catarrhalis* Collected in USA Medical Centers

Antimicrobial agent (no. of strains)	**MIC (µg/ml)**			**CLSI**	**EUCAST**
	MIC_{50}	**MIC_{90}**	**Range**	**%S/%R[a]**	**%S/%R[a]**
***S. pneumoniae* (748)**					
Ceftaroline	0.015	0.25	≤0.008 – 0.5	- / -	- / -
Penicillin[b]	≤0.03	4	≤0.03 – >4	85.0 / 1.7	- / -
Penicillin[c]	≤0.03	4	≤0.03 – >4	59.6 / 19.9	59.6 / 15.0
Amoxicillin/clavulanate	≤1	8	≤1 – 16	83.7 / 13.9	- / -
Ceftriaxone	≤0.25	2	≤0.25 – 8	88.4 / 1.9	79.4 / 1.9
Cefuroxime	≤1	8	≤1 – >8	73.8 / 23.3	73.8 / 26.2
Erythromycin	≤0.25	>2	≤0.25 – >2	60.3 / 38.9	60.3 / 38.9
Clindamycin	≤0.25	>2	≤0.25 – >2	79.8 / 19.8	80.2 / 19.8
Levofloxacin	1	1	≤0.5 – >4	99.1 / 0.9	99.1 / 0.9
Trimethoprim/sulfamethoxazole	≤0.5	>2	≤0.5 – >2	65.1 / 26.5	69.9 / 26.5
Penicillin-susceptible (MIC, ≤0.06 µg/mL; 446)					
Ceftaroline	≤0.008	0.015	≤0.008 – 0.12	- / -	- / -
Amoxicillin/clavulanate	≤1	≤1	≤1	100.0 / 0.0	- / -
Ceftriaxone	≤0.25	≤0.25	≤0.25 – 0.5	100.0 / 0.0	100.0 / 0.0
Cefuroxime	≤1	≤1	≤1 – 2	99.7 / 0.0	99.7 / 0.3
Erythromycin	≤0.25	>2	≤0.25 – >2	85.2 / 13.5	85.2 / 13.5
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	97.1 / 2.5	97.5 / 2.5
Levofloxacin	1	1	≤0.5 – >4	99.8 / 0.2	99.8 / 0.2
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	≤0.5 – >2	90.8 / 4.5	93.9 / 4.5
Penicillin-intermediate (MIC, 0.12-1 µg/mL; 153)					
Ceftaroline	0.03	0.06	≤0.008 – 0.12	- / -	- / -
Amoxicillin/clavulanate	≤1	≤1	≤1 – 2	100.0 / 0.0	- / -
Ceftriaxone	≤0.25	0.5	≤0.25 – 2	99.3 / 0.0	99.3 / 0.0
Cefuroxime	≤1	4	≤1 – 8	73.2 / 15.7	73.2 / 26.8
Erythromycin	>2	>2	≤0.25 – >2	35.9 / 64.1	35.9 / 64.1
Clindamycin	≤0.25	>2	≤0.25 – >2	75.2 / 24.8	75.2 / 24.8
Levofloxacin	1	1	≤0.5 – >4	98.0 / 2.0	98.0 / 2.0
Trimethoprim/sulfamethoxazole	1	>2	≤0.5 – >2	41.2 / 32.0	54.9 / 32.0
Penicillin-resistant (MIC, ≥2 µg/mL; 149)					
Ceftaroline	0.25	0.25	0.06 – 0.5	- / -	- / -
Amoxicillin/clavulanate	8	8	≤1 – 16	18.1 / 69.8	- / -
Ceftriaxone	2	2	≤0.25 – 8	42.3 / 9.4	3.4 / 9.4
Cefuroxime	8	>8	≤1 – >8	0.8 / 97.6	0.8 / 99.2
Erythromycin	>2	>2	≤0.25 – >2	10.7 / 89.3	10.7 / 89.3
Clindamycin	>2	>2	≤0.25 – >2	32.9 / 66.4	33.6 / 66.4
Levofloxacin	1	1	≤0.5 – >4	98.0 / 2.0	98.0 / 2.0
Trimethoprim/sulfamethoxazole	>2	>2	≤0.5 – >2	12.8 / 86.6	13.4 / 86.6
***H. influenzae* (274)**					
Ceftaroline	≤0.008	0.015	≤0.008 – 0.06	- / -	- / -
Ampicillin	≤1	>16	≤1 – >16	74.8 / 23.7	74.8 / 25.2
Amoxicillin/clavulanate	≤1	≤1	≤1 – 8	99.6 / 0.4	92.0 / 8.0
Ceftriaxone	≤0.25	≤0.25	≤0.25 – 0.5	100.0 / -	99.6 / 0.4
Cefuroxime	≤2	≤2	≤2 – 8	99.6 / 0.0	81.4 / 3.6
Azithromycin	1	2	≤0.5 – >4	98.5 / -	7.6 / 1.5
Clarithromycin	8	16	0.5 – >32	64.4 / 7.2	1.1 / 1.5
Levofloxacin	≤0.5	≤0.5	≤0.5	100.0 / -	100.0 / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	>2	≤0.5 – >2	75.2 / 23.0	75.2 / 24.1
β-lactamase-negative (206)					
Ceftaroline	≤0.008	0.015	≤0.008 – 0.03	- / -	- / -
Ampicillin	≤1	≤1	≤1 – 2	99.5 / 0.0	99.5 / 0.5
Amoxicillin/clavulanate	≤1	≤1	≤1 – 4	100.0 / 0.0	93.7 / 6.3
Ceftriaxone	≤0.25	≤0.25	≤0.25 – 0.5	100.0 / -	99.5 / 0.5
Cefuroxime	≤2	≤2	≤2 – 8	99.5 / 0.0	82.0 / 3.9
Azithromycin	1	2	≤0.5 – >4	98.5 / -	9.0 / 1.5
Clarithromycin	8	16	0.5 – >32	66.8 / 5.5	1.5 / 1.5
Levofloxacin	≤0.5	≤0.5	≤0.5	100.0 / -	100.0 / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	>2	≤0.5 – >2	72.8 / 24.8	72.8 / 26.2
β-lactamase-positive (68)					
Ceftaroline	0.015	0.03	≤0.008 – 0.06	- / -	- / -
Ampicillin	>16	>16	2 – >16	0.0 / 95.6	0.0 / 100.0
Amoxicillin/clavulanate	≤1	2	≤1 – 8	98.5 / 1.5	86.8 / 13.2
Ceftriaxone	≤0.25	≤0.25	≤0.25	100.0 / -	100.0 / 0.0
Cefuroxime	≤2	≤2	≤2 – 4	100.0 / 0.0	79.4 / 2.9
Azithromycin	2	4	≤0.5 – >4	98.5 / -	3.1 / 1.5
Clarithromycin	8	32	2 – >32	56.9 / 12.3	0.0 / 1.5
Levofloxacin	≤0.5	≤0.5	≤0.5	100.0 / -	100.0 / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	>2	≤0.5 – >2	82.4 / 17.6	82.4 / 17.6
M. catarrhalis (188)[d]					
Ceftaroline	0.06	0.12	≤0.008 – 0.25	- / -	- / -
Amoxicillin/clavulanate	≤1	≤1	≤1	100.0 / 0.0	100.0 / 0.0
Ceftriaxone	≤0.25	0.5	≤0.25 – 1	100.0 / -	100.0 / 0.0
Cefuroxime	≤1	2	≤1 – >8	99.5 / 0.5	78.7 / 1.1
Erythromycin	0.12	0.25	≤0.06 – 0.5	100.0 / -	90.4 / 0.0
Clarithromycin	≤0.25	≤0.25	≤0.25 – 0.5	100.0 / -	98.9 / 0.0
Levofloxacin	≤0.5	≤0.5	≤0.5	100.0 / -	100.0 / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	≤0.5 – >2	92.6 /3.7	92.6 / 5.3

a. Criteria as published by the CLSI [2010b] and EUCAST [2010].
b. Criteria as published by the CLSI [2010b] for 'Penicillin parenteral (non-meningitis)'.
c. Criteria as published by the CLSI [2010b] for 'Penicillin (oral penicillin V)'.
d. Criteria as published by the CLSI [2010a].

Table 3. Comparison of In Vitro Activity of Ceftaroline and Selected Antimicrobial Agents Tested Against *Staphylococcus aureus* and Enterobacteriaceae Collected in USA Medical Centers

Antimicrobial agent (no. of strains)	**MIC (µg/mL)**			**CLSI**	**EUCAST**
	MIC_{50}	**MIC_{90}**	**Range**	**%S/%R[a]**	**%S/%R[a]**
***S. aureus* (228)**					
Ceftaroline	0.5	1	0.03 – 2	- / -	- / -
Oxacillin	2	>2	≤0.25 – >2	50.0 / 50.0	50.0 / 50.0
Ceftriaxone	8	>32	0.5 – >32	50.0 / 50.0	50.0 / 50.0
Erythromycin	>2	>2	≤0.25 – >2	38.6 / 60.5	39.0 / 60.5
Clindamycin	≤0.25	>2	≤0.25 – >2	72.4 / 27.6	72.4 / 27.6
Levofloxacin	≤0.5	>4	≤0.5 – >4	52.2 / 47.4	52.2 / 47.4
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	≤0.5 – >2	97.8 / 2.2	97.8 / 2.2
Linezolid	2	2	0.5 – 8	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
Tigecycline[b]	0.12	0.25	≤0.03 – 0.5	100.0 / -	100.0 / 0.0
Methicillin-susceptible *S. aureus* (114)					
Ceftaroline	0.25	0.25	0.03 – 0.5	- / -	- / -
Ceftriaxone	4	4	0.5 – 8	100.0 / 0.0	100.0 / 0.0
Erythromycin	≤0.25	>2	≤0.25 – >2	69.3 / 28.9	70.2 / 28.9
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	93.9 / 6.1	93.9 / 6.1
Levofloxacin	≤0.5	1	≤0.5 – >4	90.4 / 8.8	90.4 / 8.8
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	≤0.5 – >2	97.4 / 2.6	97.4 / 2.6
Linezolid	1	2	1 – 2	100.0 / 0.0	100.0 / 0.0
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
Tigecycline[b]	0.12	0.25	≤0.03 – 0.5	100.0 / -	100.0 / 0.0
Methicillin-resistant *S. aureus* (114)					
Ceftaroline	0.5	1	0.25 – 2	- / -	- / -
Erythromycin	>2	>2	≤0.25 – >2	7.9 / 92.1	7.9 / 92.1
Clindamycin	≤0.25	>2	≤0.25 – >2	50.9 / 49.1	50.9 / 49.1
Levofloxacin	>4	>4	≤0.5 – >4	14.0 / 86.0	14.0 / 86.0
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	≤0.5 – >2	98.2 / 1.8	98.2 / 1.8
Linezolid	2	2	0.5 – 8	99.1 / 0.9	99.1 / 0.9
Vancomycin	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Daptomycin	0.5	0.5	0.12 – 1	100.0 / -	100.0 / 0.0
Tigecycline[b]	0.12	0.25	0.06 – 0.5	100.0 / -	100.0 / 0.0
Klebsiella spp. (95)					
Ceftaroline	0.12	>32	0.03 – >32	- / -	- / -
Ceftriaxone	≤0.25	>32	≤0.25 – >32	82.1 / 17.9	82.1 / 17.9
Cefepime	≤0.12	>16	≤0.12 – >16	87.4 / 10.5	85.3 / 14.7
Ceftazidime	0.25	>32	0.06 – >32	83.2 / 16.8	83.2 / 16.8
Imipenem	0.25	1	≤0.12 – >8	92.6 / 7.4	92.6 / 5.3
Ertapenem	≤0.06	0.25	≤0.06 – >8	91.6 / 8.4	91.6 / 8.4
Piperacillin/tazobactam	4	>64	1 – >64	85.3 / 13.7	75.8 / 14.7
Levofloxacin	≤0.5	>4	≤0.5 – >4	83.2 / 15.8	82.1 / 16.8
Amikacin	1	4	0.5 – >32	93.7 / 2.1	91.6 / 6.3
Tigecycline[b]	0.5	1	0.12 – >4	94.7 / 1.1	90.5 / 5.3
Escherichia coli (52)					
Ceftaroline	0.25	>32	0.06 – >32	- / -	- / -
Ceftriaxone	≤0.25	>32	≤0.25 – >32	82.7 / 15.4	82.7 / 15.4
Cefepime	≤0.12	16	≤0.12 – >16	88.5 / 9.6	86.5 / 11.5
Ceftazidime	0.25	32	0.06 – >32	84.6 / 15.4	84.6 / 15.4
Imipenem	≤0.12	0.25	≤0.12 – 1	100.0 / 0.0	100.0 / 0.0
Ertapenem	≤0.06	0.12	≤0.06 – 1	92.3 / 3.8	96.2 / 0.0
Piperacillin/tazobactam	2	8	1 – >64	92.3 / 3.8	90.4 / 7.7
Levofloxacin	≤0.5	>4	≤0.5 – >4	59.6 / 36.5	59.6 / 40.4
Amikacin	2	4	1 – 16	100.0 / 0.0	98.1 / 0.0
Tigecycline[b]	0.12	0.25	0.06 – 0.5	100.0 / 0.0	100.0 / 0.0
Enterobacter spp. (37)					
Ceftaroline	0.25	>32	0.06 – >32	- / -	- / -
Ceftriaxone	≤0.25	>32	≤0.25 – >32	70.3 / 27.0	70.3 / 27.0
Cefepime	≤0.12	4	≤0.12 – >16	94.6 / 2.7	78.4 / 5.4
Ceftazidime	0.5	>32	0.06 – >32	75.7 / 24.3	70.3 / 24.3
Imipenem	0.5	1	0.25 – >8	91.9 / 2.7	97.3 / 2.7
Ertapenem	≤0.06	2	≤0.06 – >8	78.4/ 18.9	81.1 / 10.8
Piperacillin/tazobactam	4	>64	1 – >64	78.4 / 18.9	75.7 / 21.6
Levofloxacin	≤0.5	2	≤0.5 – >4	94.6 / 2.7	89.2 / 5.4
Amikacin	1	2	0.5 – 4	100.0 / 0.0	100.0 / 0.0
Tigecycline[b]	0.5	1	0.12 – 2	100.0 / 0.0	94.6 / 0.0
Serratia spp. (27)					
Ceftaroline	1	2	0.25 – >32	- / -	- / -
Ceftriaxone	≤0.25	0.5	≤0.25 – >32	92.6 / 7.4	92.6 / 7.4
Cefepime	≤0.12	0.25	≤0.12 – >16	96.3 / 3.7	92.6 / 3.7
Ceftazidime	0.25	0.5	0.06 – >32	92.6 / 7.4	92.6 / 7.4
Imipenem	1	2	0.25 – 2	85.2 / 0.0	100.0 / 0.0
Ertapenem	≤0.06	≤0.06	≤0.06 – 8	96.3 / 3.7	96.3 / 3.7
Piperacillin/tazobactam	2	4	1 – >64	96.3 / 3.7	96.3 / 3.7
Levofloxacin	≤0.5	2	≤0.5 – >4	96.3 / 3.7	88.9 / 3.7
Amikacin	2	2	1 – 4	100.0 / 0.0	100.0 / 0.0
Tigecycline[b]	1	2	0.25 – 2	100.0 / 0.0	85.2 / 0.0

a. Criteria as published by the CLSI [2010b] and EUCAST [2010]; β-lactam susceptibility for *S. aureus* isolates should be directed by the oxacillin test results.
b. US FDA breakpoints were applied [Tygacil Package Insert, 2009].
EUCAST = European Committee on Antimicrobial Susceptibility Testing; R = resistant; S = susceptible.

Conclusions

- Ceftaroline exhibited potent activity against the frequently observed respiratory tract bacterial pathogens *S. pneumoniae, H. influenzae,* and *M. catarrhalis*, including strains with various resistance phenotypes

- Ceftaroline was highly active against *S. aureus*, including MRSA strains (highest MIC, 2 µg/mL). Furthermore, ceftaroline activity against Enterobacteriaceae was similar to that of ceftriaxone

- These results indicate that ceftaroline is a promising and potentially effective therapeutic option for the treatment of respiratory tract infections in USA medical centers.

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