IDWEEK 2013 164

Ceftaroline Activity Tested against Bacterial Isolates from Pediatric Patients: Results from the Assessing Worldwide Antimicrobial Resistance and Evaluation (AWARE) Program for the United States (2011-2012) HS SADER, RK FLAMM, RN JONES JMI Laboratories, North Liberty, Iowa, USA

Abstract

Background: Ceftaroline (CPT), the active form of CPT fosamil, is a cephalosporin with broad-spectrum bactericidal activity against resistant (R) gram-positive (GP) organisms, including methicillin-R S. aureus (MRSA), and many Enterobacteriaceae species. CPT fosamil is FDA-approved for treatment of acute bacterial skin/skin structure infections and community-acquired bacterial pneumonia in adults.

Methods: 5,291 consecutive unique pediatric patient strains of clinical significance were collected from 157 USA medical centers as part of the AWARE Program. The isolates were identified locally and forwarded to a central monitoring laboratory (JMI Laboratories; North Liberty, Iowa, USA) for reference antimicrobial susceptibility (S) testing. S results were analyzed according to patient age as follows: ≤1 years old (yo; 1,857 strains); 2-5 (1,342); 6-12 (1,281) and 13-17 (811).

Results: MRSA rates were slightly lower in isolates from patients 13-17 yo (39.9%) compared to other age groups, and CPT was consistently active against S. aureus (SA) isolates from all four age groups (MIC_{50/90}, 0.25-0.5/1 µg/mL 99.8-100.0% S). 99.8% of MRSA were CPT-S (MIC_{50/90}, 0.5/1 µg/mL). R rates to erythromycin, clindamycin and levofloxacin among SA did not vary significantly among age groups. All S. pneumoniae (SPN) strains (1,178) were CPT-S (MIC_{50/90}, \leq 0.015/0.12 µg/mL), while ceftriaxone S varied from 84.8 (≤1 yo) to 89.7% (13-17 yo). The highest CPT MIC among H. influenzae (HI; 587 strains) was 0.12 µg/mL (100.0% S), and β -lactamase production rates varied from 24.2 (13-17 yo) to 30.1% (6-12 yo); 27.9% overall. CPT was also very active against β -hemolytic streptococci (BHS; 556 strains, highest MIC 0.06 µg/mL). ESBL-phenotype rates among E. coli (EC)/Klebsiella spp. (KSP) were 6.0/5.1, 11.0/11.5, 5.1/8.3 and 11.4/14.7% for the ≤ 1 , 2-5, 6-12 and 13-17 age groups, respectively. CPT exhibited good activity against non-ESBL-phenotype strains of EC and KSP (MIC_{on} 0.25 µg/mL for both organisms), but limited activity against ESBL-producing strains.

Conclusion: CPT demonstrated potent in vitro activity against SA, SPN, BHS and HI isolated from pediatric patients, independent of patient age. Differences in S rates to comparator agents according to patient age group were observed mainly among EC and KSP.

Antimicrobial agent /	% Susceptible by age group (years of age)										
organisms (no. tested)	≤1	2-5	6-12	13-17	All (≤17)						
S. aureus	(633)	(493)	(527)	(464)	(2,117)						
Ceftaroline	99.8	100.0	100.0	99.8	99.9						
Oxacillin	50.9	48.5	51.8	60.1	52.6						
S. pneumoniae	(434)	(399)	(267)	(78)	(1,178)						
Ceftaroline	100.0	100.0	100.0	100.0	100.0						
Ceftriaxone	84.8	86.7	87.6	89.7	86.4						
E. coli	(167)	(91)	(118)	(88)	(464)						
Ceftaroline	91.6	83.5	92.4	84.1	88.8						
Ceftriaxone	95.2	89.0	94.9	89.8	92.9						
Klebsiella spp.	(255)	(52)	(48)	(34)	(389)						
Ceftaroline	92.5	88.5	93.8	76.5	90.7						
Ceftriaxone	95.3	90.4	95.8	88.2	94.1						

Introduction

Antimicrobial resistance has been the subject of increasing concern to pediatricians and it remains a major focus of clinical and microbiology research for pediatric infectious diseases specialists. The major challenges to pediatricians are antimicrobial resistance among community-acquired respiratory tract infections and among infections acquired in the healthcare setting. Moreover, the emergence and dissemination of communityacquired methicillin-resistant *Staphylococcus aureus* (MRSA) represents another important challenge for those physicians treating children Although much has been reported about antimicrobial susceptibility in the pediatric population, considerably less is understood regarding resistance profile patterns by pediatric patient age groupings.

Ceftaroline, the active metabolite of ceftaroline fosamil, is a cephalosporin with potent bactericidal activity against resistant gram-positive organisms, including MRSA and multidrug-resistant (MDR) Streptococcus *pneumoniae*, and common gram-negative organisms, but not those producing extended-spectrum β -lactamases (ESBLs). Ceftaroline fosamil is approved by the United States (USA) Food and Drug Administration (FDA) for the treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI) in adults, including ABSSSI caused by MRSA. It is approved by the European Medicines Agency (EMA) for similar indications. As part of the Assessing Worldwide Antimicrobial Resistance Evaluation (AWARE) Program, a global ceftaroline surveillance study, we evaluated the activity of ceftaroline tested against contemporary indicated pathogens causing infections in pediatric patients from USA hospitals.

Methods

Organism collection: A total of 5,291 consecutive unique pediatric patient isolates of clinical significance were collected from 157 USA medical centers as part of the AWARE Program in 2012. These organisms included S. aureus (2,117 strains, 47.4% MRSA), Streptococcus pneumoniae (1,178; 15.7% penicillin-non-susceptible [MIC, ≥4 µg/mL]), *Haemophilus influenzae* (587), β-hemolytic streptococci (BHS; 556), *Escherichia coli* (464; 7.8% ESBL-phenotype) and *Klebsiella* spp. (389; 7.2% ESBLphenotype). Susceptibility results were analyzed according to patient age as follows: ≤1 years old (yo; 1,857 strains); 2-5 yo (1,342); 6-12 yo (1,281) and 13-17 yo (811). Species identification was performed at the participant center and confirmed by the monitoring laboratory (JMI Laboratories, North Liberty, Iowa, USA) 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), following manufacturer instructions.

<u>Susceptibility testing methods</u>: 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. Validated MIC panels were manufactured by ThermoFisher Scientific (Cleveland, Ohio, USA). S. aureus strains were tested in cation-adjusted Mueller-Hinton broth (CA-MHB), fastidious streptococci were tested in CA-MHB supplemented with 2.5-5% lysed horse blood and *Haemophilus* spp. strains were tested in Haemophilus Test Medium (HTM) according to CLSI document M07-A9 (2012). 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 (M100-S23; 2013).

- Ceftaroline was consistently active against *S. aureus* isolates from all four age groups (MIC_{50/90}, 0.25-0.5/1 µg/mL; 99.8-100.0% susceptibility). Furthermore, 99.8% of MRSA were susceptible to ceftaroline (MIC_{50/90}, 0.5/1 μ g/mL; Tables 1 and 2). MRSA rates were slightly lower in isolates from patients 13-17 yo (39.9%) compared to other age groups (48.2 – 51.5%). Also, susceptibility to levofloxacin was lower in *S. aureus* isolates from patients 2-5 vo (67.6%) compared to other age groups (74.0 - 76.7%). Susceptibility rates to erythromycin, clindamycin, tetracycline and trimethoprim/sulfamethoxazole among *S. aureus* did not vary significantly across tabulated age groups (Table 3)
- When tested against methicillin-susceptible S. aureus (MSSA). ceftaroline (MIC₅₀ and MIC₉₀, 0.25 μ g/mL) was 16-fold more active than ceftriaxone (MIC₅₀ and MIC₉₀, 4 μ g/mL; data not shown)
- All S. pneumoniae strains (1,178) were ceftaroline-susceptible $(MIC_{50/90}, \leq 0.015/0.12 \mu g/mL; Table 1)$, while ceftriaxone susceptibility varied from only 84.8 (≤ 1 yo) to 89.7% (13-17 yo; Table 3). In general, susceptibility rates for all comparator agents were slightly lower among S. pneumoniae isolates from patients ≤ 1 yo compared to the other age groups (Table 3). Ceftaroline was highly active against penicillin-non-susceptible S. pneumoniae (MIC, \geq 4 µg/mL; 185 strains) with MIC₅₀ and MIC₉₀ values of 0.25 μ g/mL (100.0% susceptibility; Table 1), whereas ceftriaxone (MIC₅₀ and MIC₉₀, 2 µg/mL; 20.5% susceptibility), amoxicillin/clavulanate (3.2%), ervthromvcin (0.5%), clindamvcin (6.5%) tetracvcline (8.1%) and trimethoprim/sulfamethoxazole (2.2%) displayed very limited activity against these organisms (Table 3)

Results

- Table 3)

Table 1. Summary of ceftaroline activity when tested against bacterial isolates from pediatric patients (USA, 2012)

No. of isolates (cumulative %) inhibited at MIC (µg/mL) of:															
Organism (no. tested)	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	>32	MIC ₅₀	MIC ₉₀
S. aureus (2,117)		1 (0.0)	5 (0.3)	100 (5.0)	964 (50.5)	635 (80.5)	410 (99.9)	2 (100.0)						0.25	1
MSSA (1,113)		1 (0.1)	5 (0.5)	100 (9.5)	946 (94.5)	61 (100.0)								0.25	0.25
MRSA (1,004)					18 (1.8)	574 (59.0)	410 (99.8)	2 (100.0)						0.5	1
S. pneumoniae (1,178)	662 (56.2)	105 (65.1)	103 (73.9)	208 (91.5)	90 (99.2)	10 (100.0)								≤0.015	0.12
penicillin-S. (MIC, ≤2 µg/mL; 993)	662 (66.7)	105 (77.2)	102 (87.5)	124 (100.0)										≤0.015	0.12
penicillin-I (MIC, 4 µg/mL; 165)			1 (0.6)	84 (51.5)	76 (97.6)	4 (100.0)								0.12	0.25
penicillin-R (MIC, ≥8 µg/mL; 20)					14 (70.0)	6 (100.0)								0.25	0.5
H. influenzae (587)	486 (82.8)	73 (95.2)	21 (98.8)	7 (100.0)										≤0.015	0.03
β-lactamase-negative (423)	381 (90.1)	37 (98.8)	5 (100.0)											≤0.015	≤0.015
β-lactamase-positive (164)	105 (64.0)	36 (86.0)	16 (95.7)	7 (100.0)										≤0.015	0.06
β-haemolytic streptococci (556)	523 (94.1)	32 (99.8)	1 (100.0)											≤0.015	≤0.015
Group A Streptococcus (425)	424 (99.8)	1 (100.0)												≤0.015	≤0.015
Group B Streptococcus (112)	87 (77.7)	24 (99.1)	1 (100.0)											≤0.015	0.03
Group C Streptococcus (19)	12 (63.2)	7 (100.0)												≤0.015	0.03
E. coli (464)	6 (1.3)	60 (14.2)	149 (46.3)	136 (75.6)	39 (84.1)	22 (88.8)	9 (90.7)	5 (91.8)	4 (92.7)	5 (93.8)	1 (94.0)	1 (94.2)	27 (100.0)	0.12	1
non-ESBL-phenotype (428)	6 (1.4)	60 (15.4)	149 (50.2)	136 (82.0)	38 (90.9)	22 (96.0)	9 (98.1)	4 (99.1)	2 (99.5)	2 (100.0)				0.06	0.25
ESBL-phenotype (36)					1 (2.8)	0 (2.8)	0 (2.8)	1 (5.6)	2 (11.1)	3 (19.4)	1 (22.2)	1 (25.0)	27 (100.0)	>32	>32
Klebsiella spp. (389)	1 (0.3)	6 (1.8)	123 (33.4)	129 (66.6)	66 (83.5)	28 (90.7)	7 (92.5)	3 (93.3)	4 (94.3)	3 (95.1)	1 (95.4)	0 (95.4)	18 (100.0)	0.12	0.5
non-ESBL-phenotype (361)	1 (0.3)	6 (1.9)	123 (36.0)	129 (71.7)	66 (90.0)	27 (97.5)	6 (99.2)	2 (99.7)	0 (99.7)	1 (100.0)				0.12	0.25
ESBL-phenotype (28)						1 (3.6)	1 (7.1)	1 (10.7)	4 (25.0)	2 (32.1)	1 (35.7)	0 (35.7)	18 (100.0)	>32	>32

Abbreviations: MSSA = methicillin-susceptible S. aureus; MRSA = methicillin-resistant S. aureus; S = susceptible; I = intermediate; R = resistant; and ESBL = extended spectrum β-lactamase.

Table 2. Summary of ceftaroline activity tested against bacterial isolates from pediatric patients stratified by age group (USA, 2012)

Organisms/subgroup (no. tested)	Ceftaroline activity by age group:															
	≤1 year old					2-5 years old			6-12 years old				13-17 years old			
	No.	MIC ₅₀	MIC ₉₀	%S	No.	MIC ₅₀	MIC ₉₀	%S	No.	MIC ₅₀	MIC ₉₀	%S	No.	MIC ₅₀	MIC ₉₀	%S
S. aureus	633	0.5	1	99.8	493	0.5	1	100.0	527	0.25	1	100.0	464	0.25	1	99.8
MSSA	322	0.25	0.25	100.0	239	0.25	0.25	100.0	273	0.25	0.25	100.0	279	0.25	0.25	100.0
MRSA	311	0.5	1	99.7	254	0.5	1	100.0	254	0.5	1	100.0	185	0.5	1	99.5
S. pneumoniae	434	≤0.015	0.12	100.0	399	≤0.015	0.12	100.0	267	≤0.015	0.12	100.0	78	≤0.015	0.12	100.0
H. influenzae	241	≤0.015	0.03	100.0	161	≤0.015	0.03	100.0	123	≤0.015	0.03	100.0	62	≤0.015	0.03	100.0
E. coli	167	0.12	0.5	91.6	91	0.12	4	83.5	118	0.06	0.5	92.4	88	0.12	4	84.1
Non-ESBL-phenotype	157	0.12	0.5	96.8	81	0.12	0.25	93.8	112	0.06	0.25	97.3	78	0.12	0.5	94.9
ESBL-phenotype	10	>32	>32	10.0	10	>32	>32	0.0	6	>32	NA	0.0	10	32	>32	0.0
Klebsiella spp.	255	0.12	0.5	92.5	52	0.12	4	88.5	48	0.06	0.5	93.8	34	0.12	>32	76.5
Non-ESBL-phenotype	242	0.12	0.5	97.5	46	0.12	0.5	100.0	44	0.06	0.25	100.0	29	0.12	1	89.7
ESBL-phenotype	13	>32	>32	0.0	6	>32	NA	0.0	4	4	NA	25.0	5	>32	NA	0.0

Abbreviations: %S = percentage susceptible by the CLSI criteria [CLSI, 2013]; MSSA = methicillin-susceptible S. aureus; ESBL = extended spectrum β-lactamase and NA = not applicable due to reduced number of strains (<10).

• Ceftaroline was 8-fold more active than ceftriaxone (MIC_{90} , 2 μ g/mL) when tested against penicillin-susceptible (MIC_{50/90}, ≤0.015/0.12 and ≤0.06/1 µg/mL, respectively) and penicillin-nonsusceptible *S. pneumoniae* strains (MIC_{50/90}, 0.25/0.25 and 2/2 µg/mL, respectively; data not shown)

• The highest ceftaroline MIC among *H. influenzae* (587 strains) was only 0.12 μ g/mL (100.0% susceptibility), and β -lactamase production rates varied from 24.2 (13-17 yo) to 30.1% (6-12 yo); 27.9% overall (Table 3). All isolates were also susceptible to ceftriaxone and levofloxacin, whereas susceptibility to clarithromycin varied from 76.4% (6 - 12 yo) to 90.3% (13-17 yo;

 Ceftaroline was also very active against β-hemolytic streptococci (556 strains; highest MIC at 0.06 μ g/mL). All β -hemolytic streptococcal strains were susceptible to ceftaroline, ceftriaxone and penicillin, but susceptibility to clindamycin varied from 79.1% (2-5 yo) to 94.4% (6-12 yo); Table 3)

• ESBL-phenotype rates ranged from 5.1 (6 – 12 yo) to 11.4% (13 – 17 yo) among *E. coli,* and from 5.1 (≤1 yo) to 14.7% (13 – 17 yo) among Klebsiella spp. (Table 3). Ceftaroline exhibited good activity against non-ESBL-phenotype strains of *E. coli* and *Klebsiella* spp. $(MIC_{90}, 0.25 \mu g/mL$ for both organisms), but limited activity against ESBL-producing strains (Table 1 and 2).

Table 3. Activity of ceftaroline and comparator antimicrobial agents when tested against bacterial isolates from pediatric patients in USA medical centers (2012)

_		% Susceptible	by CLSI criteri	eria ^a (no. tested)		
Organism / Antimicrobial agent	≤1 year old	2-5 years old	6-12 years old	13-17 years old	All (years	
Staphylococcus aureus	(633)	(493)	(527)	(464)	(2,1	
Ceftaroline	99.8	100.0	100.0	99.8	99	
Oxacillin	50.9	48.5	51.8	60.1	52	
Erythromycin Clindamycin	38.9 93.8	35.0 94.3	40.8 93.3	42.1 91.8	39 92	
Levofloxacin	93.8 76.7	94.3 67.6	93.3 74.0	76.5	92 73	
Tetracycline	98.3	98.4	96.2	96.3	97	
TMP/SMX ^b	99.8	98.4	99.6	99.6	99	
MSSA	(322)	(239)	(273)	(279)	(1,1	
Ceftaroline	100.0	100.0	100.0	100.0	10	
Erythromycin	66.4	58.4	65.9	61.2	63	
	98.4	98.3	96.3	93.9	96	
Levofloxacin Tetracycline	94.1 98.8	92.0 97.5	92.7 95.2	91.4 96.0	92 96	
TMP/SMX ^b	99.7	99.2	99.6	99.3	99	
MRSA	(311)	(254)	(254)	(185)	(1,0	
Ceftaroline	99.7	100.0	100.0	99.5	99	
Erythromycin	10.6	13.0	13.8	13.5	12	
Clindamycin	89.0	90.6	90.1	88.6	89	
Levofloxacin	58.8	44.7	53.9	54.1	53	
	97.7 100.0	99.2 07.6	97.2 00.6	96.8 100.0	97	
TMP/SMX ^b Streptococcus pneumoniae	100.0	97.6 (399)	99.6 (267)	100.0	99	
Streptococcus pneumoniae Ceftaroline	(434) 100.0	(399) 100.0	(267) 100.0	(78) 100.0	(1,1 10	
Ceftriaxone	84.8	86.7	87.6	89.7	86	
Penicillin ^c	82.3	84.0	87.3	87.2	84	
Amoxicillin/clavulanate	78.3	81.0	82.8	83.3	80	
Erythromycin	48.5	54.1	55.1	60.3	52	
Clindamycin	76.5	79.1	83.8	80.8	79	
Levofloxacin	99.3	99.7	100.0	100.0	99	
Tetracycline TMP/SMX ^b	73.6 53.1	73.3 60.4	79.7 68.5	73.1 71.8	74 60	
Penicillin-non-susc. ^c (MIC, ≥4 µg/mL)	(77)	(64)	(34)	(10)	(18	
Ceftaroline	100.0	100.0	100.0	100.0	10	
Ceftriaxone	18.2	23.4	20.6	30.0	20	
Amoxicillin/Clavulanate	1.3	3.1	5.9	10.0	3	
Erythromycin	0.0	1.6	0.0	0.0	0	
Clindamycin	3.9	4.7	11.8	20.0	6	
Levofloxacin Tetracycline	100.0 7.8	98.4 7.8	100.0 11.8	100.0 0.0	99 8	
TMP/SMX ^b	7.8 2.6	0.0	2.9	10.0	o 2	
Haemophilus influenzae	(241)	(161)	(123)	(62)	(58	
Ceftaroline	100.0	100.0	100.0	100.0	10	
Ceftriaxone	100.0	100.0	100.0	100.0	10	
Cefuroxime	98.6	99.3	100.0	100.0	99	
Amoxicillin/clavulanate	99.6	100.0	100.0	100.0	99	
Azithromycin	99.2	100.0	98.4	98.4	99	
Clarithromycin Levofloxacin	88.0 100.0	82.6 100.0	76.4 100.0	90.3 100.0	84 10	
Levonoxacin $β$ -lactamase-positive rate	29.0	26.1	30.1	24.2	27	
3-hemolytic streptococci	(127)	(146)	(198)	(85)	(5	
Ceftaroline	100.0	100.0	100.0	100.0	10	
Ceftriaxone	100.0	100.0	100.0	100.0	10	
Penicillin	100.0	100.0	100.0	100.0	10	
Erythromycin	67.7	54.1	85.8	71.4	79	
	85.0	79.1	94.4	87.1	92	
Levofloxacin Tetracycline	100.0 45.7	99.7 73.3	100.0 86.3	98.8 55 3	93 72	
Tetracycline Escherichia coli	45.7 (167)	(91)	(118)	55.3 (88)	72 (46	
Ceftaroline	(167) 91.6	(91) 83.5	(118) 92.4	(88) 84.1	(46 88	
Ceftriaxone	91.8 95.2	83.5 89.0	92.4 94.9	89.8	92	
Ceftazidime	95.8	91.2	95.8	92.0	92	
Piperacillin/tazobactam	96.4	94.5	96.6	93.2	93	
Meropenem	100.0	100.0	100.0	100.0	10	
	90.4	83.5	89.8	81.8	87	
Levofloxacin	86.8	85.7 11.0	92.4 5.1	88.6	88	
Gentamicin	60		5.1	11.4	7	
Gentamicin ESBL-phenotype rate	6.0		(40)	(24)	(2)	
Gentamicin ESBL-phenotype rate <i>Klebsiella</i> spp.	(255)	(52)	(48) 93.8	(34) 76 5	(38	
Gentamicin ESBL-phenotype rate <i>Klebsiella</i> spp. Ceftaroline	(255) 92.5	(52) 88.5	93.8	76.5	90	
Gentamicin ESBL-phenotype rate Klebsiella spp. Ceftaroline Ceftriaxone	(255) 92.5 95.3	(52) 88.5 90.4	93.8 95.8	76.5 88.2	90 94	
Gentamicin ESBL-phenotype rate <i>Klebsiella</i> spp. Ceftaroline	(255) 92.5	(52) 88.5	93.8	76.5	90	
Gentamicin ESBL-phenotype rate Klebsiella spp. Ceftaroline Ceftriaxone Ceftazidime	(255) 92.5 95.3 97.3	(52) 88.5 90.4 88.5	93.8 95.8 95.8	76.5 88.2 94.1	90 94 95	
Gentamicin ESBL-phenotype rate <i>Klebsiella</i> spp. Ceftaroline Ceftriaxone Ceftazidime Piperacillin/tazobactam	(255) 92.5 95.3 97.3 96.8	(52) 88.5 90.4 88.5 92.3	93.8 95.8 95.8 93.8	76.5 88.2 94.1 82.4	90 94 95 94	

a. Criteria as published by the CLSI [2013]. TMP/SMX = trimethoprim/sulfamethoxazole

Criteria as published by the CLSI [2013] for 'Penicillin parenteral non-meningitis' (S≤2, I=4, R≥8 µg/mL).



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

Conclusions

- Ceftaroline demonstrated potent in vitro activity against S. aureus, S. pneumoniae, H. influenzae and β-hemolytic streptococci isolated from pediatric patients, generally independent of patient age
- Differences in susceptibility rates to β-lactams and fluoroquinolones according to patient age group were observed among E. coli and Klebsiella spp.
- These in vitro data support the further clinical development of ceftaroline for treatment of infection in children, especially those caused by MRSA and MDR S. pneumoniae.

References

- Clinical and Laboratory Standards Institute (2012). M07-A9. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard: ninth edition. Wayne, PA:
- Clinical and Laboratory Standards Institute (2013). M100-S23. Performance standards for antimicrobial susceptibility testing: 23rd informational supplement. Wayne, PA: CLSI.
- Corey GR, Wilcox M, Talbot GH, Friedland HD, Baculik T, Witherell GW, Critchley I, Das AF, Thye D (2010). Integrated analysis of CANVAS 1 and 2: Phase 3, multicenter, randomized, double-blind studies to evaluate the safety and efficacy of ceftaroline versus ancomycin plus aztreonam in complicated skin and skin-structure/ infection. *Clin Infect Dis* 51: 641-650.
- Jeyaratnam D, Reid C, Kearns A, Klein J (2006). Community associated MRSA: an alert to paediatricians. Arch Dis Child 91 511-512.
- Jones RN, Jacobs MR, Sader HS (2010). Evolving trends in *Streptococcus pneumoniae* resistance: Implications for therapy of community-acquired bacterial pneumonia. Int J Antimicrob Agents 36: 197-204.
- Kaplan SL (2006). Community-acquired methicillin-resistant Staphylococcus aureus infections in children. Semin Pediatr Infect Dis 17: 113-119
- Low DE, File TM, Jr., Eckburg PB, Talbot GH, Friedland HD, Lee J, Llorens L, Critchley IA, Thye DA (2011). FOCUS 2: a randomized, double-blinded, multicentre, Phase III trial of the efficacy and safety of ceftaroline fosamil versus ceftriaxone in community-acquired pneumonia. *J Antimicrob Chemother* 66 Suppl 3: iii33-iii44.
- Pfaller MA, Farrell DJ, Sader HS, Jones RN (2012). AWARE ceftaroline surveillance program (2008-2010); Trends in resistance patterns among *Streptococcus pneumoniae*, *Haemophilus* influenzae, and Moraxella catarrhalis in the United States. Clin Infect Dis 55 Suppl 3: S187-S193.
- Sader HS, Flamm RK, Farrell DJ, Jones RN (2012). Activity analyses of staphylococcal isolates from pediatric, adult and elderly patients; AWARE ceftaroline surveillance program. *Clin Infect Dis* 55 Suppl 3: S181-S186.
- 10. Teflaro Package Insert (2012). Available at
- <u>http://www.frx.com/pi/Teflaro_pi.pdf</u>. Accessed August 2013.

Acknowledgments

This study was supported by Cerexa, Inc., a wholly-owned subsidiary of Forest Laboratories, Inc. Forest Laboratories, Inc., was involved in the design and decision to present these results. Forest Laboratories, Inc., had no involvement in the collection, analysis, and interpretation of data. Scientific Therapeutics Information, Inc., provided editorial coordination, which was funded by Forest Research Institute, Inc.

(≤17 9.5 8 1 2.2 587) 00.0 00.0 99.2 9.8 34.3 0.00 7.9 0.00 0.00 0.00 9.6 2.8 164) 8.8 2.9 0.00 37.1