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Activity of Ceftaroline and Comparator Agents Tested Against Contemporary (2010) Pathogens Commonly Associated With Respiratory Tract Infections in Asia-Pacific Countries and South Africa

DJ BIEDENBACH, RK FLAMM, DJ FARRELL, HS SADER, RN JONES

JMI Laboratories, North Liberty, IA, USA

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JMI Laboratories
North Liberty, IA, USA
www.jmilabs.com
319.665.3370, fax 319.665.3371
robert-flamm@jmilabs.com

Abstract

Background: Ceftaroline (CPT), the active form of CPT fosamil, is a novel cephalosporin with *in vitro* activity against common respiratory tract infection (RTI) pathogens in addition to coverage of methicillin-resistant *S. aureus* (MRSA).

Methods: Consecutive non-duplicate bacterial isolates were collected from 25 medical centers in Australia, China, Hong Kong, South Korea, Malaysia, Singapore, Thailand, and South Africa (SAF) and tested for susceptibility (S) against CPT and comparators at a central laboratory by CLSI broth microdilution methods. Species identification and ß-lactamase (BL) production was confirmed when necessary.

Results: CPT was very active against *S. pneumoniae* (SPN; MIC_{50}, 0.015 µg/ml). MIC_{50} values were 0.12, 0.25 and 0.12 µg/ml among penicillin-resistant (R, ≥2 µg/ml), ceftriaxone (CRO)-non-S and levofloxacin (LEV)-non-S strains, respectively. BL production among *H. influenzae* (HI; 22.0%) and *M. catarrhalis* (MCAT; 97.8%) isolates did not significantly affect CPT MIC values. The overall collection of HI had $MIC_{50/90}$ values of ≤0.008/0.03 µg/ml with a four-fold increase among BL-producing strains (MIC_{90}, 0.06 µg/ml) compared to BL-negative strains (MIC_{90}, 0.015 µg/ml). *H. parainfluenzae* (HPAR; n=47) in this region had similar CPT MIC values compared to BL-negative isolates of HI (MIC_{90}, 0.015 µg/ml). Among the collection of MCAT (n=135), the $MIC_{50/90}$ was 0.06/0.12 µg/ml.

Conclusions: Overall S was high for CPT when tested against a diverse collection of isolates commonly associated with community-acquired RTI from Asia-Pacific countries and SAF. CPT demonstrated potent *in vitro* activity against PEN-R, CRO-non-S and LEV-non-S isolates as well as strains of HI, HPAR and MCAT that produce BL enzymes.

Table: Ceftaroline activity tested against RTI pathogens isolated in the Asia-Pacific and South Africa.

Organism (No.)	MIC_{50}	MIC_{90}	Range
Streptococcus pneumoniae (616)	0.015	0.25	≤0.008 - 2
PEN-R (MIC, ≥2 µg/ml; 202)	0.12	0.5	0.03 – 2
PEN-R (MIC, ≥8 µg/ml; 7)	0.5	-	0.25 - 2
CRO-non-S MIC, ≥2 µg/ml; 114)	0.25	0.5	0.12 - 2
LEV-non-S (MIC, ≥4 µg/ml; 14)	0.12	0.5	≤0.008 - 2
Haemophilus influenzae (454)	≤0.008	0.03	≤0.008 – 0.5
ß-lactamase-negative (354)	≤0.008	0.015	≤0.008 - 0.12
ß-lactamase-positive (100)	0.015	0.06	≤0.008 - 0.5

Introduction

Respiratory tract infections (RTIs) are common in the community and in healthcare settings where they may be associated with high mortality rates. The emergence of multidrug-resistant (MDR) organisms among the bacterial species associated with RTIs is limiting the utility of currently available antimicrobials.

Ceftaroline fosamil is a prodrug which is rapidly hydrolyzed *in vivo* to the active form ceftaroline, a novel cephalosporin with *in vitro* activity against pathogens causing community-acquired bacterial pneumonia (CABP). Ceftaroline fosamil was approved by the United States Food and Drug Administration (USA-FDA) for the treatment of CABP and acute bacterial skin and skin-structure infections (ABSSSI) in 2010.

In this study, we evaluated ceftaroline and comparator antimicrobial agents against isolates from bacterial species associated with community-acquired RTIs collected in medical centers in the Asia-Pacific (APAC) region and South Africa (SAF) during 2010.

Materials and Methods

Consecutively collected, unique isolates from patients with clinically significant infections were collected in 2010 from 25 medical centers in Australia, China, Hong Kong, Malaysia, Singapore, South Korea, Thailand and SAF, as part of the AWARE surveillance program.

Reference broth microdilution test methods (Clinical and Laboratory Standards Institute; CLSI) were conducted to determine antimicrobial susceptibility of ceftaroline and comparator agents. Validated minimum inhibitory concentration (MIC) panels were manufactured by ThermoFisher Inc, formerly TREK Diagnostics (Cleveland, Ohio, USA). *Moraxella catarrhalis* strains were tested in cation-adjusted Mueller-Hinton broth (CA-MHB; M45-A2). *S. pneumoniae* strains were tested in CA-MHB supplemented with 2.5-5% lysed horse blood and *Haemophilus influenzae* were tested in Haemophilus test medium (M07-A9, 2012). ß-lactamase production was characterized by the nitrocefin disk test (Remel; Lenexa, Kansas, USA).

Concurrent quality control (QC) testing was performed to assure proper test conditions and procedures. QC strains included: *S. aureus* ATCC 29213, *S. pneumoniae* ATCC 49619 and *H. influenzae* ATCC 49247 and 49766. Susceptibility percentages and validation of QC results were based on CLSI guidelines (M100-S22, M45-A2) and susceptibility breakpoints were used to determine susceptibility/resistance rates (CLSI and EUCAST, 2012). The interpretive criteria used for ceftaroline were those that are in the USA-FDA package insert (2012).

Results

- A total of 616 pneumococcal isolates were evaluated (Table 1). Ceftaroline *in vitro* activity, as with other ß-lactams, varied according to the susceptibility to penicillin. However, ceftaroline was the most potent of all ß-lactams tested against *S. pneumoniae* strains (MIC_{50}, 0.015 µg/ml and MIC_{90}, 0.25 µg/ml; Table 2). Over one-third (34.6% [CLSI] and 37.3% [EUCAST]) of isolates were resistant to cefuroxime and 64.0% and 55.7% (CLSI and EUCAST) were resistant to erythromycin and clindamycin, respectively (Table 3). Ceftriaxone non-susceptibility was at 18.5% (CLSI interpretive criteria; 33.8% EUCAST criteria). Also, 2.3% (14) of isolates were levofloxacin-resistant; the ceftaroline MIC_{90} for this group of isolates was 0.5 µg/ml.

- The highest *S. pneumoniae* ceftaroline MIC value observed was 2 µg/ml (1 strain [0.2%]) and 95.9% of strains were inhibited at ≤0.25 µg/ml (Table 2). The single strain with a ceftaroline MIC of 2 µg/ml was a MDR strain from South Korea with a ceftriaxone MIC of >8 µg/ml. The MIC_{50} varied from ≤0.008 µg/ml for the penicillin-susceptible (MIC, ≤0.06 µg/ml) strains to 0.12 µg/ml for the penicillin-resistant (MIC, ≥2 µg/ml) strains (Table 3).

- Against penicillin-resistant (MIC, ≥2 µg/ml) pneumococci, ceftaroline (MIC_{90}, 0.5 µg/ml) was eight- (MIC_{90}) to sixteen-fold (MIC_{50}) more active than ceftriaxone (MIC_{90}, 4 µg/ml; 43.6 and 3.0% susceptible according to CLSI and EUCAST criteria, respectively) and 16- (MIC_{90}) to 32-fold (MIC_{50}) more potent than amoxicillin/clavulanic acid (MIC_{50}, 4 µg/ml and MIC_{90}, 8 µg/ml; 42.1% susceptible according to CLSI criteria; Table 3).

- Ceftaroline was highly potent against *H. influenzae* (MIC_{50}, ≤0.008 µg/ml and MIC_{90}, 0.03 µg/ml; Table 4) and the highest ceftaroline MIC value was only 0.5 µg/ml (two isolates [0.4%]; Table 2). ß-lactamase-producing strains showed ceftaroline MIC values slightly higher (MIC_{50}, 0.015 µg/ml and MIC_{90}, 0.06 µg/ml; Table 4) than non-ß-lactamase-producing ampicillin-susceptible strains (MIC_{50}, ≤0.008 µg/ml and MIC_{90}, 0.015 µg/ml; highest MIC, 0.12 µg/ml; Table 4); but were still highly susceptible to this compound (Table 4).

Table 1. *Geographic Distribution of Isolates in the 2010 APAC and SAF Surveillance for Ceftaroline.*

Organism or group	No. of organisms (%) processed by country								
	Australia	China	Hong Kong	Korea	Malaysia	Singapore	South Africa	Thailand	Overall
Streptococcus pneumoniae	170 (27.6)	288 (46.8)	25 (4.1)	48 (7.8)	25 (4.1)	15 (2.4)	22 (3.6)	23 (3.7)	616
Haemophilus spp., all	161 (31.7)	201 (39.6)	20 (3.9)	46 (9.1)	18 (3.5)	29 (5.7)	20 (3.9)	13 (2.6)	508
Haemophilus influenzae	152 (33.5)	167 (36.8)	16 (3.5)	45 (9.9)	14 (3.1)	29 (6.4)	18 (4.0)	13 (2.9)	454
Haemophilus parainfluenzae	9 (17.7)	31 (60.8)	4 (7.8)	1 (2.0)	4 (7.8)	0 (0)	2 (3.9)	0 (0)	51
Moraxella catarrhalis	36 (26.7)	56 (41.5)	5 (3.7)	18 (13.3)	5 (3.7)	5 (3.7)	5 (3.7)	5 (3.7)	135
Total	528 (29.9)	743 (42.1)	70 (4.0)	158 (9.0)	66 (3.7)	78 (4.4)	67 (3.8)	54 (3.1)	1764

Table 2. *Summary of Ceftaroline Activity Tested Against Pathogens Associated with RTI from APAC & SAF Medical Centers (2010).*

Organism	No. of Isolates	No. of isolates (%) inhibited at antimicrobial MIC (µg/ml)										
		≤0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	MIC_{50}	MIC_{90}
Streptococcus pneumoniae	616	298 (48.4)	53 (8.6)	26 (4.2)	38 (6.2)	122 (19.8)	54 (8.8)	24 (3.9)	0 (0.0)	1 (0.2)	0.015	0.25
penicillin-susceptible	331	290 (87.6)	37 (11.2)	4 (1.2)	-	-	-	-	-	-	≤0.008	0.015
penicillin-intermediate	83	8 (9.6)	16 (19.3)	21 (25.3)	27 (32.5)	11 (13.3)	-	-	-	-	0.03	0.12
penicillin-resistant	202	0 (0.0)	0 (0.0)	1 (0.5)	11 (5.4)	111 (55.0)	54 (26.7)	24 (11.9)	0 (0.0)	1 (0.5)	0.12	0.5
Haemophilus influenzae	454	309 (68.2)	73 (16.1)	41 (9.1)	21 (4.6)	7 (1.5)	-	-	-	-	≤0.008	0.03
beta-lactamase negative	354	282 (79.7)	49 (13.8)	16 (4.5)	6 (1.7)	1 (0.3)	0 (0.0)	2 (0.4)	-	-	≤0.008	0.015
beta-lactamase positive	100	28 (28.0)	24 (24.0)	25 (25.0)	15 (15.0)	6 (6.0)	0 (0.0)	2 (2.0)	-	-	0.015	0.06
Haemophilus parainfluenzae	47	37 (78.7)	6 (12.8)	0 (0.0)	2 (4.3)	0 (0.0)	2 (4.3)	-	-	-	≤0.008	0.015
Moraxella catarrhalis	135	14 (10.4)	7 (5.2)	31 (23.0)	37 (27.4)	38 (28.1)	6 (4.4)	2 (1.5)	-	-	0.06	0.12

Table 3. *Activity of Ceftaroline and Comparator Antimicrobial Agents when Tested Against S. pneumoniae (APAC and SAF, 2010).*

Antimicrobial agent (no. tested)	MIC (µg/ml)			CLSI[a]	EUCAST[a]
	MIC_{50}	MIC_{90}	Range	%S / %R	%S / %R
Streptococcus pneumoniae, All (616)					
Ceftaroline	0.015	0.25	≤0.008 – 2	95.9[b] / -	- / -
Penicillin[c]	≤0.03	4	≤0.03 – >4	80.2 / 1.1	- / -
Penicillin[d]	≤0.03	4	≤0.03 – >4	53.7 / 32.8	53.7 / 19.8
Amoxicillin/clavulanate	≤1	8	≤1 – >8	80.7 / 15.7	- / -
Ceftriaxone	≤0.06	2	≤0.06 – >8	81.5 / 6.2	66.2 / 6.2
Cefuroxime	≤0.12	16	≤0.12 – >16	62.7 / 34.6	61.9 / 37.3
Trimethoprim/sulfamethoxazole	1	>4	≤0.5 – >4	47.1 / 45.0	52.3 / 45.0
Clindamycin	>1	>1	≤0.25 – >1	44.0 / 55.7	44.3 / 55.7
Erythromycin	>4	>4	≤0.25 – >4	35.6 / 64.0	35.6 / 64.0
Levofloxacin	1	1	≤0.5 – >4	97.7 / 2.3	97.7 / 2.3
Linezolid	1	1	≤0.12 – 2	100.0 / -	100.0 / 0.0
Vancomycin	0.25	0.5	≤0.12 – 1	100.0 / -	100.0 / 0.0
Penicillin-susceptible (331)					
Ceftaroline	≤0.008	0.015	≤0.008 – 0.03	100.0[b] / -	- / -
Penicillin[c]	≤0.03	≤0.03	≤0.03 – 0.06	100.0 / 0.0	- / -
Penicillin[d]	≤0.03	≤0.03	≤0.03 – 0.06	100.0 / 0.0	100.0 / 0.0
Amoxicillin/clavulanate	≤1	≤1	≤1 – 2	100.0 / 0.0	- / -
Ceftriaxone	≤0.06	≤0.06	≤0.06 – 0.25	100.0 / 0.0	100.0 / 0.0
Cefuroxime	≤0.12	≤0.12	≤0.12 – 1	100.0 / 0.0	99.7 / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	>4	≤0.5 – >4	70.1 / 23.0	74.0 / 23.0
Clindamycin	≤0.25	>1	≤0.25 – >1	55.9 / 43.5	56.5 / 43.5
Erythromycin	≤0.25	>8	≤0.25 – >8	52.3 / 47.1	52.3 / 47.1
Levofloxacin	1	1	≤0.5 – >4	98.8 / 1.2	98.8 / 1.2
Linezolid	1	1	≤0.12 – 2	100.0 / -	100.0 / 0.0
Vancomycin	0.25	0.5	≤0.12 – 0.5	100.0 / -	100.0 / 0.0
Penicillin-intermediate (83)					
Ceftaroline	0.03	0.12	≤0.008 – 0.12	100.0[b] / -	- / -
Penicillin[c]	0.25	1	0.12 – 1	100.0 / 0.0	- / -
Penicillin[d]	0.25	1	0.12 – 1	0.0 / 0.0	0.0 / 0.0
Amoxicillin/clavulanate	≤1	2	≤1 – 4	97.6 / 0.0	- / -
Ceftriaxone	0.25	1	≤0.06 – 1	100.0 / 0.0	85.5 / 0.0
Cefuroxime	0.25	4	≤0.12 – 8	66.3 / 16.9	61.4 / 33.7
Trimethoprim/sulfamethoxazole	1	>4	≤0.5 – >4	44.6 / 41.0	54.2 / 41.0
Clindamycin	≤0.25	>1	≤0.25 – >1	60.2 / 39.8	60.2 / 39.8
Erythromycin	4	>8	≤0.25 – >8	44.6 / 54.2	44.6 / 54.2
Levofloxacin	1	1	≤0.5 – >4	97.6 / 2.4	97.6 / 2.4
Linezolid	1	1	0.25 – 2	100.0 / -	100.0 / 0.0
Vancomycin	0.25	0.5	≤0.12 – 1	100.0 / -	100.0 / 0.0
Penicillin-resistant (202)					
Ceftaroline	0.12	0.5	0.03 – 2	87.6[b] / -	- / -
Penicillin[c]	4	4	2 – >4	39.6 / 3.5	- / -
Penicillin[d]	4	4	2 – >4	0.0 / 100.0	0.0 / 60.4
Amoxicillin/clavulanate	4	8	≤1 – >8	42.1 / 48.0	- / -
Ceftriaxone	2	4	0.5 – >8	43.6 / 18.8	3.0 / 18.8
Cefuroxime	8	>16	2 – >16	0.0 / 98.5	0.0 / 100.0
Trimethoprim/sulfamethoxazole	4	>4	≤0.5 – >4	10.4 / 82.7	15.8 / 82.7
Clindamycin	>1	>1	≤0.25 – >1	17.8 / 82.2	17.8 / 82.2
Erythromycin	>4	>4	≤0.06 – >4	4.5 / 95.5	4.5 / 95.5
Levofloxacin	1	1	≤0.5 – >4	96.0 / 4.0	96.0 / 4.0
Linezolid	0.5	1	0.25 – 1	100.0 / -	100.0 / 0.0
Vancomycin	0.25	0.5	≤0.12 – 0.5	100.0 / -	100.0 / 0.0

a. Criteria as published by the CLSI [2012] and EUCAST [2012].
b. In the absence of CLSI breakpoints, USA-FDA breakpoints were applied [Teflaro Package Insert, 2012].
c. Criteria as published by the CLSI [2012] for 'Penicillin parenteral (non-meningitis)'.
d. Criteria as published by the CLSI [2012] for 'Penicillin (oral penicillin V)'.

- Ceftaroline was very active against all 47 isolates of *H. parainfluenzae* (MIC_{50}, ≤0.008 µg/ml and MIC_{90}, 0.015 µg/ml; Table 4) inhibiting all isolates at a MIC of ≤0.25 µg/ml (Table 4).

- Ceftaroline was also very active against *M. catarrhalis* (MIC_{50}, 0.06 µg/ml and MIC_{90}, 0.12 µg/ml).

Table 4. *Activity of Ceftaroline and Comparator Antimicrobial Agents when Tested Against Haemophilus spp. and Moraxella catarrhalis (APAC and SAF, 2010).*

Antimicrobial agent (no. tested)	MIC (µg/ml)			CLSI[a]	EUCAST[a]
	MIC_{50}	MIC_{90}	Range	%S / %R	%S / %R
H. influenzae, All (453)					
Ceftaroline	≤0.008	0.03	≤0.008 – 0.5	99.6[b] / -	- / -
Ampicillin	≤1	>8	≤1 – >8	75.5 / 21.6	75.5 / 24.5
Amoxicillin/clavulanate	≤1	2	≤1 – 8	99.1 / 0.9	84.1 / 15.9
Ceftriaxone	≤0.06	≤0.06	≤0.06 – 0.25	100.0 / -	99.3 / 0.7
Cefuroxime	1	2	≤0.12 – >16	98.0 / 0.4	73.3 / 7.9
Trimethoprim/sulfamethoxazole	≤0.5	>4	≤0.5 – >4	50.8 / 45.7	50.8 / 47.7
Azithromycin	1	2	≤0.25 – >4	98.9 / -	0.2 / 1.1
Levofloxacin	≤0.5	≤0.5	≤0.5 – 2	100.0 / -	99.8 / 0.2
ß-lactamase-negative (354)					
Ceftaroline	≤0.008	0.015	≤0.008 – 0.12	100.0[b] / -	- / -
Ampicillin	≤1	≤1	≤1 – 8	96.6 / 0.6	96.6 / 3.4
Amoxicillin/clavulanate	≤1	2	≤1 – 8	99.7 / 0.3	89.5 / 10.5
Ceftriaxone	≤0.06	≤0.06	≤0.06 – 0.12	100.0 / -	100.0 / 0.0
Cefuroxime	1	2	≤0.12 – 8	98.0 / 0.0	77.1 / 7.9
Trimethoprim/sulfamethoxazole	≤0.5	>4	≤0.5 – >4	53.3 / 42.5	53.3 / 44.8
Azithromycin	1	2	≤0.25 – >4	99.2 / -	0.3 / 0.8
Levofloxacin	≤0.5	≤0.5	≤0.5 – 2	100.0 / -	99.7 / 0.3
ß-lactamase-positive (100)					
Ceftaroline	0.015	0.06	≤0.008 – 0.5	98.0[b] / -	- / -
Ampicillin	>8	>8	≤1 – >8	1.0 / 96.0	1.0 / 99.0
Amoxicillin/clavulanate	≤1	2	≤1 – 8	97.0 / 3.0	65.0 / 35.0
Ceftriaxone	≤0.06	≤0.06	≤0.06 – 0.25	100.0 / -	97.0 / 3.0
Cefuroxime	1	2	0.25 – >16	98.0 / 2.0	60.0 / 8.0
Trimethoprim/sulfamethoxazole	4	>4	≤0.5 – >4	42.0 / 57.0	42.0 / 58.0
Azithromycin	1	2	0.25 – >4	98.0 / -	0.0 / 2.0
Levofloxacin	≤0.5	≤0.5	≤0.5	100.0 / -	100.0 / 0.0
H. parainfluenzae (47)					
Ceftaroline	≤0.008	0.015	≤0.008 – 0.25	95.7[b] / -	- / -
Ampicillin	≤1	≤1	≤1 – >8	91.5 / 8.5	- / -
Amoxicillin/clavulanate	≤1	≤1	≤1 – 2	100.0 / 0.0	- / -
Ceftriaxone	≤0.06	≤0.06	≤0.06 – 0.25	100.0 / -	- / -
Cefuroxime	0.25	1	≤0.12 – 2	100.0 / 0.0	- / -
Trimethoprim/sulfamethoxazole	2	>4	≤0.5 – >4	38.3 / 42.6	- / -
Azithromycin	0.5	2	≤0.25 – >4	95.7 / -	- / -
Levofloxacin	1	2	≤0.5 – >4	91.5 / -	- / -
M. catarrhalis, All (135)					
Ceftaroline	0.06	0.12	≤0.008 – 0.5	- / -	- / -
Amoxicillin/clavulanate	≤1	≤1	≤1 – 2	100.0 / 0.0	99.3 / 0.7
Ceftriaxone	0.25	1	≤0.06 – 2	100.0 / -	99.3 / 0.0
Cefuroxime	1	2	≤0.12 – 8	99.3 / 0.0	72.6 / 3.0
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	≤0.5 – >4	94.1 / 3.7	94.1 / 4.4
Erythromycin	0.25	0.5	≤0.06 – >8	95.9 / -	77.0 / 4.9
Levofloxacin	≤0.5	≤0.5	≤0.5 – 1	100.0 / -	100.0 / 0.0

a. Criteria as published by the CLSI [2012] and EUCAST [2012].
b. In the absence of CLSI breakpoints, USA-FDA breakpoints were applied [Teflaro Package Insert, 2012].

Conclusions

- Ceftaroline showed potent *in vitro* activity against pneumococci, including ceftriaxone-non-susceptible and levofloxacin-non-susceptible *S. pneumoniae* isolates, as well as Gram-negative pathogens (*H. influenzae*, *H. parainfluenzae* and *M. catarrhalis*) associated with community-acquired respiratory tract infections.
- Penicillin-susceptible strains of *S. pneumoniae* were highly susceptible to ceftaroline, ceftriaxone and cefuroxime. However, against penicillin-resistant (MIC, ≥2 µg/ml) pneumococci, ceftaroline was eight- to 16-fold more active than ceftriaxone and 16- to 32-fold more potent than amoxicillin/clavulanic acid.
- Ceftaroline was highly active against *H. influenzae* regardless of ß-lactamase production (MIC_{90}, 0.015 – 0.06 µg/ml). *H. parainfluenzae* (MIC_{90}, 0.015 µg/ml) and *M. catarrhalis* (MIC_{50}, 0.06 µg/ml and MIC_{90}, 0.12 µg/ml) strains were also very susceptible to ceftaroline.

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References

1. Clinical and Laboratory Standards Institute (2010). *M45-A2. Methods for antimicrobial dilution and disk susceptibility testing of infrequently isolated or fastidious bacteria: second edition*. Wayne, PA: CLSI.
2. 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: CLSI.
3. Clinical and Laboratory Standards Institute (2012). *M100-S22. Performance standards for antimicrobial susceptibility testing: 22nd informational supplement*. Wayne, PA: CLSI.
4. European Committee on Antimicrobial Susceptibility Testing (2012). Breakpoint tables for interpretation of MICs and zone diameters. Version 2.0, January 2012. Available at: http://www.eucast.org/clinical_breakpoints/. Accessed January 1, 2012.
5. File TM, Jr., Low DE, Eckburg PB, Talbot GH, Friedland HD, Lee J, Llorens L, Critchley I, Thye D (2010). Integrated analysis of FOCUS 1 and FOCUS 2: Randomized, doubled-blinded, multicenter phase 3 trials of the efficacy and safety of ceftaroline fosamil versus ceftriaxone in patients with community-acquired pneumonia. *Clin Infect Dis* 51: 1395-1405.
6. File TM, Jr., Low DE, Eckburg PB, Talbot GH, Friedland HD, Lee J, Llorens L, Critchley IA, Thye DA (2011). FOCUS 1: 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: iii19-iii32.
7. Flamm RK, Sader HS, Farrell DJ, Jones RN (2012). Summary of ceftaroline activity against pathogens in the United States, 2010: Report from the Assessing Worldwide Antimicrobial Resistance Evaluation (AWARE) Surveillance Program. *Antimicrob Agents Chemother* 56: 2933-2940.
8. Jones RN, Farrell DJ, Mendes RE, Sader HS (2011). Comparative ceftaroline activity tested against pathogens associated with community-acquired pneumonia: Results from an international surveillance study. *J Antimicrob Chemother* 66 Suppl 3: iii69-iii80.
9. Teflaro Package Insert (2012). Available at http://www.frx.com/pi/Teflaro_pi.pdf. Accessed June 2012.