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Antimicrobial Activity of Ceftaroline and Comparator Agents Tested Against Organisms Causing Skin and Soft Tissue Infections in European Medical Centres (2011)

HS Sader, RK Flamm, RN Jones

JMI Laboratories, North Liberty, Iowa, USA

Contact Information:
Helio S. Sader, MD, PhD
JMI Laboratories
345 Beaver Kreek Ctr, Ste A.
North Liberty, Iowa, 52317, USA
Phone: 319-665-3370
Fax: 319-665-3371
Email: helio-sader@jmilabs.com

Amended Abstract

Objective: To evaluate the spectrum and potency of ceftaroline (CPT) against contemporary (2011) pathogens causing complicated skin and soft tissue infections (cSSTI) isolated in Europe. CPT is the active metabolite of the prodrug CPT fosamil, a new parenteral cephalosporin recently approved by the European Medicines Agency for treatment of adults with cSSTI and community-acquired pneumonia. CPT is the only cephalosporin currently approved for the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) cSSTI infections.

Methods: 2205 organisms from the SENTRY Antimicrobial Surveillance Programme as part of the 2011 AWARE CPT surveillance study in Europe were isolated from cSSTI. Isolates were collected from patients in 41 medical centres in 16 European countries (including Israel and Turkey). Susceptibility (S) testing for CPT and commonly used antimicrobials was performed by CLSI broth microdilution method. S interpretations for CPT and comparators were as published by EUCAST. Extended spectrum beta-lactamase (ESBL) phenotype was determined per CLSI guidelines.

Results: 25.7% of *Staphylococcus aureus* isolates were resistant (R) to oxacillin (MRSA). CPT was very active against methicillin-S *S. aureus* (MSSA; MIC_{90}, 0.25 mg/L; 100.0% S) and MRSA (MIC_{90}, 2 mg/L; 89.7% S). Against MSSA, CPT was 16-, four- and four-fold more active than ceftriaxone (CRO), linezolid and vancomycin, respectively. MRSA showed high R rates to levofloxacin (LEV; 75.8%) and clindamycin (33.0%). Beta-haemolytic streptococci were highly CPT-S (MIC_{90}, ≤0.015 mg/L; highest MIC, 0.06 mg/L). CPT exhibited good activity against non-ESBL-phenotype strains of *Klebsiella* spp. and *Escherichia coli* (MIC_{90}, 0.5-1 mg/L), but limited activity against ESBL-producing and/or CRO-R strains. ESBL-phenotype *Klebsiella* spp. and *E. coli* also exhibited high R rates to LEV (58.2% and 72.2%, respectively) and gentamicin (51.9% and 40.9%, respectively). Furthermore, 21.5% of ESBL-phenotype *Klebsiella* spp. showed decreased S (MIC, ≥4 mg/L) to meropenem. Among *Morganella morganii* strains, 67.9% and 82.1% were S to CPT and CRO, respectively (see Table 1).

Conclusions: CPT demonstrated *in vitro* activity against Gram-positive organisms, including MRSA strains, and non-ESBL-phenotype *Enterobacteriaceae* isolated from patients with documented cSSTI in Europe. These results indicate that CPT has a good in vitro activity profile against contemporary pathogens responsible for cSSTI in Europe, including MRSA.

Introduction

Ceftaroline fosamil is the prodrug form of ceftaroline, a novel cephalosporin with bactericidal activity *in vitro* against Gram-positive organisms (including methicillin-susceptible and -resistant *Staphylococcus aureus* [MSSA and MRSA], β-haemolytic streptococci, viridans group streptococci, and *Streptococcus pneumoniae*), as well as many common Gram-negative organisms associated with skin infections. In two Phase 3 complicated skin and skin structure infection (cSSSI) trials (CANVAS 1 [NCT00424190] and CANVAS 2 [NCT00423657]), ceftaroline fosamil demonstrated high rates of clinical cure and microbiological efficacy, and was shown to be non-inferior to the comparison regimen of vancomycin plus aztreonam.

Ceftaroline fosamil was approved by the United States Food and Drug Administration (USA-FDA) for acute bacterial skin and skin-structure infection (ABSSSI) and community-acquired bacterial pneumonia (CABP) in late 2010, and more recently, by the European Medicines Agency (EMA) for the treatment of complicated skin and soft-tissue infections (cSSTIs) and community-acquired pneumonia (CAP) in August 2012.

In this study, we evaluated ceftaroline and selected other antimicrobial agents tested against 2,205 organisms collected from patients in European medical centres during 2011 from SENTRY as part of the **A**ssessing **W**orldwide **A**ntimicrobial **R**esistance **E**valuation (AWARE) Programme, a global ceftaroline surveillance study.

Materials and Methods

Clinically significant, consecutively collected, non-duplicate isolates from patients hospitalized with cSSTI in 41 medical centres in 2011 were utilized for this study. A total of 2,205 isolates were collected from 14 European countries, including (no. of medical centres) Belgium (1), Czech Republic (2), France (5), Germany (3), Greece (1), Italy (3), Poland (3), Portugal (1), Romania (3), Russia (3), Slovenia (1), Spain (3), Sweden (2) and the United Kingdom (UK; 2), plus Turkey (5) and Israel (3). The organism collection included: *S. aureus* (n = 1,319; 25.7% MRSA), β-haemolytic streptococci (n=210), *Escherichia coli* (n = 437; 26.3% extended spectrum β-lactamase [ESBL]-phenotype), *Klebsiella* spp. (n=183; 43.2% ESBL-phenotype) and *Morganella morganii* (n=56).

Broth microdilution test methods conducted according to the Clinical and Laboratory Standards Institute (CLSI) were performed to determine antimicrobial susceptibility of ceftaroline and comparators. Validated MIC panels were manufactured by ThermoFisher Scientific, formerly 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-A9, 2012). *E.coli* and *Klebsiella* spp. isolates were grouped as 'ESBL-phenotype' and 'non-ESBL-phenotype' based on the CLSI screening criteria for ESBL production (CLSI, 2013). Those isolates with positive ESBL screening test (i.e. MIC ≥2 mg/L for ceftazidime or ceftriaxone or aztreonam) were categorized as 'ESBL-phenotype' for the purpose of susceptibility testing results analysis.

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 *E. coli* ATCC 25922. Validation of QC results were based on the CLSI guidelines (M100-S23) and susceptibility breakpoints were used to determine susceptibility/resistance rates (CLSI and EUCAST, 2013).

Table 1. *Antimicrobial activity of ceftaroline when tested against bacterial isolates from cSSTIs in European medical centres (2011)*

Organism/region (no. tested)	no. of isolates (cumulative %) inhibited at ceftaroline MIC (mg/L) of:									MIC_{50}	MIC_{90}
	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	≥4		
S. aureus (1,319)	–	–	5 (0.4)	147 (11.5)	814 (73.2)	174 (86.4)	144 (97.3)	35 (100.0)	–	0.25	1
MSSA (980)	–	–	5 (0.5)	147 (15.5)	803 (97.5)	25 (100.0)	–	–	–	0.25	0.25
MRSA (339)	–	–	–	–	11 (3.2)	149 (47.2)	144 (89.7)	35 (100.0)	–	1	2
β-haemolytic streptococci (210)	197 (93.8)	11 (99.1)	2 (100.0)	–	–	–	–	–	–	≤0.015	≤0.015
E. coli (437)	1 (0.2)	39 (9.2)	102 (32.5)	79 (50.6)	37 (59.0)	27 (65.2)	21 (70.0)	9 (72.1)	7 (73.7)	0.12	>32
Non-ESBL-phenotype (322)	1 (0.3)	39 (12.4)	102 (44.1)	79 (68.6)	37 (80.1)	26 (88.2)	20 (94.4)	8 (96.9)	4 (98.1)	0.12	1
ESBL-phenotype (115)	–	–	–	–	–	1 (0.9)	1 (1.7)	1 (2.6)	3 (5.2)	>32	>32
Klebsiella spp. (183)	–	6 (3.3)	41 (25.7)	24 (33.8)	19 (49.2)	9 (54.1)	3 (55.7)	1 (56.3)	4 (58.5)	0.5	>32
Non-ESBL-phenotype (104)	–	6 (5.8)	41 (45.2)	24 (68.3)	19 (86.5)	9 (95.2)	3 (98.1)	1 (99.0)	1 (100.0)	0.12	0.5
ESBL-phenotype (79)	–	–	–	–	–	–	–	–	3 (3.8)	>32	>32
M. morganii (56)	–	6 (10.7)	14 (35.7)	11 (55.4)	3 (60.7)	4 (67.9)	2 (71.4)	0 (71.4)	2 (75.0)	0.12	>32

ESBL-phenotype defined as an MIC ≥2 mg/L for ceftazidime or ceftriaxone or aztreonam (CLSI, 2013).

Table 2. *Activity of ceftaroline and comparator antimicrobial agents when tested against isolates from cSSTIs (Europe, 2011)*

Organism (no. tested)/ antimicrobial agent	MIC (mg/L)			CLSI[a] %S / %R	EUCAST[a] %S / %R
	50%	90%	Range		
S. aureus (1,319)					
Ceftaroline	0.25	1	0.06 – 2	97.3 / 0.0	97.3 / 2.7
Oxacillin	0.5	>2	≤0.25 – >2	74.3 / 25.7	74.3 / 25.7
Ceftriaxone	4	>8	1 – >8	74.3 / 25.7	74.3 / 25.7
Cefuroxime	2	>16	≤0.5 – >16	74.3 / 25.7	74.3 / 25.7
Erythromycin	0.25	>16	≤0.12 – >16	71.0 / 26.6	71.3 / 28.1
Clindamycin	≤0.25	>2	≤0.25 – >2	89.8 / 10.2	89.5 / 10.2
Levofloxacin	≤0.12	>4	≤0.12 – >4	76.6 / 22.6	76.6 / 22.6
Tetracycline	≤0.25	>8	≤0.25 – >8	88.8 / 10.5	88.2 / 11.6
TMP/SMX[b]	≤0.5	≤0.5	≤0.5 – >4	99.2 / 0.8	99.2 / 0.6
Teicoplanin	≤2	≤2	≤2 – 4	100.0 / 0.0	99.8 / 0.2
Vancomycin	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Linezolid	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Daptomycin	0.25	0.5	0.12 – 2	99.8 / –	99.8 / 0.2
Tigecycline[c]	0.06	0.12	≤0.03 – 0.5	100.0 / –	100.0 / 0.0
MSSA (980)					
Ceftaroline	0.25	0.25	0.06 – 0.5	100.0 / 0.0	100.0 / 0.0
Ceftriaxone	4	4	1 – 8	100.0 / 0.0	100.0 / 0.0
Cefuroxime	2	2	≤0.5 – 8	100.0 / 0.0	100.0 / 0.0
Erythromycin	0.25	>16	≤0.12 – >16	83.5 / 14.6	83.8 / 15.9
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	97.8 / 2.2	97.6 / 2.2
Levofloxacin	≤0.12	0.25	≤0.12 – >4	95.6 / 4.2	95.6 / 4.2
Tetracycline	≤0.25	0.5	≤0.25 – >8	93.0 / 6.6	92.3 / 7.4
TMP/SMX[b]	≤0.5	≤0.5	≤0.5 – >4	99.5 / 0.5	99.5 / 0.2
Teicoplanin	≤2	≤2	≤2	100.0 / 0.0	100.0 / 0.0
Vancomycin	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Linezolid	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Daptomycin	0.25	0.5	0.12 – 2	99.9 / –	99.9 / 0.1
Tigecycline[c]	0.06	0.06	≤0.03 – 0.25	100.0 / –	100.0 / 0.0
MRSA (339)					
Ceftaroline	1	2	0.25 – 2	89.7 / 0.0	89.7 / 10.3
Ceftriaxone	>8	>8	4 – >8	0.0 / 100.0	0.0 / 100.0
Cefuroxime	>16	>16	2 – >16	0.0 / 100.0	0.0 / 100.0
Erythromycin	>16	>16	≤0.12 – >16	34.8 / 61.4	35.4 / 63.1
Clindamycin	≤0.25	>2	≤0.25 – >2	66.7 / 33.0	66.1 / 33.3
Levofloxacin	>4	>4	≤0.12 – >4	21.8 / 75.8	21.8 / 75.8
Tetracycline	≤0.25	>8	≤0.25 – >8	76.7 / 21.8	76.1 / 23.6
TMP/SMX[b]	≤0.5	≤0.5	≤0.5 – >4	98.2 / 1.8	98.2 / 1.8
Teicoplanin	≤2	≤2	≤2 – 4	100.0 / 0.0	99.4 / 0.6
Vancomycin	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Linezolid	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Daptomycin	0.25	0.5	0.12 – 2	99.4 / –	99.4 / 0.6
Tigecycline[c]	0.06	0.12	≤0.03 – 0.5	100.0 / –	100.0 / 0.0
β-haemolytic streptococci[d] (210)					
Ceftaroline	≤0.015	≤0.015	≤0.015 – 0.06	100.0 / –	100.0 / 0.0
Penicillin	≤0.06	≤0.06	≤0.06	100.0 / –	100.0 / 0.0
Ceftriaxone	≤0.06	0.12	≤0.06 – 1	99.5 / –	100.0 / 0.0
Erythromycin	≤0.12	16	≤0.12 – >16	78.6 / 21.0	78.6 / 21.0
Clindamycin	≤0.25	>2	≤0.25 – >2	89.0 / 11.0	89.0 / 11.0
Tetracycline	>8	>8	≤0.25 – >8	47.6 / 51.4	46.7 / 52.4
Levofloxacin	0.5	1	≤0.12 – 2	100.0 / 0.0	91.9 / 0.0
Vancomycin	0.5	0.5	0.25 – 1	100.0 / –	100.0 / 0.0
Linezolid	1	1	0.5 – 2	100.0 / –	100.0 / 0.0
Daptomycin	≤0.06	0.25	≤0.06 – 0.5	100.0 / –	100.0 / 0.0
Tigecycline[c]	≤0.03	≤0.03	≤0.03 – 0.12	100.0 / –	100.0 / 0.0
All *E. coli* (437)					
Ceftaroline	0.12	>32	≤0.015 – >32	65.2 / 30.0	65.2 / 34.8
Ceftriaxone	≤0.06	>8	≤0.06 – >8	73.9 / 25.6	73.9 / 25.6
Ceftazidime	0.25	16	0.06 – >32	81.5 / 15.1	76.2 / 18.5
Cefepime	≤0.5	>16	≤0.5 – >16	82.2 / 16.0	76.2 / 20.6
Ampicillin/sulbactam	16	>32	1 – >32	40.3 / 43.2	40.3 / 59.7
Piperacillin/tazobactam	2	64	≤0.5 – >64	85.4 / 8.0	79.4 / 14.6
Meropenem	≤0.06	≤0.06	≤0.06 – >8	99.5 / 0.5	99.5 / 0.2
Levofloxacin	≤0.12	>4	≤0.12 – >4	66.6 / 30.4	65.9 / 33.4
Gentamicin	≤1	>8	≤1 – >8	83.1 / 16.5	81.7 / 16.9
Amikacin	2	8	0.5 – >32	98.2 / 0.7	95.4 / 1.8
Tigecycline[c]	0.12	0.25	0.06 – 1	100.0 / 0.0	100.0 / 0.0
Non-ESBL–phenotype *E. coli* (322)					
Ceftaroline	0.12	1	≤0.015 – >32	88.2 / 5.6	88.2 / 11.8
Ceftriaxone	≤0.06	0.12	≤0.06 – 0.5	100.0 / 0.0	100.0 / 0.0
Ceftazidime	0.12	0.25	0.06 – 1	100.0 / 0.0	100.0 / 0.0
Cefepime	≤0.5	≤0.5	≤0.5 – 8	100.0 / 0.0	98.8 / 0.3
Meropenem	≤0.06	≤0.06	≤0.06	100.0 / 0.0	100.0 / 0.0
Ampicillin/sulbactam	8	>32	1 – >32	52.5 / 29.8	52.5 / 47.5
Piperacillin/tazobactam	2	16	≤0.5 – >64	90.4 / 5.9	87.3 / 9.6
Levofloxacin	≤0.12	>4	≤0.12 – >4	80.4 / 16.5	79.8 / 19.6
Gentamicin	≤1	2	≤1 – >8	91.6 / 8.4	90.4 / 8.4
Tigecycline[c]	0.12	0.12	0.06 – 1	100.0 / 0.0	100.0 / 0.0

Table 2. *(Cont)*

Organism (no. tested)/ antimicrobial agent	MIC (mg/L)			CLSI[a] %S / %R	EUCAST[a] %S / %R
	50%	90%	Range		
ESBL-phenotype *E.coli* (115)					
Ceftaroline	>32	>32	0.5 – >32	0.9 / 98.3	0.9 / 99.1
Ceftriaxone	>8	>8	0.25 – >8	0.9 / 97.4	0.9 / 97.4
Ceftazidime	16	>32	0.5 – >32	29.6 / 57.4	9.6 / 70.4
Cefepime	>16	>16	≤0.5 – >16	32.2 / 60.9	13.0 / 77.4
Meropenem	≤0.06	≤0.06	≤0.06 – >8	98.3 / 1.7	98.3 / 0.9
Ampicillin/sulbactam	32	>32	2 – >32	6.1 / 80.9	6.1 / 93.9
Piperacillin/tazobactam	8	>64	≤0.5 – >64	71.3 / 13.9	57.4 / 28.7
Levofloxacin	>4	>4	≤0.12 – >4	27.8 / 69.6	27.0 / 72.2
Gentamicin	2	>8	≤1 – >8	59.1 / 39.1	57.4 / 40.9
Amikacin	4	16	1 – >32	94.8 / 2.6	87.0 / 5.2
Tigecycline[c]	0.12	0.25	0.06 – 0.5	100.0 / 0.0	100.0 / 0.0
All *Klebsiella* spp.[e] (183)					
Ceftaroline	0.5	>32	0.03 – >32	54.1 / 44.3	54.1 / 45.9
Ceftriaxone	0.12	>8	≤0.06 – >8	60.7 / 39.3	60.7 / 39.3
Ceftazidime	0.5	>32	0.03 – >32	63.9 / 33.3	57.9 / 36.1
Cefepime	≤0.5	>16	≤0.5 – >16	65.0 / 31.7	60.7 / 36.6
Meropenem	≤0.06	2	≤0.06 – >8	89.6 / 9.3	90.7 / 5.5
Ampicillin/sulbactam	16	>32	2 – >32	45.9 / 45.9	45.9 / 54.1
Piperacillin/tazobactam	4	>64	≤0.5 – >64	67.8 / 24.6	59.6 / 32.2
Levofloxacin	≤0.12	>4	≤0.12 – >4	72.7 / 21.3	68.3 / 27.3
Gentamicin	≤1	>8	≤1 – >8	75.4 / 23.0	74.3 / 24.6
Amikacin	2	16	0.5 – >32	93.4 / 3.8	86.3 / 6.6
Tigecycline[c]	0.25	1	0.06 – 4	99.5 / 0.0	96.2 / 0.5
Non-ESBL-phenotype *Klebsiella* spp.[f] (104)					
Ceftaroline	0.12	0.5	0.03 – 4	95.2 / 1.9	95.2 / 4.8
Ceftriaxone	≤0.06	0.25	≤0.06 – 0.5	100.0 / 0.0	100.0 / 0.0
Ceftazidime	0.12	0.5	0.03 – 1	100.0 / 0.0	100.0 / 0.0
Cefepime	≤0.5	≤0.5	≤0.5 – 2	100.0 / 0.0	99.0 / 0.0
Meropenem	≤0.06	≤0.06	≤0.06 – 0.5	100.0 / 0.0	100.0 / 0.0
Ampicillin/sulbactam	4	16	2 – >32	80.8 / 5.8	80.8 / 19.2
Piperacillin/tazobactam	2	8	≤0.5 – >64	96.2 / 1.9	90.4 / 3.8
Levofloxacin	≤0.12	0.5	≤0.12 – >4	96.2 / 1.9	95.2 / 3.8
Gentamicin	≤1	≤1	≤1 – >8	96.2 / 3.8	96.2 / 3.8
Amikacin	1	2	0.5 – 4	100.0 / 0.0	100.0 / 0.0
Tigecycline[c]	0.25	0.5	0.06 – 2	100.0 / 0.0	96.2 / 0.0
ESBL-phenotype *Klebsiella* spp.[g] (79)					
Ceftaroline	>32	>32	4 – >32	0.0 / 100.0	0.0 / 100.0
Ceftriaxone	>8	>8	0.25 – >8	8.9 / 91.1	8.9 / 91.1
Ceftazidime	32	>32	0.25 – >32	16.5 / 77.2	2.5 / 83.5
Cefepime	>16	>16	≤0.5 – >16	19.0 / 73.4	10.1 / 84.8
Meropenem	≤0.06	>8	≤0.06 – >8	75.9 / 21.5	78.5 / 12.7
Ampicillin/sulbactam	>32	>32	16 – >32	0.0 / 98.7	0.0 / 100.0
Piperacillin/tazobactam	>64	>64	2 – >64	30.4 / 54.4	19.0 / 69.6
Levofloxacin	4	>4	≤0.12 – >4	41.8 / 46.8	32.9 / 58.2
Gentamicin	8	>8	≤1 – >8	48.1 / 48.1	45.6 / 51.9
Amikacin	4	32	0.5 – >32	84.8 / 8.9	68.4 / 15.2
Tigecycline[c]	0.5	1	0.06 – 4	98.7 / 0.0	96.2 / 1.3
M. morganii (56)					
Ceftaroline	0.12	>32	0.03 – >32	67.9 / 28.6	67.9 / 32.1
Ceftriaxone	≤0.06	2	≤0.06 – >8	82.1 / 8.9	82.1 / 8.9
Ceftazidime	0.12	16	0.06 – >32	83.9 / 14.3	76.8 / 16.1
Cefepime	≤0.5	≤0.5	≤0.5 – 1	100.0 / 0.0	100.0 / 0.0
Meropenem	≤0.06	0.12	≤0.06 – 0.25	100.0 / 0.0	100.0 / 0.0
Ampicillin/sulbactam	16	32	2 – >32	21.4 / 44.6	21.4 / 78.6
Piperacillin/tazobactam	≤0.5	2	≤0.5 – 64	98.2 / 0.0	94.6 / 1.8
Levofloxacin	≤0.12	>4	≤0.12 – >4	82.1 / 12.5	76.8 / 17.9
Gentamicin	≤1	>8	≤1 – >8	87.5 / 10.7	82.1 / 12.5
Amikacin	2	4	0.5 – 16	100.0 / 0.0	98.2 / 0.0
Tigecycline[c]	0.5	1	0.12 – 4	98.2 / 0.0	96.4 / 1.8

[a]Criteria as published by the CLSI (2013) and EUCAST (2013), β-lactam susceptibility should be directed by the oxacillin test results. [b]TMP/SMX = trimethoprim/sulfamethoxazole. [c]USA-FDA breakpoints were applied (Tygacil Package Insert, 2012). [d]Includes: Group A *Streptococcus* (131 strains), Group B *Streptococcus* (72 strains), and Group C *Streptococcus* (7 strains). [e]Includes: *Klebsiella oxytoca* (31 strains) and *K. pneumoniae* (152 strains). [f]Includes: *K. oxytoca* (26 strains) and *K. pneumoniae* (78 strains). [g]Includes: *K. oxytoca* (5 strains) and *K. pneumoniae* (74 strains).

Results

- Ceftaroline exhibited *in vitro* activity against MSSA isolates (MIC_{50} and MIC_{90}, 0.25 mg/L; 100.0% susceptible) and MRSA isolates ($MIC_{50/90}$, 1/2 mg/L; 89.7% susceptible by CLSI and EUCAST criteria). The highest MIC results observed among MSSA and MRSA were 0.5 and 2 mg/L, respectively (Tables 1 and 2). The overall MRSA rate was 25.7%.
- Ceftaroline (MIC_{50} and MIC_{90}, 0.25 mg/L) was 16-fold more active than ceftriaxone (MIC_{50} and MIC_{90}, 4 mg/L) and 8-fold more active than cefuroxime (MIC_{50} and MIC_{90}, 2 mg/L) when tested against MSSA. All tested agents were ≥92.3% susceptible against MSSA, except erythromycin (83.5–83.8% susceptible; Table 2).
- The most active agents against MRSA were: ceftaroline ($MIC_{50/90}$, 1/2 mg/L; 89.7% susceptible by CLSI/EUCAST criteria; all isolates inhibited at ≤2 mg/L), linezolid (MIC_{50} and MIC_{90}, 1 mg/L; 100.0% susceptible), vancomycin (MIC_{50} and MIC_{90}, 1 mg/L; 100.0% susceptible), daptomycin ($MIC_{50/90}$, 0.25/0.5 mg/L; 99.4% susceptible), and tigecycline ($MIC_{50/90}$, 0.06/0.12 mg/L; 100.0% susceptible). In contrast, only 21.8% of MRSA strains were susceptible to levofloxacin (Table 2).
- Against β-haemolytic streptococci, ceftaroline (MIC_{50} and MIC_{90}, ≤0.015 mg/L; highest MIC of 0.06 mg/L) was more active than ceftriaxone ($MIC_{50/90}$, ≤0.06/0.12 mg/L). Decreased susceptibility was observed for tetracycline (46.7–47.6% susceptible), erythromycin (78.6% susceptible) and clindamycin (89.0% susceptible; Table 2).
- *E. coli* isolates were generally susceptible to ceftaroline ($MIC_{50/90}$, 0.12/1 mg/L for non ESBL-strains). Among non-ESBL strains, 88.2% and 94.4% were inhibited at a ceftaroline MIC of ≤0.5 and ≤1 mg/L, respectively (Tables 1 and 2). An ESBL-phenotype was observed in 26.3% of *E. coli* strains, and ESBL-phenotype strains were markedly less susceptible to ceftaroline (MIC_{50} and MIC_{90}, >32 mg/L) and all other cephalosporins tested, such as ceftriaxone and ceftazidime (Table 2).
- High rates of ESBL-phenotypes were observed among *Klebsiella* spp. (43.2%). Ceftaroline exhibited good activity against non-ESBL-phenotype strains ($MIC_{50/90}$, 0.12/0.5 mg/L), while ESBL-producing strains had a ceftaroline MIC_{50} of >32 mg/L (Tables 1 and 2). Decreased susceptibility to meropenem was observed in 24.1% (MIC, ≥2 mg/L) and 21.5% (MIC, ≥4 mg/L) of ESBL-phenotype *Klebsiella* spp. by CLSI and EUCAST, respectively (Table 2).
- Among *M. morganii* strains, 67.9% and 82.1% were susceptible to ceftaroline ($MIC_{50/90}$, 0.12/>32 mg/L) and ceftriaxone ($MIC_{50/90}$, ≤0.06/2 mg/L; Table 2), respectively.

Conclusions

- Ceftaroline demonstrated activity *in vitro* against *S. aureus* (including MRSA), β-haemolytic streptococci and non-ESBL-phenotype *Enterobacteriaceae* isolated from patients with documented cSSTI in medical centres from 14 European countries, Israel and Turkey (2011).
- Activity of ceftaroline against *S. aureus* was similar to that of vancomycin, daptomycin and linezolid; activity against β-haemolytic streptococci was most similar to that of penicillin and ceftriaxone.
- These results indicate that ceftaroline has an excellent *in vitro* activity profile against contemporary pathogens responsible for cSSTI in Europe, including MRSA.

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