ECCMID 2018 Poster #P1805

Community-Acquired Skin and Soft Tissue Infection in Europe, Asia, and Latin America: Frequency of Organism Occurrence and Antimicrobial Activity of Ceftaroline and Comparator Agents HS Sader, JM Streit, MD Huband, MA Pfaller

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Introduction

- Skin and soft tissue infection (SSTI) encompasses a wide range of clinical presentations, from mild cases of cellulitis and subcutaneous tissue infections to complicated deepseated infections with systemic signs of sepsis and the presence of complicating co-morbidities, and represents a common cause of hospitalisation
- Ceftaroline is a cephalosporin with broad-spectrum *in vitro* bactericidal activity against gram-positive and common gram-negative pathogens causing SSTI, including oxacillin (methicillin)-susceptible (MSSA) and -resistant S. aureus (MRSA), β-haemolytic streptococci, and non-ESBL-producing Escherichia coli and Klebsiella pneumoniae
- Ceftaroline fosamil is approved by the European Medicine Agency (EMA) and by the US Food and Drug Administration (FDA) for the treatment of complicated SSTIs, including those caused by MRSA
- The SENTRY Antimicrobial Surveillance Program monitors the frequency of occurrence and antimicrobial susceptibility of organisms from various infection types worldwide
- In this investigation we evaluated the frequency and antimicrobial susceptibility of organisms isolated from patients hospitalised with community-acquired (CA) SSTI in Europe (EUR), the Asia-Pacific region (APAC), and Latin America (LATAM)

Materials and Methods

Organism collection

- A total of 5,120 bacterial isolates were consecutively collected in 2014–2016 from 63 medical centres distributed as follows (Table 1)
- Western Europe (W-EUR): 3,250 isolates from 20 centres in 10 nations
- Eastern Europe and the Mediterranean region (E-EUR): 839 isolates from 16 centres in 12 nations
- Asia-Pacific region (APAC): 666 isolates from 16 centres in 10 nations
- Latin America (LATAM): 365 isolates from 11 centres in 9 nations
- Each participating centre was asked to collect consecutive bacterial isolates from patients hospitalised with SSTI
- An isolate obtained from an outpatient or collected earlier than 48 hours after hospitalisation was considered community-acquired (CA-SSTI)
- An extended-spectrum β -lactamase screen-positive phenotype (ESBL-phenotype) was defined as MIC $\geq 2 \text{ mg/L}$ for ceftriaxone, ceftazidime, or aztreonam (CLSI, 2018)

Susceptibility methods

- Broth microdilution tests were conducted according to the Clinical and Laboratory Standards Institute (CLSI) documents to determine antimicrobial susceptibility of ceftaroline and numerous comparator antimicrobials used to treat patients with SSTI
- MIC panels were prepared at JMI Laboratories (2015-2016) or manufactured by ThermoFisher Scientific[®] (2014; Cleveland, Ohio, USA)
- Susceptibility percentages and QC results validation were based on the EUCAST (2018) and CLSI (M100, 2018) guidelines

Table 1 List of nations and number of participating centres surveyed in each geographic region

Western Europe (W-EUR)	Eastern Europe (E-EUR)	Asia-Pacific region (APAC)	Latin America (LATAM)
Belgium (1)	Belarus (1)	Australia (5)	Argentina (1)
France (4)	Croatia (1)	Hong Kong (1)	Brazil (2)
Germany (2)	Czech Republic (1)	Japan (1)	Chile (1)
Greece (1)	Hungary (1)	Malaysia (1)	Colombia (1)
Ireland (2)	Israel (1)	New Zealand (2)	Costa Rica (1)
Italy (3)	Poland (1)	Philippines (1)	Ecuador (1)
Portugal (1)	Romania (2)	Singapore (1)	Mexico (2)
Spain (3)	Russia (3)	South Korea (2)	Peru (1)
Sweden (1)	Slovakia (1)	Taiwan (1)	Venezuela (1)
United Kingdom (2)	Slovenia (1)	Thailand (1)	
	Turkey (2)		
	Ukraine (1)		

- and Figure 3)
- (Figure 1)

- (APAC); 8.4% overall (Figure 2)

- ≤2 mg/L

are employees of JMI Laboratories.

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Results

S. aureus was the most common CA-SSTI organism in W-EUR, E-EUR, and APAC and represented 43.3% of the overall collection (Figures 1a to 1d)

• MRSA rates varied from 15.8% (E-EUR) to 27.6% (LATAM); 18.5% overall (Figure 2) • In general, 98.9% of S. aureus and 94.2% of MRSA isolates were susceptible to ceftaroline, with 99.5% of MRSA isolates inhibited at ≤2 mg/L (0.5% resistant; Table 2

• Escherichia coli was second overall (14.2%) and first in LATAM (31.5%) with ESBL-phenotype rates varying from 16.5% (W-EUR) to 34.8% (APAC); 22.8% overall

• β-haemolytic streptococci (BHS; 8.2%), *Enterococcus* spp. (7.5%), *Klebsiella* spp. (6.0%), and *Enterobacter* spp. (5.5%) ranked third, fourth, fifth, and sixth overall, respectively; but, the rank order varied among geographic regions (Figures 1a to 1d)

• β -haemolytic streptococci were highly susceptible to ceftaroline (MIC₀₀, ≤ 0.015 mg/L; highest MIC, 0.03 mg/L; 100.0% susceptible; Table 2), but exhibited decreased susceptibility to tetracycline (59.4%) and erythromycin (82.8%; data not shown) • Vancomycin resistance among enterococci varied from 2.8% (E-EUR) to 10.5%

• ESBL-phenotype rates among *Klebsiella* spp. varied from 28.6% (APAC) to 56.7% (E-EUR); 38.0% overall (Figure 2)

• Among *Enterobacter* spp., overall susceptibility to ceftaroline and ceftazidime were 62.8% and 67.0%, respectively, but varied from 70.8% and 75.8% in W-EUR to 44.8% and 48.3% in LATAM, respectively (Figure 3)

Conclusions

• The frequency and antimicrobial susceptibility of bacteria isolated from patients with CA-SSTI varied broadly by geographic region

S. aureus represented 43.3% of the bacterial isolates collected from patients with CA-SSTI and was very susceptible (98.9% overall) to ceftaroline

Ceftaroline was very active against MRSA from all geographic regions evaluated in this investigation with an overall susceptibility of 94.2% and 99.5% inhibited at

Ceftaroline spectrum of activity against *Enterobacteriaceae* was similar to those of ceftriaxone and ceftazidime

Acknowledgements

JMI Laboratories received financial support from Pfizer in connection with the study and the development of this poster. The authors HS Sader, JM Streit, MD Huband, and MA Pfaller

References

Figure 1 Frequency of occurrence of organisms isolated from patients hospitalised with community-acquired skin and soft tissue infections (CA-SSTI) stratified by geographic region

A. Western Europe



Table 2 Antimicrobial activity of ceftaroline tested against the main organisms and organism groups of isolates from all geographic regions combined

Organism/organism group (no. of isolates)	No. of isolates at MIC (mg/L; cumulative %)													
	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	> ^a	
Staphylococcus aureus (2,216)			13 0.6	227 10.8	1,530 79.9	262 91.7	160 98.9	22 99.9	2 100.0					0.2
Methicillin-susceptible (1,805)			13 0.7	227 13.3	1,516 97.3	49 100.0								0.2
Methicillin-resistant (411)					14 3.4	213 55.2	160 94.2	22 99.5	2 100.0					0.5
β-haemolytic streptococci (418)	413 98.8	5 100.0												≤0.0
Enterococcus spp. (382)					7 1.8	12 5.0	78 25.4	132 59.9	28 67.3	18 72.0			107 100.0	2
E. faecalis (277)					4 1.4	5 3.2	77 31.0	130 78.0	27 87.7	18 94.2			12 100.0	2
Coagulase-negative staphylococci (215)			62 28.8	28 41.9	68 73.5	37 90.7	13 96.7	7 100.0						0.2
Methicillin-susceptible (116)			61 52.6	21 70.7	30 96.6	4 100.0								≤0.0
Methicillin-resistant (99)			1 1.0	7 8.1	38 46.5	33 79.8	13 92.9	7 100.0						0.5
Viridans group streptococci (66)	35 53.0	24 89.4	3 93.9	2 97.0	0 97.0	2 100.0								≤0.0 ⁻
Enterobacteriaceae (1,822)	22 1.2	97 6.5	388 27.8	388 49.1	224 61.4	140 69.1	89 74.0	41 76.2	28 77.8	21 78.9	22 80.1	35 82.1	327 100.0	0.2
Escherichia coli (729)	15 2.1	59 10.2	192 36.5	162 58.7	72 68.6	35 73.4	23 76.5	11 78.1	9 79.3	5 80.0	6 80.8	3 81.2	137 100.0	0.12
Ceftriaxone-susceptible (572)	15 2.6	59 12.9	192 46.5	162 74.8	72 87.4	35 93.5	21 97.2	7 98.4	4 99.1	2 99.5	0 99.5	1 99.7	2 100.0	0.12
Klebsiella spp. (305)	2 0.7	9 3.6	69 26.2	52 43.3	33 54.1	21 61.0	4 62.3	1 62.6	3 63.6	6 65.6	0 65.6	3 66.6	102 100.0	0.2
Ceftriaxone-susceptible (198)	2 1.0	9 5.6	69 40.4	52 66.7	33 83.3	21 93.9	4 96.0	1 96.5	2 97.5	4 99.5	0 99.5	0 99.5	1 100.0	0.12
Enterobacter spp. (282)		4 1.4	19 8.2	67 31.9	64 54.6	23 62.8	12 67.0	4 68.4	8 71.3	2 72.0	9 75.2	19 81.9	51 100.0	0.2
Ceftriaxone-susceptible (186)		4 2.2	19 12.4	66 47.8	64 82.3	19 92.5	9 97.3	1 97.8	4 100.0					0.2
Proteus mirabilis (193)		10 5.2	73 43.0	51 69.4	15 77.2	6 80.3	10 85.5	1 86.0	2 87.0	3 88.6	4 90.7	1 91.2	17 100.0	0.12
Serratia marcescens (83)					6 7.2	33 47.0	25 77.1	13 92.8	1 94.0	1 95.2	2 97.6	1 98.8	1 100.0	1
Morganella morganii (90)		9 10.0	13 24.4	27 54.4	15 71.1	6 77.8	4 82.2	2 84.4	0 84.4	1 85.6	0 85.6	2 87.8	11 100.0	0.1
Citrobacter spp. (70)		2 2.9	17 27.1	26 64.3	12 81.4	9 94.3	0 94.3	0 94.3	0 94.3	1 95.7	0 95.7	1 97.1	2 100.0	0.12
Other Enterobacteriaceae (70)	5 7.1	4 12.9	5 20.0	3 24.3	7 34.3	7 44.3	11 60.0	9 72.9	5 80.0	2 82.9	1 84.3	5 91.4	6 100.0	1

^a Greater than the highest dilution tested

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MIC 0.25 ≤0.015 >8 0.5 0.25 >32 0.5 >32 0.5 >32 >32 0.5 20

Figure 2 Frequency of occurrence of key resistance phenotypes among the main organisms isolated from patients hospitalised with SSTI



Figure 3 Ceftaroline resistance rates among the main organisms isolated from patients hospitalised with SSTI



Abbreviations: MRSA, methicillin-resistant S. aureus; BHS, β-haemolytic streptococci