

In vitro Activities of Ceftaroline and Comparator Agents against Gram-positive Bacterial Pathogens Causing Blood Stream Infections in a Global Population: ATLAS Surveillance Program 2012-2018

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Introduction

Typical gram-positive organisms causing bloodstream infections (BSI) include *Staphylococcus aureus* (methicillin-susceptible [MSSA] and -nonsusceptible [MRSA]), coagulase negative staphylococci, *Streptococcus pneumoniae* and beta hemolytic streptococci. The parenteral cephem ceftaroline fosamil is currently approved by the FDA for the treatment of adult and pediatric patients with acute bacterial skin and skin structure infections caused by *S. aureus* (including MSSA and MRSA isolates), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Klebsiella oxytoca*, as well as for community-acquired bacterial pneumonia caused by *S. pneumoniae* (including cases with concurrent bacteremia), *S. aureus* (MSSA isolates only), *Haemophilus influenzae*, *E. coli*, *K. pneumoniae*, and *K. oxytoca* [1]. Limited data have been published on the *in vitro* activity of ceftaroline against recent gram-positive clinical isolates known to be frequent bacterial causes of blood stream infections. The ATLAS (Antimicrobial Testing Leadership and Surveillance) program is a worldwide surveillance study that summarizes the *in vitro* activities of ceftaroline and comparator agents against common pathogens isolated from patients with bloodstream infections and other infection types.

Materials & Methods

Clinically relevant, non-duplicate, isolates cultured from blood by clinical laboratories in 2012-2018 were collected as part of the ATLAS program. Isolates were shipped to a central laboratory (IHMA, Inc., Schaumburg, IL, USA) for testing. Identifications were confirmed by MALDI-TOF mass spectroscopy (Bruker Daltronics, Bremen, Germany; library version MBT Compass 4.1.90. and 4.1.100). In total, 10,998 non-duplicate isolates of *S. aureus*, *S. epidermidis*, *S. pneumoniae* and beta hemolytic streptococci from BSI collected between 2012 and 2018 were tested. Isolates came from (n(%)): Asia/South Pacific (1,739/15.8%), Europe (5,448/49.5%), Latin America (1,805/16.4%), Middle East/Africa (861/7.8%), and North America (1,145/10.4%). Minimum inhibitory concentration (MIC) values were determined by broth microdilution according to Clinical Laboratory Standards Institute (CLSI) guidelines [2] and percent susceptibility (%S) interpreted using 2020 CLSI MIC breakpoints [3].

Results

Table 1. *In vitro* activity of ceftaroline and comparator agents against isolates from bloodstream infections, 2012-2018

Organism	Antimicrobial	Global				Asia/South Pacific				Europe				Latin America				MidEast/Africa				North America			
		N	%S	MIC ₉₀	Range	N	%S	MIC ₉₀	Range	N	%S	MIC ₉₀	Range	N	%S	MIC ₉₀	Range	N	%S	MIC ₉₀	Range	N	%S	MIC ₉₀	Range
<i>Staphylococcus aureus</i> , MSSA	Ceftaroline	2692	100	0.25	≤0.015 - 2	454	99.8	0.5	0.06 - 2	1264	100	0.25	≤0.015 - 0.5	544	100	0.25	≤0.06 - 0.5	203	100	0.25	≤0.015 - 0.5	227	100	0.25	≤0.06 - 0.5
	Ceftriaxone	4712	na	4	≤0.03 - >64	494	na	4	0.5 - >64	2737	na	4	≤0.03 - >64	552	na	4	0.12 - >64	204	na	4	≤0.03 - 8	725	na	4	≤0.03 - 32
	Clindamycin	2692	96.1	0.12	≤0.03 - >4	454	93.2	0.25	≤0.03 - >4	1264	97.0	0.12	≤0.03 - >4	544	97.1	0.12	≤0.03 - >4	203	99.5	0.12	≤0.03 - >4	227	92.1	0.25	≤0.03 - >4
	Daptomycin	2692	100	0.5	≤0.06 - 1	454	100	0.5	≤0.06 - 1	1264	100	0.5	≤0.06 - 1	544	100	0.5	0.12 - 1	203	100	0.5	0.12 - 1	227	100	0.5	0.12 - 1
	Erythromycin	2692	77.3	8	≤0.12 - >8	454	78.9	>4	≤0.12 - >8	1264	81.7	>4	≤0.12 - >8	544	71.9	>8	≤0.12 - >8	203	81.8	>4	0.25 - >8	227	58.1	8	≤0.12 - >8
	Gentamicin	2692	95.0	≤2	≤0.06 - >32	454	90.1	2	≤0.06 - >32	1264	97.6	≤2	≤0.06 - >32	544	93.6	≤2	≤0.06 - >32	203	91.6	2	≤0.06 - >32	227	96.9	≤2	0.12 - >32
	Levofloxacin	5806	92.0	0.5	≤0.03 - >32	671	88.1	4	0.03 - >32	3265	92.9	0.5	≤0.03 - >32	703	97.7	0.25	0.03 - 32	297	91.2	0.5	≤0.06 - 8	870	87.5	4	≤0.06 - >32
	Linezolid	5806	100	2	≤0.5 - >8	671	99.9	2	≤0.5 - >8	3265	100	2	≤0.5 - 4	703	100	2	≤0.5 - 4	297	100	2	≤0.5 - 4	870	100	2	≤0.5 - 4
	Trimethoprim Sulfa	2692	99.0	≤1	≤0.03 - >4	454	97.4	≤1	≤0.03 - >4	1264	99.7	≤1	≤0.03 - >4	544	99.6	≤1	≤0.03 - >4	203	97.0	≤1	≤0.03 - >4	227	98.7	≤1	≤0.03 - >2
	Vancomycin	5806	100	1	≤0.12 - 2	671	100	1	≤0.25 - 2	3265	100	1	≤0.12 - 2	703	100	2	0.25 - 2	297	100	1	≤0.12 - 2	870	100	1	≤0.12 - 2
<i>Staphylococcus aureus</i> , MRSA	Ceftaroline	2454	91.4	1	≤0.015 - 8	474	81.6	2	0.06 - 8	1147	95.4	1	0.25 - 4	464	87.9	2	≤0.015 - 2	159	90.6	1	0.25 - 2	210	99.5	1	0.25 - 2
	Ceftriaxone	3655	na	>64	≤0.03 - >64	621	na	>64	0.12 - >64	1780	na	>64	≤0.03 - >64	474	na	>64	1 - >64	193	na	>64	0.06 - >64	587	na	>64	1 - >64
	Clindamycin	2454	64.9	>4	≤0.03 - >4	474	58.6	>4	≤0.03 - >4	1147	73.0	>4	≤0.03 - >4	464	45.9	>4	≤0.03 - >4	159	69.8	>4	≤0.03 - >4	210	73.3	>4	≤0.03 - >4
	Daptomycin	2454	99.8	1	0.12 - 4	474	99.8	1	0.12 - 2	1147	99.7	1	0.25 - 2	464	100	1	0.25 - 1	159	99.4	1	0.25 - 4	210	99.5	1	0.25 - 2
	Erythromycin	2454	33.8	>8	≤0.12 - >8	474	30.4	>8	≤0.12 - >8	1147	39.3	>8	≤0.12 - >8	464	29.3	>8	≤0.12 - >8	159	43.4	>8	≤0.12 - >8	210	14.3	>8	≤0.12 - >8
	Gentamicin	2454	80.1	>32	≤0.06 - >32	474	64.3	>32	≤0.06 - >32	1147	87.0	32	≤0.06 - >32	464	79.3	>32	≤0.06 - >32	159	59.7	>32	≤0.06 - >32	210	94.8	≤2	0.12 - >32
	Levofloxacin	4056	28.8	16	≤0.06 - >32	686	43.1	8	≤0.06 - >32	1936	18.9	32	≤0.06 - >32	575	41.7	>4	≤0.06 - >32	223	32.7	>4	0.12 - 16	636	30.2	>32	≤0.06 - >32
	Linezolid	4056	100	2	≤0.5 - 4	686	100	2	≤0.5 - 4	1936	100.0	2	≤0.5 - 4	575	100	2	≤0.5 - 4	223	100	2	≤0.5 - 4	636	100	2	≤0.5 - 4
	Trimethoprim Sulfa	2454	95.0	≤1	≤0.03 - >4	474	89.0	4	≤0.03 - >4	1147	98.8	≤1	≤0.03 - >4	464	97.6	≤1	≤0.03 - >4	159	83.0	>4	0.06 - >4	210	91.4	≤1	0.06 - >4
	Vancomycin	4056	100	1	≤0.12 - 2	686	100	1	≤0.25 - 2	1936	100	1	≤0.12 - 2	575	100	2	≤0.25 - 2	223	100	2	0.5 - 2	636	100	1	0.25 - 2
<i>Staphylococcus epidermidis</i>	Ceftaroline	1978	na	0.5	≤0.015 - 4	234	na	0.5	0.03 - 2	1035	na	0.5	≤0.015 - 2	357	na	0.5	≤0.015 - 2	166	na	0.5	0.03 - 2	186	na	0.5	0.03 - 4
	Ceftriaxone	2440	na	>32	≤0.03 - >64	155	na	>32	≤0.5 - >32	1795	na	>32	≤0.03 - >64	270	na	>32	≤0.5 - >32	127	na	>32	≤0.5 - >32	93	na	>32	≤0.5 - >32
	Clindamycin	1978	55.1	>4	≤0.03 - >4	234	56.0	>4	≤0.03 - >4	1035	57.3	>4	≤0.03 - >4	357	51.0	>4	≤0.03 - >4	166	48.8	>4	≤0.03 - >4	186	55.4	>4	≤0.03 - >4
	Daptomycin	1978	99.8	1	≤0.06 - 2	234	100	1	≤0.06 - 2	1035	99.7	1	≤0.06 - 2	357	100	1	≤0.06 - 1	166	100	1	≤0.06 - 1	186	100	1	0.12 - 1
	Erythromycin	1978	30.1	>8	≤0.12 - >8	234	31.2	>8	≤0.12 - >8	1035	30.4	>8	≤0.12 - >8	357	27.5	>8	≤0.12 - >8	166	26.5	>8	≤0.12 - >8	186	35.5	>8	≤0.12 - >8
	Gentamicin	1978	48.8	>32	≤0.06 - >32	234	51.3	>32	≤0.06 - >32	1035	46.5	>32	≤0.06 - >32	357	44.8	>32	≤0.06 - >32	166	48.8	>32	≤0.06 - >32	186	66.1	32	≤0.06 - >32
	Levofloxacin	3015	37.3	8	≤0.03 - >32	234	41.5	>4	≤0.03 - >4	2070	34.8	8	≤0.03 - >32	358	43.3	>4	0.06 - >4	167	44.9	>4	0.12 - >4	186	41.9	>4	≤0.03 - >4
	Linezolid	3015	98.7	2	≤0.5 - >8	234	100	2	≤0.5 - 2	2070	98.5	2	≤0.5 - 2	358	98.6	2	≤0.5 - >8	167	99.4	2	≤0.5 - >8	186	100	2	≤0.5 - 2
	Trimethoprim Sulfa	1978	54.3	>4	≤0.03 - >4	234	53	>4	≤0.03 - >4	1035	58.5	>4	≤0.03 - >4	357	49	>4	≤0.03 - >4	166	45.8	>4	0.06 - >4	186	50.5	>4	≤0.03 - >4
	Vancomycin	3015	99.8	2	≤0.12 - 8	234	99.6	2	0.5 - 8	2070	100	2	≤0.12 - 8	358	99.2	2	≤0.25 - 8	167	100	2	0.5 - 4	186	100	2	≤0.25 - 4
<i>Streptococcus pneumoniae</i> , penicillin-susceptible	Ceftaroline	1821	100	0.015	≤0.004 - 0.12	201	100	0.015	≤0.004 - 0.12	1124	100	0.015	≤0.004 - 0.12	146	100	0.015	≤0.004 - 0.06	126	100	0.015	≤0.004 - 0.03	224	100	0.008	≤0.004 - 0.06
	Ceftriaxone	3672	100	0.06	≤0.015 - 1	226	100	0.06	≤0.015 - 0.5	2350	100	0.06	≤0.015 - 1	224	100	0.06	≤0.015 - 0.25	160	100	0.06	≤0.015 - 0.25	712	100	0.03	≤0.015 - 0.5
	Erythromycin	3554	88.9	>1	≤0.008 - >64	223	78.9	>1	≤0.008 - >64	2283	92.6	0.06	≤0.008 - >64	212	90.6	0.06	≤0.008 - >64	158	91.8	0.06	≤0.008 - 64	678	78.8	4	≤0.015 - >64
	Linezolid	3672	99.7	1	≤0.06 - 16	226	99.6	1	≤0.12 - >8	2350	99.6	1	≤0.06 - 16	224	99.6	1	≤0.06 - 4	160	100	1	≤0.06 - 2	712	99.7	1	≤0.06 - 8
	Vancomycin	3672	100	0.5	≤0.008 - 1	226	100	0.5	0.015 - 1	2350	100	0.5	≤0.008 - 1	224	100	0.5	0.06 - 0.5	160	100	0.5	0.06 - 1	712	100	0.5	≤0.03 - 1
<i>Streptococcus pneumoniae</i> , penicillin-non-susceptible	Ceftaroline	600	99.7	0.25	≤0.004 - 2	126	99.2	0.25	0.008 - 2	240	99.6	0.25	≤0.004 - 1	91	100	0.25	≤0.004 - 0.25	78	100	0.25	0.008 - 0.5	65	100	0.12	≤0.004 - 0.25
	Ceftriaxone	1413	90.7	1	≤0.015 - 64	157	79.6	2	≤0.03 - 8	715	92.7	1	≤0.015 - >4	156	87.8	2	≤0.03 - 2	122	87.7	2	≤0.03 - >4	263	95.1	1	≤0.015 - 64
	Erythromycin	1372	42.5	>64	≤0.015 - >64	154	30.5	16	≤0.015 - >64	697	52.8	>64	≤0.015 - >64	152	30.3	64	≤0.015 - >64	118	38.1	64	≤0.015 - >64	251	30.7	>64	≤0.015 - >64
	Linezolid	1413	98.5	1	≤0.06 - 16	157	95.5	2	0.25 - 16	715	99.0	1	≤0.06 - 16	156	98.7	1	≤0.06 - >8	122	97.5	1	≤0.06 - >8	263	99.2	1	0.12 - >8
	Vancomycin	1413																							