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In Vitro Activity of Ceftaroline against 623 Diverse Strains of Anaerobic Bacteria▽

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The *in vitro* activities of ceftaroline, a novel, parenteral, broad-spectrum cephalosporin, and four comparator antimicrobials were determined against anaerobic bacteria. Against Gram-positive strains, the activity of ceftaroline was similar to that of amoxicillin-clavulanate and four to eight times greater than that of ceftriaxone. Against Gram-negative organisms, ceftaroline showed good activity against β-lactamase-negative strains but not against the members of the *Bacteroides fragilis* group. Ceftaroline showed potent activity against a broad spectrum of anaerobes encountered in respiratory, skin, and soft tissue infections.

With the continuing emergence of novel patterns of resistance to commonly used antimicrobial agents, alternative therapies are needed to treat serious infections. Ceftaroline is a novel, parenteral, broad-spectrum cephalosporin that exhibits bactericidal activity against Gram-positive organisms, such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-intermediate *S. aureus*, and multidrug-resistant *Streptococcus pneumoniae* (MDRSP) strains, as well as common Gram-negative pathogens (8, 12, 14, 16, 18–22). Ceftaroline is currently in development for the treatment of complicated skin and skin structure infections and community-acquired pneumonia.

Anaerobic bacteria are common pathogens in a variety of pleuropulmonary infections, including aspiration pneumonia, lung abscesses, and empyema (1, 3, 6, 15). However, many laboratories do not culture for anaerobes (9), diminishing awareness of the role of anaerobes in these infections. The main anaerobic pathogens isolated from these infections include *Prevotella melaninogenica* (~25%), *Prevotella intermedia* (~30%), *Fusobacterium* species (~39%), Gram-positive cocci (~30%), and *Veillonella* species (~35%) (7). Cephalosporins such as cefoxitin have been used for the therapy of aspiration pneumonias. Although cefoxitin is active against most respiratory anaerobes, it has poor activity against the newer resistant strains of members of the family *Enterobacteriaceae* and MRSA. The activity of ceftaroline against Gram-positive anaerobes is similar to that of amoxicillin-clavulanate, and non-β-lactamase-producing Gram-negative strains generally have low ceftaroline MICs (present study), suggesting that ceftaroline might have an adequate spectrum of activity for therapy for some cases of aspiration pneumonia.

To investigate the broader potential of ceftaroline, we compared its *in vitro* activity against 623 unique clinical isolates of anaerobic bacteria representing 5 Gram-negative bacterial genera and 17 Gram-positive bacterial genera to the activities of ceftriaxone, metronidazole, clindamycin, and amoxicillin-clavulanate.

The reference agar dilution procedure described in CLSI document M11-A7 was used (5). The organisms were recovered from a variety of clinical specimens and were stored at −70°C in 20% skim milk. Identification was accomplished by standard phenotypic methods or by partial 16S rRNA gene sequencing for strains that could not be identified phenotypically (13, 17). Quality control strains *Bacteroides fragilis* ATCC 25285, *Clostridium difficile* ATCC 700057, and *Staphylococcus aureus* ATCC 29213 were included on each day of testing.

The antimicrobial agents were obtained as follows: ceftaroline was from Forest Laboratories, Inc. (New York, NY); ceftriaxone, vancomycin, and metronidazole were from Sigma-Aldrich, Inc. (St. Louis, MO); and amoxicillin and clavulanate were from GlaxoSmithKline (Research Triangle Park, NC). The agar dilution plates were prepared on the day of testing.

The strains were taken from the freezer and transferred twice to ensure purity and good growth. Cell paste from 48-h cultures was suspended in brucella broth to achieve the turbidity of a 0.5 McFarland standard, and the mixture was applied to plates with a Steers replicator to deliver approximately 10^5 CFU/spot. The plates were incubated for 44 h at 37°C in an anaerobic chamber. The MIC was the lowest concentration that completely inhibited growth or that resulted in a marked reduction in growth compared with that for the drug-free growth control (5).

A summary showing the MIC range, MIC_{50}, MIC_{90}, and percent susceptibility is presented in Table 1. The cumulative ceftaroline MIC distributions for all groups of strains are displayed in Table 2.

The ceftaroline MIC_{50}s for *B. fragilis* and other *B. fragilis* group species were 16 and 64 μg/ml, respectively, and the MIC_{90}s were >64 μg/ml for both for *B. fragilis* and other *B. fragilis* group species. Ceftaroline was effective against all other Gram-negative, non-β-lactamase-producing strains and had activity similar to that of ceftriaxone. For *Prevotella* species, the ceftaroline MICs varied according to β-lactamase production, with the MIC_{50} and the MIC_{90} being 1 and 32 μg/ml, respectively. Most *Porphyromonas* species were susceptible to ceftaroline at ≤0.5 μg/ml; four β-lactamase-positive strains of

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TABLE 1. Summary of ceftaroline and comparator agent MICs, by species or group

Organism	No. of isolates	MIC (μg/ml)			% susceptible	% resistant
		Range	50%	90%		
Gram-negative bacteria						
Bacteroides fragilis	30					
Ceftaroline		4–>64	16	64	NA[a]	NA
Ceftriaxone (≤16, ≥64)[b]		4–>64	32	64	27	43
Clindamycin (≤2, ≥8)		0.06–>128	1	128	63	37
Metronidazole (≤8, ≥32)		0.25–2	1	2	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		0.5–64	0.5	2	93	7
Bacteroides thetaiotaomicron	20					
Ceftaroline		32–>64	64	>64	NA	NA
Ceftriaxone (≤16, ≥64)		64–>64	>64	>64	0	100
Clindamycin (≤2, ≥8)		0.06–>128	4	128	45	45
Metronidazole (≤8, ≥32)		0.5–1	1	1	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		0.5–8	2	4	95	0
Bacteroides fragilis group spp.[c]	26					
Ceftaroline		2–>64	64	>64	NA	NA
Ceftriaxone (≤16, ≥64)		4–>64	>64	>64	23	58
Clindamycin (≤2, ≥8)		0.06–>128	4	>128	42	50
Metronidazole (≤8, ≥32)		0.5–2	1	2	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		0.125–32	2	8	77	4
Prevotella bivia	20					
Ceftaroline		0.125–>64	2	64	NA	NA
Ceftriaxone (≤16, ≥64)		0.125–>64	2	>64	75	15
Clindamycin (≤2, ≥8)		0.03–>128	≤0.03	>128	85	15
Metronidazole (≤8, ≥32)		≤0.03–4	1	2	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–4	0.25	4	100	0
Prevotella buccae	20					
Ceftaroline		0.125–>64	0.5	64	NA	NA
Ceftriaxone (≤16, ≥64)		0.125–>64	0.25	64	50	30
Clindamycin (≤2, ≥8)		≤0.03–>128	≤0.03	>128	80	20
Metronidazole (≤8, ≥32)		0.25–1	0.5	1	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		0.06–4	0.06	1	100	0
Prevotella melaninogenica	18					
Ceftaroline		≤0.008–32	2	32	NA	NA
Ceftriaxone (≤16, ≥64)		0.03–32	2	32	78	0
Clindamycin (≤2, ≥8)		≤0.03–>128	≤0.03	>128	72	28
Metronidazole (≤8, ≥32)		0.06–2	0.5	1	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–2	0.125	2	100	0
Prevotella intermedia	20					
Ceftaroline		≤0.008–64	1	16	NA	NA
Ceftriaxone (≤16, ≥64)		0.03–64	1	16	80	10
Clindamycin (≤2, ≥8)		≤0.03–>128	≤0.03	16	85	15
Metronidazole (≤8, ≥32)		0.125–2	0.25	1	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–1	0.06	0.5	100	0
Prevotella spp.[d]	20					
Ceftaroline		≤0.008–32	2	32	NA	NA
Ceftriaxone (≤16, ≥64)		≤0.008–64	1	8	90	5
Clindamycin (≤2, ≥8)		≤0.03–>128	≤0.03	128	70	30
Metronidazole (≤8, ≥32)		0.06–8	0.5	2	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–2	0.125	1	100	0
Porphyromonas asaccharolytica	21					
Ceftaroline		≤0.008–0.5	0.015	0.03	NA	NA
Ceftriaxone (≤16, ≥64)		≤0.008–1	0.06	0.06	100	0
Clindamycin (≤2, ≥8)		≤0.03–>128	≤0.03	>128	81	19
Metronidazole (≤8, ≥32)		≤0.03–0.25	0.06	0.125	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–≤0.03	≤0.03	≤0.03	100	0
Porphyromonas somerae	10					
Ceftaroline		≤0.008–16	0.015	16	NA	NA
Ceftriaxone (≤16, ≥64)		≤0.008–64	0.015	64	80	20
Clindamycin (≤2, ≥8)		≤0.03–>128	≤0.03	>128	80	20
Metronidazole (≤8, ≥32)		0.25–0.5	0.5	0.5	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–0.5	≤0.03	0.125	100	0
Fusobacterium nucleatum	22					
Ceftaroline		≤0.008–0.125	≤0.008	0.125	NA	NA
Ceftriaxone (≤16, ≥64)		0.015–1	0.125	0.5	100	0
Clindamycin (≤2, ≥8)		≤0.03–0.5	0.06	0.06	100	0
Metronidazole (≤8, ≥32)		≤0.03–0.25	≤0.03	0.25	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–0.5	≤0.03	0.06	100	0
Fusobacterium necrophorum	22					
Ceftaroline		0.015–0.06	0.03	0.06	NA	NA
Ceftriaxone (≤16, ≥64)		≤0.008–0.125	0.015	0.03	100	0
Clindamycin (≤2, ≥8)		≤0.03–0.25	≤0.03	0.06	100	0
Metronidazole (≤8, ≥32)		0.06–0.25	0.125	0.25	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–1	0.125	0.5	100	0

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TABLE 1—*Continued*

Organism	No. of isolates	MIC (μg/ml)			% susceptible	% resistant
		Range	50%	90%		
Fusobacterium mortiferum	10					
Ceftaroline		1–64	8	32	NA	NA
Ceftriaxone (≤16, ≥64)		16–>64	>64	>64	10	90
Clindamycin (≤2, ≥8)		≤0.03–0.25	0.06	1	100	0
Metronidazole (≤8, ≥32)		0.25–2	0.5	1	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		0.25–8	4	8	80	0
Fusobacterium varium	10					
Ceftaroline		0.015–0.5	0.25	0.5	NA	NA
Ceftriaxone (≤16, ≥64)		0.15–8	1	8	100	0
Clindamycin (≤2, ≥8)		0.06–64	2	4	90	10
Metronidazole (≤8, ≥32)		0.25–0.5	0.25	0.5	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		0.125–2	1	2	100	0
Veillonella spp.	19					
Ceftaroline		0.015–1	0.125	0.5	NA	NA
Ceftriaxone (≤16, ≥64)		0.03–8	4	8	79	16
Clindamycin (≤2, ≥8)		≤0.03–>128	0.125	128	79	21
Metronidazole (≤8, ≥32)		1–8	2	8	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–8	0.25	4	95	0
Gram-positive bacteria						
Anaerococcus prevotii-Anaerococcus tetradius[e]	20					
Ceftaroline		≤0.008–2	0.03	0.125	NA	NA
Ceftriaxone (≤16, ≥64)		0.03–32	0.25	0.5	95	0
Clindamycin (≤2, ≥8)		≤0.03–>128	0.5	128	60	40
Metronidazole (≤8, ≥32)		0.125–4	1	2	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–8	≤0.03	0.125	95	0
Finegoldia magna	19					
Ceftaroline		0.03–1	0.25	0.5	NA	NA
Ceftriaxone (≤16, ≥64)		2–8	4	8	100	0
Clindamycin (≤2, ≥8)		0.06–>128	2	>128	53	37
Metronidazole (≤8, ≥32)		0.06–1	0.5	1	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–0.25	0.125	0.25	100	0
Parvimonas micra	22					
Ceftaroline		0.015–0.5	0.06	0.25	NA	NA
Ceftriaxone (≤16, ≥64)		0.125–2	0.5	1	100	0
Clindamycin (≤2, ≥8)		0.06–128	0.25	16	86	14
Metronidazole (≤8, ≥32)		0.125–1	0.25	0.25	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–1	0.125	0.5	100	0
Peptoniphilus asaccharolyticus	21					
Ceftaroline		≤0.008–0.25	0.06	0.25	NA	NA
Ceftriaxone (≤16, ≥64)		0.03–1	0.125	0.25	100	0
Clindamycin (≤2, ≥8)		≤0.03–>128	0.125	>128	76	24
Metronidazole (≤8, ≥32)		0.125–2	1	1	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–0.06	≤0.03	0.06	100	0
Peptostreptococcus anaerobius-Peptostreptococcus stomatis[f]	23					
Ceftaroline		0.125–8	0.5	4	NA	NA
Ceftriaxone (≤16, ≥64)		0.5–16	2	8	100	0
Clindamycin (≤2, ≥8)		≤0.03–32	≤0.03	0.25	96	4
Metronidazole (≤8, ≥32)		0.125–1	0.5	1	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–32	0.125	0.5	91	9
Anaerobic Gram-positive cocci[g]	22					
Ceftaroline		≤0.008–8	0.06	1	NA	NA
Ceftriaxone (≤16, ≥64)		0.03–64	0.25	16	91	5
Clindamycin (≤2, ≥8)		≤0.03–>128	0.125	64	73	27
Metronidazole (≤8, ≥32)		0.25–>64	1	4	91	9
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–4	0.06	0.5	100	0
Actinomyces spp.[h]	13					
Ceftaroline		≤0.008–0.25	0.015	0.25	NA	NA
Ceftriaxone (≤16, ≥64)		≤0.008–0.5	0.125	0.5	100	0
Clindamycin (≤2, ≥8)		≤0.03–>128	0.06	128	77	23
Metronidazole (≤8, ≥32)		>32–>32	>32	>32	0	100
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–0.5	0.06	0.5	100	0
Propionibacterium acnes	20					
Ceftaroline		≤0.008–0.125	≤0.008	0.06	NA	NA
Ceftriaxone (≤16, ≥64)		≤0.008–0.125	0.015	0.06	100	0
Clindamycin (≤2, ≥8)		0.125–>128	0.125	0.125	95	5
Metronidazole (≤8, ≥32)		>32–>32	>32	>32	0	100
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–0.25	≤0.03	0.06	100	0
Propionibacterium avidum	11					
Ceftaroline		0.015–0.25	0.25	0.25	NA	NA
Ceftriaxone (≤16, ≥64)		0.03–0.5	0.25	0.5	100	0
Clindamycin (≤2, ≥8)		0.125–0.5	0.25	0.25	100	0
Metronidazole (≤8, ≥32)		>32–>32	>32	>32	0	100
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–0.25	0.25	0.25	100	0

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TABLE 1—*Continued*

Organism	No. of isolates	MIC (μg/ml)			% susceptible	% resistant
		Range	50%	90%		
Eggerthella lenta	17					
Ceftaroline		2–16	8	16	NA	NA
Ceftriaxone (≤16, ≥64)		16–>64	>64	>64	6	94
Clindamycin (≤2, ≥8)		0.06–8	0.5	2	94	6
Metronidazole (≤8, ≥32)		0.5–1	0.5	1	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		0.5–1	1	1	100	0
"*Eubacterium*" group[j]	25					
Ceftaroline		0.015–0.25	0.125	0.25	NA	NA
Ceftriaxone (≤16, ≥64)		0.03–16	0.5	2	100	0
Clindamycin (≤2, ≥8)		≤0.03–>128	0.06	2	92	8
Metronidazole (≤8, ≥32)		0.125–4	0.5	1	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–0.5	0.125	0.25	100	0
Lactobacillus casei-Lactobacillus rhamnosus group[j]	10					
Ceftaroline		0.25–8	0.5	1	NA	NA
Ceftriaxone (≤16, ≥64)		8–>64	32	64	40	30
Clindamycin (≤2, ≥8)		0.25–2	1	2	100	0
Metronidazole (≤8, ≥32)		>64–>64	>64	>64	0	100
Amoxicillin-clavulanate (≤4/2, ≥16/8)		0.25–2	0.5	1	100	0
Clostridium perfringens	20					
Ceftaroline		≤0.008–0.5	0.125	0.25	NA	NA
Ceftriaxone (≤16, ≥64)		≤0.008–4	0.5	2	100	0
Clindamycin (≤2, ≥8)		≤0.03–2	0.25	1	100	0
Metronidazole (≤8, ≥32)		0.5–4	2	4	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–0.125	0.03	0.125	100	0
Clostridium ramosum	21					
Ceftaroline		1–2	1	1	NA	NA
Ceftriaxone (≤16, ≥64)		0.25–0.5	0.25	0.5	100	0
Clindamycin (≤2, ≥8)		1–>128	4	8	24	43
Metronidazole (≤8, ≥32)		0.5–2	1	1	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–0.25	0.06	0.25	100	0
Clostridium innocuum	21					
Ceftaroline		0.5–4	1	2	NA	NA
Ceftriaxone (≤16, ≥64)		8–32	8	16	95	0
Clindamycin (≤2, ≥8)		0.125–>128	0.5	>128	86	14
Metronidazole (≤8, ≥32)		0.5–4	1	4	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		0.125–1	0.5	0.5	100	0
Clostridium clostridioforme group[k]	20					
Ceftaroline		0.25–2	1	2	NA	NA
Ceftriaxone (≤16, ≥64)		2–>64	4	32	75	10
Clindamycin (≤2, ≥8)		≤0.03–4	0.5	2	95	0
Metronidazole (≤8, ≥32)		≤0.03–0.25	0.06	0.25	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		0.25–1	0.5	0.5	100	0
Clostridium spp., other[l]	24					
Ceftaroline		0.015–16	0.5	16	NA	NA
Ceftriaxone (≤16, ≥64)		0.015–>64	2	64	75	21
Clindamycin (≤2, ≥8)		≤0.03–>128	2	128	54	38
Metronidazole (≤8, ≥32)		0.125–4	0.5	4	100	0
Amoxicillin-clavulanate (≤4/2, ≥16/8)		≤0.03–2	0.125	1	100	0

[a] NA, not applicable.
[b] Values in parentheses are the breakpoints for susceptibility, resistance (in μg/ml).
[c] *Bacteroides caccae* (*n* = 6), *B. distasonis* (*n* = 3), *B. merdae* (*n* = 1), *B. ovatus* (*n* = 5), *B. uniformis* (*n* = 4), and *B. vulgatus* (*n* = 7).
[d] *Prevotella bergensis* (*n* = 2), *P. corporis* (*n* = 1), *P. denticola* (*n* = 5), *P. disiens* (*n* = 5), *P. loescheii* (*n* = 3), *P. nanceiensis* (*n* = 2), *P. oris* (*n* = 1), and *P. tannerae* (*n* = 1).
[e] *Anaerococcus prevotii* (*n* = 12) and *A. tetradius* (*n* = 8).
[f] *Peptostreptococcus anaerobius* (*n* = 17) and *P. stomatis* (*n* = 6).
[g] *Anaerococcus lactolyticus* (*n* = 1), *Anaerococcus murdochii* (*n* = 1), *Anaerococcus octavius* (*n* = 1), *Anaerococcus vaginalis* (*n* = 5), *Anaerococcus* species, no PCR match (*n* = 3), *Gemella morbillorum* (*n* = 1), *Gemella sanguinis* (*n* = 1), *Peptoniphilus harei* (*n* = 7), and *Peptoniphilus lacrimalis* (*n* = 2).
[h] *Actinomyces israelii* (*n* = 1), *A. meyeri* (*n* = 2), *A. neuii* subsp. *anitratus* (*n* = 2), *A. odontolyticus* (*n* = 3), and *A. turicensis* (*n* = 5).
[i] *Atopobium parvulum* (*n* = 1), *Collinsella aerofaciens* (*n* = 4), *Eubacterium contortum* (*n* = 1), *Eubacterium cylindroides* (*n* = 1), *Eubacterium limosum* (*n* = 8), *Eubacterium saburreum* (*n* = 2), *Mogibacterium timidum* (*n* = 3), *Slackia exigua* (*n* = 4), and *Solobacterium moorei* (*n* = 1).
[j] *Lactobacillus casei* (*n* = 3) and *L. rhamnosus* (*n* = 7).
[k] *Clostridium aldenense* (*n* = 4), *C. bolteae* (*n* = 5), *C. citroniae* (*n* = 3), *C. hathewayi* (*n* = 4), and *C. clostridioforme* (*n* = 4).
[l] *Clostridium barati* (*n* = 1), *C. bifermentans* (*n* = 1), *C. butyricum* (*n* = 2), *C. cadaveris* (*n* = 2), *C. celerecrescens* (*n* = 1), *C. difficile* (*n* = 4), *C. glycolicum* (*n* = 2), *C. hylemonae* (*n* = 2), *C. paraputrificum* (*n* = 2), *C. sordellii* (*n* = 1), *C. sphenoides* (*n* = 1), *C. subterminale* (*n* = 1), *C. symbiosum* (*n* = 2), and *C. tertium* (*n* = 2).

Porphyromonas somerae (previously *Porphyromonas levii*), however, had ceftaroline MICs of 8 to 16 μg/ml. *Fusobacterium nucleatum* and *Fusobacterium necrophorum*, including two β-lactamase-positive strains, had a ceftaroline MIC_{50} and a ceftaroline MIC_{90} of 0.015 and 0.125 μg/ml, respectively. The bile-resistant *Fusobacterium varium* strains were susceptible to ceftaroline, with the highest MIC observed being 0.5 μg/ml, whereas *Fusobacterium mortiferum* had high MICs of ceftaroline (MIC_{90}, 32 μg/ml), ceftriaxone (MIC_{90}, >64 μg/ml), and amoxicillin-clavulanate (MIC_{90}, 8 μg/ml). All *Veillonella* species were inhibited by ≤1 μg/ml ceftaroline.

Almost all of the Gram-negative species were susceptible to

TABLE 2. Ceftaroline MIC distributions for Gram-negative and Gram-positive anaerobes

Organism group and organism	Total	Cumulative % of isolates with the following ceftaroline MIC (μg/ml):														
		≤0.008	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	>64
Gram-negative anaerobes																
Bacteroides fragilis	30										7	37	63		73	100
Bacteroides fragilis group, other[a]	46									4	7	9	20	37	57	100
Prevotella species[b]	98	3.1	4.1	12	18	27	37	43	50	55	63	74	82	91	96	100
Porphyromonas species[c]	31	13	71	81		84		87						90	100	
Fusobacterium nucleatum/*Fusobacterium necrophorum*[d]	44	25	50	77	89	100										
Fusobacterium mortiferum	10								10	20		70	80	90	100	
Fusobacterium varium	10		20			30	80	100								
Veillonella species	19		5	32		84	89	95	100							
Total	288															
Gram-positive anaerobes																
All Gram-positive cocci[e]	127	10	20	30	47	61	82	92	96	97	98	100				
Propionibacterium and *Actinomyces* species[f]	44	43	57	64	77	82	100									
Lactobacillus casei-Lactobacillus rhamnosus group[g]	10						20	80	90			100				
Eggerthella lenta	17									6	12	88	100			
"*Eubacterium*" group, other[h]	25		8	20	28	92	100									
Clostridium perfringens	20	15	35			60	90	100								
Clostridium ramosum	21								90	100						
Clostridium innocuum	21							29	67	95	100					
Clostridium clostridioforme group[i]	20						15	35	80	100						
Clostridium species, other[j]	24		4		8	21	46	54	67	75		83	100			
Total	329															

[a] *Bacteroides thetaiotaomicron* (*n* = 20), *B. caccae* (*n* = 6), *B. distasonis* (*n* = 3), *B. merdae* (*n* = 1), *B. ovatus* (*n* = 5), *B. uniformis* (*n* = 4), and *B. vulgatus* (*n* = 7).
[b] *Prevotella bivia* (*n* = 20), *P. buccae* (*n* = 20), *P. melaninogenica* (*n* = 18), *P. intermedia* (*n* = 20), *P. bergensis* (*n* = 2), *P. corporis* (*n* = 1), *P. denticola* (*n* = 5), *P. disiens* (*n* = 5), *P. loescheii* (*n* = 3), *P. nanceiensis* (*n* = 2), *P. oris* (*n* = 1), and *P. tannerae* (*n* = 1).
[c] *Porphyromonas asaccharolytica* (*n* = 21) and *P. somerae* (*n* = 10).
[d] *Fusobacterium nucleatum* (*n* = 22) and *F. necrophorum* (*n* = 22).
[e] *Finegoldia magna* (*n* = 19), *Parvimonas micra* (*n* = 22), *Peptostreptococcus anaerobius* (*n* = 17), *Peptostreptococcus stomatis* (*n* = 6), *Anaerococcus prevotii* (*n* = 12), *Anaerococcus tetradius* (*n* = 8), *Anaerococcus lactolyticus* (*n* = 1), *Anaerococcus murdochii* (*n* = 1), *Anaerococcus octavius* (*n* = 1), *Anaerococcus vaginalis* (*n* = 5), *Anaerococcus* species, no PCR match (*n* = 3), *Gemella morbillorum* (*n* = 1), *Gemella sanguinis* (*n* = 1), *Peptoniphilus asaccharolyticus* (*n* = 21), *Peptoniphilus harei* (*n* = 7), and *Peptoniphilus lacrimalis* (*n* = 2).
[f] *Propionibacterium acnes* (*n* = 21), *Propionibacterium avidum* (*n* = 11), *Actinomyces israelii* (*n* = 1), *Actinomyces meyeri* (*n* = 2), *Actinomyces neuii* subsp. *anitratus* (*n* = 2), *Actinomyces odontolyticus* (*n* = 3), and *Actinomyces turicensis* (*n* = 5).
[g] *Lactobacillus casei* (*n* = 3) and *L. rhamnosus* (*n* = 7).
[h] *Atopobium parvulum* (*n* = 1), *Collinsella aerofaciens* (*n* = 4), *Eubacterium contortum* (*n* = 1), *Eubacterium cylindroides* (*n* = 1), *Eubacterium limosum* (*n* = 8), *Eubacterium saburreum* (*n* = 2), *Mogibacterium timidum* (*n* = 3), *Slackia exigua* (*n* = 4), and *Solobacterium moorei* (*n* = 1).
[i] *Clostridium aldenense* (*n* = 4), *C. bolteae* (*n* = 5), *C. citroniae* (*n* = 3), *C. hathewayi* (*n* = 4), and *C. clostridioforme* (*n* = 4).
[j] *Clostridium barati* (*n* = 1), *C. bifermentans* (*n* = 1), *C. butyricum* (*n* = 2), *C. cadaveris* (*n* = 2), *C. celerecrescens* (*n* = 1), *C. difficile* (*n* = 4), *C. glycolicum* (*n* = 2), *C. hylemonae* (*n* = 2), *C. paraputrificum* (*n* = 2), *C. sordellii* (*n* = 1), *C. sphenoides* (*n* = 1), *C. subterminale* (*n* = 1), *C. symbiosum* (*n* = 2), and *C. tertium* (*n* = 2).

metronidazole; four strains of *Veillonella* species and one strain of *Prevotella nanceiensis*, however, showed elevated MICs of 4 to 8 μg/ml. Clindamycin resistance was present in 37% of *B. fragilis* strains, 43% of *Bacteroides thetaiotaomicron* strains, 45% of *B. fragilis* group species, 21% of *Prevotella* species, and 19% of *Porphyromonas asaccharolytica* strains. Resistance to amoxicillin-clavulanate at >8/4 μg/ml was present in one *B. fragilis* strain and one *Bacteroides ovatus* strain, both of which were also resistant to imipenem; however, 19% of the *B. fragilis* group species showed an intermediate-susceptible amoxicillin-clavulanate MIC.

Ceftaroline exhibited excellent activity against Gram-positive strains. The MIC_{50} and MIC_{90} for 127 strains of Gram-positive cocci were 0.125 and 0.5 μg/ml, respectively; and the MIC_{50} and MIC_{90} for 44 strains of *Propionibacterium acnes*, *Propionibacterium avidum*, and *Actinomyces* species were 0.015 and 0.25 μg/ml, respectively. The MIC_{50} and MIC_{90} for 106 strains of *Clostridium* species were 0.5 and 2 μg/ml, respectively, with higher MICs of 8 to 16 μg/ml being noted for 4 strains of *Clostridium difficile*, 1 strain of *Clostridium celerecrescens*, and 1 strain of *Clostridium tertium*. The MIC_{50} and MIC_{90} for 10 strains of vancomycin-resistant lactobacilli were 0.5 and 1 μg/ml, respectively. All "*Eubacterium*" group Gram-positive rods except *Eggerthella lenta* were inhibited by ≤0.25 μg/ml; the MIC_{50} and MIC_{90} for *Eggerthella lenta* were 8 and 16 μg/ml, respectively. Ceftaroline was four- to eightfold more active than ceftriaxone against Gram-positive organisms, with the MICs being the most similar to those of amoxicillin-clavulanate.

Clindamycin resistance was present in 37% of the *Finegoldia magna* strains and 40% of the strains in the *Anaerococcus prevotii* and *Anaerococcus tetradius* groups. All strains of *Actinomyces*, *Propionibacterium*, and *Lactobacillus* were resistant to metronidazole, as were one strain of anaerobic *Gemella morbillorum* and one strain of *Gemella sanguinis.* All except two Gram-positive strains were susceptible to amoxicillin-clavulanate; the exceptions were two strains of *Peptostreptococcus anaerobius* (MICs, 32 μg/ml).

Ceftaroline has been demonstrated to have excellent activity against strains commonly encountered in skin and respiratory

infections, including MRSA, group A *Streptococcus*, MDRSP, and non-extended-spectrum β-lactamase (ESBL)-producing members of the family *Enterobacteriaceae* (8, 12, 14, 16, 18–22). The present study is the first to focus on the activity of ceftaroline against anaerobes and expands the known spectrum of species against which ceftaroline shows activity. The findings reported here are consistent with those of a limited study by Sader et al. (21).

Although ceftaroline has a low level of activity against most *Bacteroides* isolates, its use in combination with a β-lactamase inhibitor might overcome this resistance and increase the clinical potential of the use of ceftaroline against intra-abdominal infections and some skin and soft tissue infections. Many skin infections contain anaerobes that are predominantly Gram-positive anaerobic cocci and relatively few *Bacteroides* species (2, 10), suggesting that ceftaroline may have activity in these instances as well.

Our study confirmed the increasing resistance to clindamycin currently being reported by many investigators. Of particular interest was the resistance demonstrated by 2 of 19 strains of *P. asaccharolytica*, a species previously thought to be very susceptible to clindamycin (11). Additionally, four strains of *P. somerae* were β-lactamase producers, which is of interest because most studies do not report MICs for *Porphyromonas* and, to date, β-lactamase-producing strains have been a rare finding. We also noted an increase in the number of *B. fragilis* group strains with amoxicillin-clavulanate MICs reaching the intermediate level, similar to the increase in the ampicillin-sulbactam MICs reported in the CLSI M11-A7 supplement, which includes an antibiogram for the *B. fragilis* group (4).

Except for *Bacteroides* species and β-lactamase-producing *Prevotella* isolates, ceftaroline showed potent activity against a broad spectrum of anaerobic bacteria frequently recovered from a variety of clinical infections.

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