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In Vitro Activities of the Des-Fluoro(6) Quinolone BMS-284756 against Aerobic and Anaerobic Pathogens Isolated from Skin and Soft Tissue Animal and Human Bite Wound Infections

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BMS-284756, a new des-fluoro(6) quinolone, was very active against 240 aerobic and 180 anaerobic isolates from bite victims. It inhibited 403 of 420 (96%) isolates, including those of *Moraxella* spp., CDC group EF-4, and *Eikenella corrodens* at ≤2 μg/ml and those of all *Pasteurella* spp. and *Bergeyella zoohelcum* at ≤0.015 μg/ml. *Fusobacterium russii* and 6 of 11 *Fusobacterium nucleatum* isolates of animal bite origin were resistant, but isolates of human bite origin were susceptible, which suggests that they were of a different subspecies.

Many of the 4.5 million Americans bitten by animals or humans each year require either therapeutic or prophylactic antimicrobial therapy; approximately 30,000 of these patients visit an emergency department for medical treatment, and an additional 10,000 are hospitalized with serious wound infections involving complex polymicrobial floras (4, 18). While many patients receive a beta-lactam agent such as amoxicillin-clavulanate, approximately 20% report a history of an adverse reaction to penicillin or other beta-lactam antibiotics (2) and require an appropriate alternative agent.

Older fluoroquinolones, such as ciprofloxacin, have limited activities against certain gram-positive aerobes and many anaerobic species typically encountered in human and animal bite wounds (5, 7). BMS-284756 {T-3811ME; 1-cyclopropyl-8-(difluoromethoxy)-7-[(1*R*)-1-methyl-2,3-dihydro-1H-5-isoindolyl]-4-oxo-1,4-dihydro-3-quinolinecarboxylic acid methanesulfonate monohydrate)} is a new des-fluoro(6) quinolone that lacks the six-position fluorine characterizing the previous generation of fluoroquinolones. Preliminary data indicate that this drug has a broad spectrum of activity against most gram-positive and gram-negative aerobes and anaerobes, including certain strains that are resistant to other fluoroquinolones (3, 8).

Studies have focused on more typical isolates, especially respiratory and intra-abdominal pathogens (8, 17), but have not evaluated the drug against the specific range of bacteria, such as *Pasteurella* species, *Eikenella corrodens*, *Prevotella heparinolytica*, and *Porphyromonas macacae*, commonly found in human and animal bite wound infections. In this study, we determined the activity of BMS-284756 against 420 aerobic and anaerobic strains recently isolated from such infections in humans. The specific sources of the strains were 117 dog bite, 156 cat bite, 132 human bite, and 15 other animal bite wounds. All isolates were identified by standard criteria (1, 9–13, 16); the numbers and species tested are given in Table 1. Control strains included *Staphylococcus aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, *Escherichia coli* ATCC 25922, *Bacteroides fragilis* ATCC 25285, and *Bacteroides thetaiotaomicron* ATCC 29741.

Standard laboratory powders were supplied as follows: BMS-284756 by Bristol-Myers Squibb Co., Princeton, N.J.; amoxicillin-clavulanate by SmithKline Beecham Pharmaceuticals, Philadelphia, Pa.; ampicillin-sulbactam by Pfizer Inc., New York, N.Y.; cefotetan by Astra Zeneca Pharmaceuticals, Wilmington, Del.; levofloxacin by Ortho-McNeil Pharmaceuticals, Raritan, N.J.; ciprofloxacin and moxifloxacin by Bayer Corp., West Haven, Conn.; and doxycycline and penicillin G by Sigma Chemical Co., St. Louis, Mo. Antimicrobial agents were reconstituted according to the manufacturers' instructions. Serial twofold dilutions were added to the media on the day of testing.

To ensure purity and good growth, frozen cultures were transferred twice on Trypticase soy blood or chocolate agar (Hardy Diagnostics, Santa Maria, Calif.) for the aerobes and on brucella agar supplemented with hemin, vitamin K_1, and 5% sheep blood (Anaerobe Systems, Morgan Hill, Calif.) for the anaerobes. Susceptibility testing was performed according to NCCLS standards (14, 15). Supplemented brucella agar was the basal medium used for the anaerobic species and for *Eikenella corrodens* and *Bergeyella zoohelcum*. Mueller-Hinton agar was used for staphylococci, and Mueller-Hinton agar supplemented with 5% sheep blood was used for the remainder of the organisms.

The agar plates were inoculated with a Steers replicator (Craft Machine Inc., Chester, Pa.). The inocula used were 10^4 CFU per spot for aerobic bacteria and 10^5 CFU for *Eikenella corrodens* and anaerobic bacteria. Control plates without antimicrobial agents were inoculated before and after the inoculation of each set of plates containing drugs. Plates with aerobic isolates were incubated at 35°C in an aerobic environment for 18 to 20 h and then examined; *Eikenella corrodens*, fastidious gram-negative bacilli, *B. Zoohelcum*, and streptococci were incubated in 5% CO_2 for 42 to 44 h. Plates with anaerobes

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TABLE 1. In vitro activities of BMS-284756 and eight other antimicrobial agents against aerobic and anaerobic human and animal bite pathogens

Organism and agent (no. of isolates)	MIC (μg/ml)[s]		
	Range	50%	90%
Bergeyella zoohelcum (11)			
BMS-284756	≤0.015–≤0.015	≤0.015	≤0.015
Moxifloxacin	≤0.015–≤0.015	≤0.015	≤0.015
Levofloxacin	0.06–0.125	0.06	0.06
Ciprofloxacin	0.03–0.125	0.06	0.06
Amoxicillin-clavulanate	≤0.06–0.25	≤0.06	0.125
Cefotetan	≤0.06–8	2	8
Penicillin G	≤0.06–0.25	≤0.06	0.125
Ampicillin-sulbactam	≤0.06–0.25	≤0.06	0.125
Doxycycline	0.25–2	2	2
Corynebacterium spp. (19)[a]			
BMS-284756	≤0.015–8	0.25	1
Moxifloxacin	≤0.015–2	0.25	0.5
Levofloxacin	0.06–8	2	8
Ciprofloxacin	≤0.015–>8	2	4
Amoxicillin-clavulanate	≤0.06–2	1	2
Cefotetan	≤0.06–>32	32	>32
Penicillin G	≤0.06–2	1	2
Ampicillin-sulbactam	≤0.06–2	1	2
Doxycycline	0.05–1	0.25	0.25
CDC groups EF-4a and EF-4b (15)[b]			
BMS-284756	≤0.015–0.125	≤0.015	0.06
Moxifloxacin	≤0.015–0.125	≤0.015	0.06
Levofloxacin	≤0.015–0.06	≤0.015	0.06
Ciprofloxacin	≤0.015–0.06	≤0.015	0.03
Amoxicillin-clavulanate	≤0.06–0.5	0.25	0.5
Cefotetan	0.125–4	0.5	1
Penicillin G	≤0.06–0.5	0.25	0.5
Ampicillin-sulbactam	≤0.06–0.5	0.25	0.5
Doxycycline	0.125–0.25	0.25	0.25
Eikenella corrodens (16)			
BMS-284756	≤0.015–0.125	0.03	0.06
Moxifloxacin	≤0.015–0.03	≤0.015	0.03
Levofloxacin	≤0.015–≤0.015	≤0.015	≤0.015
Ciprofloxacin	≤0.015–≤0.015	≤0.015	≤0.015
Amoxicillin-clavulanate	≤0.06–0.5	0.25	0.5
Cefotetan	0.125–1	0.5	1
Penicillin G	0.125–0.5	0.5	0.5
Ampicillin-sulbactam	0.125–0.5	0.5	0.6
Doxycycline	2–16	4	8
Enterococcus spp. (14)[c]			
BMS-284756	≤0.015–0.25	0.03	0.25
Moxifloxacin	0.03–0.25	0.06	0.25
Levofloxacin	0.06–1	0.5	1
Ciprofloxacin	0.06–1	0.5	1
Amoxicillin-clavulanate	≤0.06–1	≤0.06	1
Cefotetan	0.125–>32	16	>32
Penicillin G	≤0.06–1	≤0.06	1
Ampicillin-sulbactam	≤0.06–1	≤0.06	1
Doxycycline	≤0.06–16	0.125	16
Fastidious gram-negative bacilli (16)[d]			
BMS-284756	≤0.015–1	≤0.015	0.125
Moxifloxacin	≤0.015–4	0.06	0.5
Levofloxacin	≤0.015–>8	0.03	1
Ciprofloxacin	≤0.015–8	0.03	2
Amoxicillin-clavulanate	≤0.06–4	0.25	1
Cefotetan	≤0.06–>32	1	>32
Penicillin G	≤0.06–4	0.25	0.5
Ampicillin-sulbactam	≤0.06–4	0.25	0.5
Doxycycline	0.125–4	1	4
Moraxella spp. (21)[e]			
BMS-284756	≤0.015–0.06	≤0.015	0.03
Moxifloxacin	≤0.015–0.06	≤0.015	0.06
Levofloxacin	≤0.015–0.06	≤0.015	0.06
Ciprofloxacin	≤0.015–0.06	≤0.015	0.06
Amoxicillin-clavulanate	≤0.06–0.5	≤0.06	0.5
Cefotetan	≤0.06–1	0.125	0.5
Penicillin G	≤0.06–0.5	≤0.06	0.25
Ampicillin-sulbactam	≤0.06–0.5	≤0.06	0.25
Doxycycline	≤0.06–0.5	0.25	0.5
Neisseria spp. (20)[f]			
BMS-284756	≤0.015–0.125	≤0.015	0.06
Moxifloxacin	≤0.015–0.25	≤0.015	0.03
Levofloxacin	≤0.015–0.25	≤0.015	0.06
Ciprofloxacin	≤0.015–0.25	≤0.015	0.125
Amoxicillin-clavulanate	≤0.06–8	0.25	0.5
Cefotetan	≤0.06–0.5	0.25	0.5
Penicillin G	≤0.06–4	0.125	0.25
Ampicillin-sulbactam	≤0.06–4	0.125	0.25
Doxycycline	0.125–2	0.25	0.5
Pasteurella canis-Pasteurella dagmatis group (15)[g]			
BMS-284756	≤0.015–≤0.015	≤0.015	≤0.015
Moxifloxacin	≤0.015–0.03	≤0.015	0.03
Levofloxacin	≤0.015–0.03	≤0.015	0.03
Ciprofloxacin	≤0.015–≤0.015	≤0.015	≤0.015
Amoxicillin-clavulanate	≤0.06–0.25	0.125	0.25
Cefotetan	≤0.06–0.25	0.125	0.125
Penicillin G	≤0.06–0.25	0.125	0.125
Ampicillin-sulbactam	≤0.06–0.25	0.125	0.125
Doxycycline	0.125–0.25	0.125	0.125
Pasteurella multocida subsp. *multocida* (15)			
BMS-284756	≤0.015–≤0.015	≤0.015	≤0.015
Moxifloxacin	≤0.015–0.03	≤0.015	0.03
Levofloxacin	≤0.015–0.03	≤0.015	0.03
Ciprofloxacin	≤0.015–≤0.015	≤0.015	≤0.015
Amoxicillin-clavulanate	0.125–0.25	0.25	0.25
Cefotetan	0.125–0.25	0.25	0.25
Penicillin G	0.125–0.25	0.25	0.25
Ampicillin-sulbactam	0.125–0.25	0.25	0.25
Doxycycline	0.125–0.25	0.125	0.125
Pasteurella multocida subsp. *septica* (11)			
BMS-284756	≤0.015–≤0.015	≤0.015	≤0.015
Moxifloxacin	≤0.015–0.03	≤0.015	0.03
Levofloxacin	≤0.015–0.03	≤0.015	0.03
Ciprofloxacin	≤0.015–≤0.015	≤0.015	≤0.015
Amoxicillin-clavulanate	0.125–0.25	0.25	0.25
Cefotetan	0.125–0.25	0.25	0.25
Penicillin G	0.125–0.25	0.25	0.25
Ampicillin-sulbactam	0.125–0.25	0.25	0.25
Doxycycline	0.125–0.25	0.125	0.125
Staphylococcus aureus (18)			
BMS-284756	≤0.015–0.03	≤0.015	≤0.015
Moxifloxacin	≤0.015–0.06	0.03	0.06
Levofloxacin	0.125–0.25	0.125	0.25
Ciprofloxacin	0.125–0.5	0.25	0.5
Amoxicillin-clavulanate	≤0.06–2	0.25	1
Cefotetan	4–32	8	8
Penicillin G	≤0.06–4	0.5	2
Ampicillin-sulbactam	≤0.06–4	0.5	2
Doxycycline	0.125–0.125	0.125	0.125
Staphylococcus epidermidis (11)			
BMS-284756	≤0.015–0.03	0.03	0.03
Moxifloxacin	0.03–0.06	0.06	0.06
Levofloxacin	0.125–0.25	0.25	0.25
Ciprofloxacin	0.06–0.25	0.125	0.25
Amoxicillin-clavulanate	≤0.06–0.25	≤0.06	0.25
Cefotetan	0.5–>32	8	>32
Penicillin G	≤0.06–2	≤0.06	1
Ampicillin-sulbactam	≤0.06–2	≤0.06	1
Doxycycline	≤0.06–16	0.125	0.5

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TABLE 1—*Continued*

Organism and agent (no. of isolates)	MIC (μg/ml)[s]		
	Range	50%	90%
Staphylococcus spp. (19)[h]			
BMS-284756	≤0.015–0.125	≤0.015	0.06
Moxifloxacin	≤0.015–0.5	0.06	0.125
Levofloxacin	≤0.015–2	0.125	0.25
Ciprofloxacin	≤0.015–2	0.125	0.25
Amoxicillin-clavulanate	≤0.06–0.5	0.125	0.25
Cefotetan	≤0.06–32	8	16
Penicillin G	≤0.06–1	≤0.06	0.5
Ampicillin-sulbactam	≤0.06–1	≤0.06	0.5
Doxycycline	≤0.06–8	≤0.06	4
"Streptococcus milleri" group (19)[i]			
BMS-284756	0.03–0.5	0.06	0.125
Moxifloxacin	0.06–2	0.25	0.25
Levofloxacin	0.5–8	1	2
Ciprofloxacin	0.5–8	1	4
Amoxicillin-clavulanate	≤0.06–0.5	≤0.06	0.25
Cefotetan	1–16	4	16
Penicillin G	≤0.06–0.5	0.125	0.5
Ampicillin-sulbactam	≤0.06–0.5	0.125	0.5
Doxycycline	≤0.06–>32	1	>32
Bacteroides tectus (10)			
BMS-284756	≤0.015–0.125	0.03	0.06
Moxifloxacin	0.06–0.125	0.06	0.125
Levofloxacin	0.125–0.5	0.25	0.25
Ciprofloxacin	0.5–2	0.5	1
Amoxicillin-clavulanate	≤0.06–0.5	≤0.06	0.125
Cefotetan	0.25–8	0.5	0.5
Penicillin G	0.03–32	0.03	0.125
Ampicillin-sulbactam	≤0.06–1	≤0.06	0.25
Doxycycline	0.125–8	0.25	0.5
Bacteroides ureolyticus group (13)[j]			
BMS-284756	≤0.015–2	≤0.015	1
Moxifloxacin	≤0.015–>8	0.125	>8
Levofloxacin	≤0.015–>8	0.125	>8
Ciprofloxacin	≤0.015–>8	0.06	>8
Amoxicillin-clavulanate	≤0.06–>32	0.25	>32
Cefotetan	0.125–>32	1	>32
Penicillin G	≤0.015–>32	0.25	>32
Ampicillin-sulbactam	≤0.06–>32	0.25	>32
Doxycycline	0.125–2	0.25	2
Eubacterium spp. (13)[k]			
BMS-284756	0.03–0.5	0.06	0.25
Moxifloxacin	0.125–1	0.125	0.5
Levofloxacin	0.125–2	0.25	2
Ciprofloxacin	0.25–4	0.5	2
Amoxicillin-clavulanate	≤0.06–0.25	≤0.06	0.25
Cefotetan	0.25–8	0.5	4
Penicillin G	≤0.015–0.5	0.06	0.25
Ampicillin-sulbactam	≤0.06–0.25	≤0.06	0.125
Doxycycline	≤0.06–2	0.5	2
Fusobacterium russii (9)			
BMS-284756	4–>8	8	NA
Moxifloxacin	4–8	8	NA
Levofloxacin	>8–>8	>8	NA
Ciprofloxacin	>8–>8	>8	NA
Amoxicillin-clavulaNAte	≤0.06–0.125	≤0.06	NA
Cefotetan	≤0.06–0.25	≤0.06	NA
Penicillin G	≤0.015–>32	0.03	NA
Ampicillin-sulbactam	≤0.06–2	≤0.06	NA
Doxycycline	≤0.06–0.25	≤0.06	NA
Fusobacterium spp., animal isolates (12)[l]			
BMS-284756	0.125–>8	1	>8
Moxifloxacin	0.25–>8	1	>8
Levofloxacin	0.25–>8	1	>8
Ciprofloxacin	0.125–>8	4	>8
Amoxicillin-clavulanate	≤0.06–≤0.06	≤0.06	≤0.06
Cefotetan	≤0.06–0.25	≤0.06	0.25
Penicillin G	≤0.015–0.25	≤0.015	0.5
Ampicillin-sulbactam	≤0.06–0.125	≤0.06	≤0.06
Doxycycline	0.125–0.5	0.125	0.25
Fusobacterium spp., human isolates (14)[m]			
BMS-284756	≤0.015–0.5	0.25	0.5
Moxifloxacin	0.125–0.25	0.125	0.25
Levofloxacin	0.125–1	0.25	1
Ciprofloxacin	0.25–4	2	4
Amoxicillin-clavulanate	≤0.06–0.125	≤0.06	≤0.06
Cefotetan	≤0.06–1	≤0.06	0.5
Penicillin G	≤0.015–0.06	≤0.015	0.06
Ampicillin-sulbactam	≤0.06–0.125	≤0.06	≤0.06
Doxycycline	≤0.06–0.25	0.125	0.25
Peptostreptococcus spp. (23)[n]			
BMS-284756	0.03–0.25	0.06	0.25
Moxifloxacin	0.06–2	0.25	0.5
Levofloxacin	0.25–>8	0.5	4
Ciprofloxacin	0.25–>8	0.5	2
Amoxicillin-clavulanate	≤0.06–2	0.125	1
Cefotetan	≤0.06–8	1	4
Penicillin G	≤0.015–2	0.06	0.25
Ampicillin-sulbactam	≤0.06–2	0.25	0.5
Doxycycline	≤0.06–>32	0.5	32
Porphyromonas macacae (10)			
BMS-284756	0.03–0.06	0.06	0.06
Moxifloxacin	0.03–0.125	0.125	0.125
Levofloxacin	0.125–0.5	0.25	0.25
Ciprofloxacin	0.5–1	0.5	1
Amoxicillin-clavulanate	≤0.06–0.125	≤0.06	≤0.06
Cefotetan	0.25–1	0.5	1
Penicillin G	0.03–1	0.5	1
Ampicillin-sulbactam	≤0.06–0.125	≤0.06	≤0.06
Doxycycline	0.125–16	0.125	0.25
Porphyromonas spp. (12)[o]			
BMS-284756	0.03–0.06	0.03	0.06
Moxifloxacin	0.03–0.125	0.06	0.125
Levofloxacin	0.125–0.5	0.125	0.5
Ciprofloxacin	0.5–2	0.5	1
Amoxicillin-clavulanate	≤0.06–≤0.06	≤0.06	≤0.06
Cefotetan	≤0.06–0.25	0.125	0.25
Penicillin G	≤0.015–1	≤0.015	≤0.015
Ampicillin-sulbactam	≤0.06–≤0.06	≤0.06	≤0.06
Doxycycline	0.125–0.25	0.125	0.25
Prevotella heparinolytica (10)			
BMS-284756	0.06–0.25	0.125	0.25
Moxifloxacin	0.125–0.25	0.125	0.25
Levofloxacin	0.5–1	0.5	0.5
Ciprofloxacin	2–4	2	4
Amoxicillin-clavulanate	0.125–0.25	0.25	0.25
Cefotetan	1–2	1	2
Penicillin G	0.125–0.25	0.125	0.25
Ampicillin-sulbactam	0.25–0.5	0.25	0.5
Doxycycline	0.125–4	0.125	4
Prevotella spp., pigmented (17)[p]			
BMS-284756	0.06–0.25	0.125	0.25
Moxifloxacin	0.06–0.5	0.25	0.5
Levofloxacin	0.25–1	0.25	1
Ciprofloxacin	0.25–2	0.5	2
Amoxicillin-clavulanate	≤0.06–0.25	≤0.06	0.25
Cefotetan	≤0.06–8	1	4
Penicillin G	≤0.015–16	0.5	8

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TABLE 1—*Continued*

Organism and agent (no. of isolates)	MIC (μg/ml)[s]		
	Range	50%	90%
Ampicillin-sulbactam	≤0.06–0.5	0.125	0.5
Doxycycline	≤0.06–8	0.25	2
Prevotella spp., non pigmented (15)[q]			
BMS-284756	0.06–0.25	0.125	0.25
Moxifloxacin	0.06–0.5	0.25	0.5
Levofloxacin	0.25–1	0.5	1
Ciprofloxacin	0.5–2	1	2
Amoxicillin-clavulanate	≤0.06–1	≤0.06	1
Cefotetan	0.5–32	2	16
Penicillin G	≤0.015–16	0.5	8
Ampicillin-sulbactam	≤0.06–2	0.125	1
Doxycycline	≤0.06–8	0.25	8
Veillonella spp. (11)			
BMS-284756	0.125–4	0.25	0.5
Moxifloxacin	0.125–2	0.25	0.5
Levofloxacin	0.25–4	0.25	0.5
Ciprofloxacin	0.125–4	0.125	0.25
Amoxicillin-clavulanate	≤0.06–2	0.125	0.5
Cefotetan	0.5–4	1	2
Penicillin G	0.125–4	0.25	4
Ampicillin-sulbactam	0.125–2	0.25	1
Doxycycline	1–16	1	2
Gram-positive *Bacillus* spp. (11)[r]			
BMS-284756	0.06–2	0.125	1
Moxifloxacin	0.125–2	0.5	1
Levofloxacin	0.25–4	1	2
Ciprofloxacin	0.25–8	1	4
Amoxicillin-clavulanate	≤0.06–0.5	≤0.06	0.125
Cefotetan	≤0.06–8	1	4
Penicillin G	≤0.015–0.25	0.03	0.125
Ampicillin-sulbactam	≤0.06–1	≤0.06	0.125
Doxycycline	0.125–1	0.5	0.5

[a] *Corynebacterium accolens* (*n* = 1), *C. amycolatum* (*n* = 1), *"C. aquaticum"* (*n* = 10), *C. argentoratense* (*n* = 1), *C. jeikeium* (*n* = 1), *C. minutissimum* (*n* = 3), *C. propinquum* (*n* = 1), and *C. ulcerans* (*n* = 1).
[b] Centers for Disease Control and Prevention (CDC) groups EF-4a (*n* = 4) and EF-4b (*n* = 11).
[c] *Enterococcus avium* (*n* = 2), *E. durans* (*n* = 5), *E. faecalis* (*n* = 6), and *E. malodoratus* (*n* = 1).
[d] *Actinobacillus actinomycetemcomitans* (*n* = 1) and *Actinobacillus* sp. (*n* = 1); *Capnocytophaga canimorsus* (*n* = 3), *C. gingivalis* (*n* = 1), and *Capnocytophaga* spp. (*n* = 2); *Haemophilus aphrophilus* (*n* = 1), *H. influenzae* (*n* = 1), and *H. parainfluenzae* (*n* = 5); and *Weeksella virosa* (*n* = 1).
[e] *Moraxella atlantae* (*n* = 3), *M. bovis* (*n* = 1), *M. catarrhalis* (*n* = 10), *M. lacunata* (*n* = 2), *M. nonliquefaciens* (*n* = 3), and *M. osloensis* (*n* = 2).
[f] *Neisseria cinerea-N. flavescens* group (*n* = 1), *N. elongata* subsp. *elongata* (*n* = 2), *N. elongata* subsp. *nitroreducens*(*n* = 2), *N. subflava* (*n* = 4), *N. weaveri* (*n* = 10), and an unidentifiable *Neisseria* sp. (*n* = 1).
[g] *Pasteurella canis* (*n* = 9) and *P. dagmatis* (*n* = 6).
[h] *Staphylococcus hominis* (*n* = 2), *S. hyicus* (*n* = 2), *S. intermedius* (*n* = 6), *S. saprophyticus* (*n* = 1), *S. sciuri* subsp. *lentus*(*n* = 1), and *S. warneri* (*n* = 7).
[i] *Streptococcus anginosus* (*n* = 7), *S. constellatus* (*n* = 6), and *S. intermedius* (*n* = 6).
[j] *Bacteroides ureolyticus* (*n* = 3), *Campylobacter gracilis* (*n* = 5), *C. mucosalis* (*n* = 2), and *C. rectus* (*n* = 3).
[k] *Eubacterium aerofaciens* (*n* = 1), *E. lentum* (*n* = 1), *E. saburreum* (*n* = 3), *E. yurii* subsp. *yurii* (*n* = 2), and organisms with no good fit (*n* = 6).
[l] *Fusobacterium nucleatum* (*n* = 10), *F. nucleatum* subsp. *animalis* (*n* = 1), and *F. necrophorum* (*n* = 1).
[m] *Fusobacterium necrophorum* (*n* = 3) and *F. nucleatum* (*n* = 11).
[n] *Peptostreptococcus anaerobius* (*n* = 7), *P. asaccharolyticus* (*n* = 1), *P. ivorii* (*n* = 1), *P. magnus* (*n* = 3), *P. micros* (*n* = 8), *P. prevotii* (*n* = 2), and *P. tetradius* (*n* = 1).
[o] *Porphyromonas cangingivalis* (*n* = 4) and *P. gingivalis* (*n* = 8).
[p] *Prevotella denticola* (*n* = 2), *P. intermedia-P. nigrescens* group (*n* = 7), *P. melaninogenica* (*n* = 4), *P. pallens* (*n* = 3), and *P. tannerae* (*n* = 1).
[q] *Prevotella buccae* (*n* = 7), *P. buccalis* (*n* = 1), *P. disiens* (*n* = 1), *P. oris* (*n* = 5), and an organism with no good fit (*n* = 1).
[r] *Actinomyces israelii* (*n* = 1), *A. meyeri* (*n* = 1), *A. naeslundii* (*n* = 2), and *A. viscosus* (*n* = 2); *Lactobacillus catenaformis* (*n* = 1), *L. lactis* (*n* = 1), *L. plantarum* (*n* = 2), and a *Lactobacillus* species with no good fit (*n* = 1).
[s] 50% and 90%, MIC_{50} and MIC_{90}, respectively; NA, not applicable.

were incubated in an anaerobic chamber (Anaerobe Systems) at 35°C for 44 to 48 h. The MIC was defined as the lowest concentration of an agent that yielded no growth or a marked change in growth compared to that on the control plate.

The full results of the study are presented in Table 1. At ≤2 μg/ml, BMS-284756 inhibited 96% (403 of 420) of the isolates studied and was the most active of the tested quinolones against enterococci, staphylococci, streptococci, and most of the anaerobic species. Overall, BMS-284756 and moxifloxacin had comparable activities, with BMS-284756 MICs generally being 1 dilution lower. All aerobic isolates except one (239 of 240; 99%), a strain of *Corynebacterium jeikeium*, were susceptible to BMS-284756 at ≤1 μg/ml, while all *Pasteurella* species and *Bergeyella zoohelcum* were susceptible to BMS-284756 at ≤0.015 μg/ml. BMS-284756 was also highly active against fastidious gram-negative organisms such as *Haemophilus* spp. and *Capnocytophaga* spp. It was slightly less active than the other quinolones against *Neisseria* spp. and *Eikenella corrodens* but still demonstrated a high level of effectiveness (MIC_{90} [the MIC at which 90% of the organisms were inhibited], 0.06 μg/ml) against both.

Hoellman et al. (8) studied the activity of BMS-284756 against 357 recently isolated anaerobes of human origin and found the MIC_{50} and MIC_{90} to be 0.5 and 2.0 μg/ml, respectively. In our study, BMS-284756 was active against 164 of 180 (91%) anaerobic isolates at ≤2 μg/ml (overall MIC_{90}, 1μg/ml), and it compared favorably with the other quinolones against *Campylobacter* spp. (MIC_{90}, 1 μg/ml) and *Eubacterium* spp. (MIC_{90}, 0.25 μg/ml), as well as against *Porphyromonas* spp., *Peptostreptococcus* spp., *Bacteroides tectus*, and most strains of *Prevotella* spp. The overall MIC_{90}s of the other quinolones were as follows: 2 μg/ml for moxifloxacin, 4 μg/ml for levofloxacin, and 8 μg/ml for ciprofloxacin.

BMS-284756, along with the other quinolones, including moxifloxacin, was less active against many strains of fusobacteria of animal bite origin. All nine strains of *Fusobacterium russii* and 6 of 11 animal bite strains of *Fusobacterium nucleatum* were resistant and required ≥4 μg of BMS-284756 per ml for inhibition. Conversely, all 14 *F. nucleatum* strains of human bite origin were susceptible to BMS-284756 at ≤0.5 μg/ml. While 3 of 12 *F. nucleatum* isolates from animal bites produced beta-lactamase, none of the 14 isolates from human bites produced beta-lactamase.

Prior studies (6, 7) have noted that some strains of *F. nu-*

cleatum are resistant to ciprofloxacin, levofloxacin, moxifloxacin, and other quinolones but did not differentiate between animal and human sources. One could speculate that the resistance found in the present study might be associated with the use of fluoroquinolones for veterinary infections and in animal feed for growth enhancement. However, this explanation seems unlikely. A more likely cause of resistance appears to be that the animal strains of *F. nucleatum* are of one subspecies with an intrinsic resistance to quinolones, which they also share with other species, such as *F. russii*, and that the human strains are of a different subspecies. Further molecular studies are in progress to clarify this finding.

BMS-284756 has an excellent broad spectrum of activity and consequently merits further evaluation as a therapeutic alternative in animal and human bite wound infections.

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