

NOTES

Comparative Antianaerobic Activity of BMS 284756

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Agar dilution MIC methodology was used to compare the activity of BMS 284756 with those of ciprofloxacin, levofloxacin, moxifloxacin, trovafloxacin, amoxicillin-clavulanate, piperacillin-tazobactam, imipenem, clindamycin, and metronidazole against 357 anaerobes. Overall, the respective MICs at which 50% of the isolates tested were inhibited (MIC₅₀s) and MIC₉₀s (in micrograms per milliliter) were as follows: BMS 284756, 0.5 and 2.0; ciprofloxacin, 2.0 and 16.0; levofloxacin, 1.0 and 8.0; moxifloxacin, 0.5 and 4.0; trovafloxacin, 0.5 and 2.0; amoxicillin-clavulanate, 0.5 and 2.0; piperacillin-tazobactam, 0.25 and 8.0; imipenem, 0.06 and 1.0; clindamycin, 0.25 and 8.0; and metronidazole, 1.0 and >16.0. BMS 284756 is a promising new quinolone with excellent antianaerobic activity.

Anaerobes are becoming increasingly resistant to β -lactams due to β -lactamase production and other mechanisms. Although β -lactamase production, and concomitant resistance to β -lactams, is the norm among the *Bacteroides fragilis* group, other anaerobic gram-negative bacilli in the genera *Prevotella*, *Porphyromonas*, and *Fusobacterium* have increasingly become β -lactamase positive. β -Lactamase production also has been described for clostridia. Metronidazole resistance in organisms other than non-spore-forming gram-positive bacilli has been described, as has clindamycin resistance in anaerobic gram-negative bacilli (1–5).

Quinolones such as ciprofloxacin, ofloxacin, fleroxacin, pefloxacin, enoxacin, and lomefloxacin are inactive or marginally active against anaerobes. Newer quinolones with increased antianaerobic activity include (i) those with slightly increased activity against aerobic gram-positive and some nonfermentative gram-negative bacteria (sparfloxacin, grepafloxacin, and levofloxacin) and (ii) those with significantly improved antianaerobic activity (with clinafloxacin and sitafloxacin being the most active, followed by trovafloxacin, moxifloxacin, and gatifloxacin) (6–11, 13, 16).

BMS 284756 (T-3811) (15) is a novel des-F(6)-quinolone with a broad spectrum of activity. The present study tested the antianaerobic activity of BMS 284756 compared to those of ciprofloxacin, levofloxacin, moxifloxacin, trovafloxacin, amoxicillin-clavulanate, piperacillin-tazobactam, imipenem, clindamycin, and metronidazole against 357 anaerobes.

All anaerobes were clinical strains, isolated during the past four years, identified by standard procedures (14) and kept frozen in 200 g of dehydrated skim milk (Difco Laboratories, Detroit, Mich.) per liter at -70°C until use. No history regarding prior in vivo exposure to quinolones or other antibiotics

tested is available, and no advanced quinolone-resistant strains or very recent clinical strains (isolated within a few months prior to the study) were included. Prior to testing, strains were subcultured twice onto enriched sheep blood agar plates (14). BMS 284756 susceptibility powder was obtained from Bristol-Myers Squibb Laboratories, Wallingford, Conn., and other drugs were obtained from their manufacturers. β -Lactamase testing was by the nitrocefin disk method (Cefinase; BBL Microbiology Systems, Cockeysville, Md.). Agar dilution susceptibility testing was according to the latest method recommended by the National Committee for Clinical Laboratory Standards (NCCLS) (12), using brucella agar with 5% sterile defibrinated sheep blood for non-*B. fragilis* group strains. Clavulanate was added to amoxicillin at a fixed ratio of 1:2, and tazobactam was added to piperacillin at a fixed concentration of 4.0 $\mu\text{g}/\text{ml}$. All quality control gram-negative and -positive strains recommended by NCCLS were included with each run; in every case, results (where available) were in the control range.

Among the anaerobic gram-negative bacilli tested, 76 of 80 *B. fragilis* group strains (95%) 54 of 89 *Prevotella* and *Porphyromonas* strains (60.7%), and 3 of 41 fusobacterial strains (7.3%) produced β -lactamase.

Results of MIC testing are presented in Table 1. Overall, the respective MICs at which 50% of the strains tested were inhibited (MIC₅₀s) and MIC₉₀s (in micrograms per milliliter) were as follows: BMS 284756, 0.5 and 2.0; ciprofloxacin, 2.0 and 16.0; levofloxacin, 1.0 and 8.0; moxifloxacin, 0.5 and 4.0; trovafloxacin, 0.5 and 2.0; amoxicillin-clavulanate, 0.5 and 2.0; piperacillin-tazobactam, 0.25 and 8.0; imipenem, 0.06 and 1.0; clindamycin, 0.25 and 8.0; and metronidazole, 1.0 and >16.0.

BMS 284756 and trovafloxacin had the lowest MICs of all quinolones tested (MIC₅₀ and MIC₉₀s of 0.5 and 2.0 $\mu\text{g}/\text{ml}$, respectively), followed by moxifloxacin (0.5 and 4.0), levofloxacin (1.0 and 8.0), and ciprofloxacin (2.0 and 16.0).

Thirteen strains (3.6%) required BMS 284756 MICs of ≥ 4.0 $\mu\text{g}/\text{ml}$, and these comprised one *Bacteroides thetaiotaomicron*

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TABLE 1. MICs of agents

Organism and agent ^a	MIC ($\mu\text{g/ml}$)			Organism and agent ^a	MIC ($\mu\text{g/ml}$)		
	Range	MIC ₅₀	MIC ₉₀		Range	MIC ₅₀	MIC ₉₀
<i>Bacteroides fragilis</i> (35/35)				Amoxicillin-clavulanate			
BMS 284756	0.125-2.0	0.25	1.0	Piperacillin-tazobactam	$\leq 0.125-2.0$	≤ 0.125	≤ 0.125
Ciprofloxacin	4.0->32.0	4.0	32.0	Imipenem	$\leq 0.016-0.25$	0.06	0.125
Levofloxacin	1.0-32.0	2.0	8.0	Clindamycin	$\leq 0.016-0.06$	0.03	0.03
Moxifloxacin	0.25-8.0	0.5	1.0	Metronidazole	1.0->16.0	4.0	8.0
Trovafoxacin	0.125-4.0	0.25	0.5	<i>Prevotella corporis</i> (3/11)			
Amoxicillin-clavulanate	0.25-32.0	0.5	4.0	BMS 284756	0.125-0.5	0.125	0.25
Piperacillin-tazobactam	$\leq 0.125->128.0$	1.0	4.0	Ciprofloxacin	0.5-2.0	1.0	1.0
Imipenem	0.06->8.0	0.25	1.0	Levofloxacin	0.5-1.0	1.0	1.0
Clindamycin	0.5->32.0	2.0	4.0	Moxifloxacin	0.5-1.0	0.5	0.5
Metronidazole	0.5-4.0	1.0	2.0	Trovafoxacin	0.5-1.0	1.0	1.0
<i>Bacteroides thetaiotaomicron</i> (15/15)				Amoxicillin-clavulanate			
BMS 284756	0.25-16.0	0.5	1.0	Piperacillin-tazobactam	$\leq 0.125-0.5$	≤ 0.125	0.5
Ciprofloxacin	8.0->32.0	16.0	>32.0	Imipenem	$\leq 0.125-\leq 0.125$	≤ 0.125	≤ 0.125
Levofloxacin	2.0->32.0	8.0	8.0	Clindamycin	0.03-0.06	0.03	0.06
Moxifloxacin	1.0->8.0	1.0	2.0	Metronidazole	$\leq 0.016-0.125$	≤ 0.016	0.03
Trovafoxacin	0.25-8.0	0.5	2.0		$\leq 0.125-1.0$	0.25	0.5
Amoxicillin-clavulanate	0.5-8.0	1.0	4.0	<i>Prevotella intermedia</i> (6/10)			
Piperacillin-tazobactam	2.0-32.0	16.0	32.0	BMS 284756	0.25-0.25	0.25	0.25
Imipenem	0.125-1.0	0.25	1.0	Ciprofloxacin	1.0-1.0	1.0	1.0
Clindamycin	0.5->32.0	4.0	>32.0	Levofloxacin	0.5-1.0	0.5	1.0
Metronidazole	0.5-2.0	1.0	1.0	Moxifloxacin	0.25-0.5	0.5	0.5
<i>Bacteroides distasonis</i> (6/10)				Trovafoxacin			
BMS 284756	0.125-8.0	0.25	0.5	Amoxicillin-clavulanate	$\leq 0.125-0.5$	≤ 0.125	0.25
Ciprofloxacin	2.0->32.0	4.0	8.0	Piperacillin-tazobactam	$\leq 0.125-\leq 0.125$	≤ 0.125	≤ 0.125
Levofloxacin	1.0-32.0	2.0	2.0	Imipenem	$\leq 0.016-0.06$	0.03	0.06
Moxifloxacin	0.25-4.0	0.25	0.5	Clindamycin	$\leq 0.016-\leq 0.016$	≤ 0.016	≤ 0.016
Trovafoxacin	0.25-2.0	0.5	0.5	Metronidazole	0.25-1.0	0.5	1.0
Amoxicillin-clavulanate	1.0-128.0	4.0	32.0	<i>Prevotella melaninogenica</i> (8/10)			
Piperacillin-tazobactam	1.0-128.0	4.0	8.0	BMS 284756	0.25-1.0	0.25	0.5
Imipenem	0.5-2.0	1.0	1.0	Ciprofloxacin	1.0-4.0	2.0	4.0
Clindamycin	0.5-8.0	2.0	8.0	Levofloxacin	0.5-2.0	1.0	2.0
Metronidazole	0.125-1.0	0.5	1.0	Moxifloxacin	0.5-1.0	1.0	1.0
<i>Bacteroides vulgatus</i> (10/10)				Trovafoxacin			
BMS 284756	0.25-2.0	0.5	2.0	Amoxicillin-clavulanate	$\leq 0.125-2.0$	≤ 0.125	1.0
Ciprofloxacin	16.0->32.0	32.0	>32.0	Piperacillin-tazobactam	$\leq 0.125-\leq 0.125$	≤ 0.125	≤ 0.125
Levofloxacin	1.0->32.0	2.0	>32.0	Imipenem	$\leq 0.016-0.06$	0.03	0.03
Moxifloxacin	0.5->8.0	1.0	>8.0	Clindamycin	$\leq 0.016-\leq 0.016$	≤ 0.016	≤ 0.016
Trovafoxacin	0.25-8.0	0.5	8.0	Metronidazole	0.5-1.0	0.5	1.0
Amoxicillin-clavulanate	0.5-8.0	1.0	8.0	Miscellaneous <i>Prevotella</i> and <i>Porphyromonas</i> strains (13/23) ^b			
Piperacillin-tazobactam	4.0-64.0	8.0	32.0	BMS 284756	0.016-0.5	0.25	0.5
Imipenem	0.25-1.0	1.0	1.0	Ciprofloxacin	0.25-4.0	1.0	2.0
Clindamycin	$\leq 0.016->32.0$	0.25	1.0	Levofloxacin	$\leq 0.125-8.0$	1.0	1.0
Metronidazole	0.5-2.0	1.0	2.0	Moxifloxacin	0.03-1.0	0.5	1.0
<i>Bacteroides ovatus</i> (10/10)				Trovafoxacin			
BMS 284756	0.5-2.0	0.5	2.0	Amoxicillin-clavulanate	$\leq 0.125-1.0$	0.5	0.5
Ciprofloxacin	16.0->32.0	32.0	>32.0	Piperacillin-tazobactam	$\leq 0.125-\leq 0.125$	0.125	≤ 0.125
Levofloxacin	8.0-32.0	8.0	16.0	Imipenem	$\leq 0.016-0.25$	0.06	0.125
Moxifloxacin	2.0->8.0	4.0	4.0	Clindamycin	$\leq 0.016->32$	≤ 0.016	0.03
Trovafoxacin	0.5-2.0	1.0	2.0	Metronidazole	$\leq 0.125-4.0$	2.0	4.0
Amoxicillin-clavulanate	0.5-8.0	2.0	4.0	<i>Prevotella</i> and <i>Porphyromonas</i> (54/89)			
Piperacillin-tazobactam	4.0-32.0	8.0	16.0	BMS 284756	0.016-4.0	0.5	2.0
Imipenem	0.25-2.0	0.5	2.0	Ciprofloxacin	0.25-32.0	2.0	16.0
Clindamycin	2.0->32.0	4.0	>32.0	Levofloxacin	$\leq 0.125-16.0$	1.0	8.0
Metronidazole	0.25-2.0	1.0	2.0	Moxifloxacin	0.03-8.0	1.0	4.0
<i>Bacteroides fragilis</i> group (76/80)				Trovafoxacin			
BMS 284756	0.125-16.0	0.5	2.0	Amoxicillin-clavulanate	$\leq 0.125-4.0$	0.25	1.0
Ciprofloxacin	2.0->32.0	8.0	>32.0	Piperacillin-tazobactam	$\leq 0.125-2.0$	≤ 0.125	≤ 0.125
Levofloxacin	1.0->32.0	2.0	32.0	Imipenem	$\leq 0.016-0.25$	0.06	0.125
Moxifloxacin	0.25->8.0	0.5	4.0	Clindamycin	$\leq 0.016->32.0$	≤ 0.016	0.03
Trovafoxacin	0.125-8.0	0.5	2.0	Metronidazole	$\leq 0.125->16.0$	2.0	4.0
Amoxicillin-clavulanate	0.25-128.0	1.0	8.0	<i>Fusobacterium nucleatum</i> (1/10)			
Piperacillin-tazobactam	$\leq 0.125->128.0$	4.0	32.0	BMS 284756	0.25-1.0	0.5	0.5
Imipenem	0.06->8.0	0.25	1.0	Ciprofloxacin	1.0-4.0	2.0	2.0
Clindamycin	$\leq 0.016->32.0$	2.0	>32.0	Levofloxacin	0.5-1.0	1.0	1.0
Metronidazole	0.125-4.0	1.0	2.0	Moxifloxacin	0.125-0.5	0.125	0.125
<i>Prevotella bivia</i> (24/35)				Trovafoxacin			
BMS 284756	0.25-4.0	1.0	2.0	Amoxicillin-clavulanate	$\leq 0.125-1.0$	≤ 0.125	0.5
Ciprofloxacin	2.0-32.0	16.0	32.0	Piperacillin-tazobactam	$\leq 0.125-0.5$	≤ 0.125	0.5
Levofloxacin	1.0-16.0	4.0	8.0	Imipenem	$\leq 0.016-0.25$	0.03	0.06
Moxifloxacin	0.5-8.0	2.0	4.0				
Trovafoxacin	0.5-4.0	2.0	4.0				

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TABLE 1—Continued

Organism and agent ^a	MIC ($\mu\text{g/ml}$)			Organism and agent ^a	MIC ($\mu\text{g/ml}$)		
	Range	MIC ₅₀	MIC ₉₀		Range	MIC ₅₀	MIC ₉₀
Clindamycin	0.03–0.125	0.06	0.125	Other gram-positive non-spore-forming bacilli (0/18) ^d			
Metronidazole	≤ 0.125 –0.5	≤ 0.125	0.25		BMS 284756	0.5–2.0	2.0
<i>Fusobacterium necrophorum</i> (0/10)				Ciprofloxacin	1.0–32.0	1.0	16.0
BMS 284756	0.125–0.5	0.25	0.5	Levofloxacin	0.5–8.0	1.0	4.0
Ciprofloxacin	0.5–2.0	1.0	1.0	Moxifloxacin	0.25–2.0	0.25	2.0
Levofloxacin	0.5–2.0	1.0	2.0	Trovafoxacin	1.0–4.0	1.0	4.0
Moxifloxacin	0.03–1.0	0.25	1.0	Amoxicillin-clavulanate	≤ 0.125 –2.0	0.25	1.0
Trovafoxacin	0.03–0.5	0.25	0.5	Piperacillin-tazobactam	≤ 0.125 –16.0	1.0	16.0
Amoxicillin-clavulanate	≤ 0.125 –0.25	≤ 0.125	≤ 0.125	Imipenem	≤ 0.016 –0.5	0.5	0.5
Piperacillin-tazobactam	≤ 0.125 –0.5	≤ 0.125	≤ 0.125	Clindamycin	0.03–8.0	0.125	1.0
Imipenem	≤ 0.016 –0.03	≤ 0.016	≤ 0.016	Metronidazole	0.5–>16.0	2.0	>16.0
Clindamycin	0.03–0.06	0.06	0.06	<i>Lactobacillus</i> (0/10)			
Metronidazole	≤ 0.125 –1.0	0.25	0.5	BMS 284756	0.06–1.0	0.125	0.25
<i>Fusobacterium mortiferum</i> (2/10)				Ciprofloxacin	1.0–>32.0	2.0	16.0
BMS 284756	0.125–0.5	0.25	0.25	Levofloxacin	1.0–>32.0	2.0	16.0
Ciprofloxacin	1.0–2.0	1.0	2.0	Moxifloxacin	0.25–8.0	0.25	1.0
Levofloxacin	0.5–1.0	1.0	1.0	Trovafoxacin	0.125–8.0	0.25	1.0
Moxifloxacin	0.25–0.5	0.25	0.5	Amoxicillin-clavulanate	0.25–1.0	1.0	1.0
Trovafoxacin	0.5–1.0	0.5	1.0	Piperacillin-tazobactam	0.5–4.0	2.0	4.0
Amoxicillin-clavulanate	0.5–32.0	1.0	16.0	Imipenem	0.25–4.0	2.0	4.0
Piperacillin-tazobactam	0.25–1.0	0.25	1.0	Clindamycin	0.5–8.0	1.0	4.0
Imipenem	0.25–1.0	0.5	1.0	Metronidazole	>16.0–>16.0	>16.0	>16.0
Clindamycin	0.06–0.125	0.125	0.125	<i>Clostridium perfringens</i> (0/21)			
Metronidazole	≤ 0.125 –0.5	≤ 0.125	0.5	BMS 284756	0.125–2.0	0.5	1.0
<i>Fusobacterium varium</i> (0/11)				Ciprofloxacin	0.25–16.0	1.0	2.0
BMS 284756	2.0–>32.0	4.0	8.0	Levofloxacin	0.25–4.0	0.5	1.0
Ciprofloxacin	4.0–>32.0	8.0	16.0	Moxifloxacin	0.25–2.0	0.5	1.0
Levofloxacin	4.0–>32.0	4.0	8.0	Trovafoxacin	0.06–2.0	0.25	0.25
Moxifloxacin	2.0–>8.0	4.0	8.0	Amoxicillin-clavulanate	≤ 0.125 –0.5	≤ 0.125	0.25
Trovafoxacin	2.0–8.0	4.0	4.0	Piperacillin-tazobactam	≤ 0.125 –0.5	0.25	0.5
Amoxicillin-clavulanate	1.0–2.0	1.0	2.0	Imipenem	0.06–0.25	0.125	0.125
Piperacillin-tazobactam	2.0–8.0	8.0	8.0	Clindamycin	0.06–>32.0	2.0	8.0
Imipenem	0.5–1.0	1.0	1.0	Metronidazole	0.5–2.0	1.0	2.0
Clindamycin	2.0–32.0	8.0	32.0	<i>Clostridium difficile</i> (0/10)			
Metronidazole	0.25–0.5	0.25	0.5	BMS 284756	0.5–4.0	1.0	1.0
<i>Fusobacteria</i> (3/41)				Ciprofloxacin	8.0–>32.0	8.0	16.0
BMS 284756	0.125–>32.0	0.5	4.0	Levofloxacin	4.0–>32.0	4.0	4.0
Ciprofloxacin	0.5–>32.0	2.0	8.0	Moxifloxacin	1.0–8.0	1.0	2.0
Levofloxacin	0.5–>32.0	1.0	8.0	Trovafoxacin	1.0–4.0	1.0	1.0
Moxifloxacin	0.03–>8.0	0.25	4.0	Amoxicillin-clavulanate	0.5–2.0	0.5	2.0
Trovafoxacin	0.03–8.0	0.5	4.0	Piperacillin-tazobactam	8.0–32.0	8.0	16.0
Amoxicillin-clavulanate	≤ 0.125 –32.0	0.5	2.0	Imipenem	2.0–4.0	2.0	4.0
Piperacillin-tazobactam	≤ 0.125 –8.0	0.25	8.0	Clindamycin	2.0–>32.0	4.0	>32.0
Imipenem	≤ 0.016 –1.0	0.25	1.0	Metronidazole	0.25–0.5	0.25	0.25
Clindamycin	0.03–32.0	0.06	16.0	Miscellaneous clostridia (0/20) ^e			
Metronidazole	≤ 0.125 –1.0	0.25	0.5	BMS 284756	0.25–2.0	0.5	2.0
Peptostreptococci (0/49) ^f				Ciprofloxacin	0.5–8.0	1.0	8.0
BMS 284756	0.03–0.5	0.125	0.25	Levofloxacin	0.5–4.0	1.0	4.0
Ciprofloxacin	0.25–16.0	1.0	2.0	Moxifloxacin	0.25–2.0	1.0	2.0
Levofloxacin	0.25–16.0	0.5	4.0	Trovafoxacin	0.25–1.0	0.5	0.5
Moxifloxacin	0.03–4.0	0.25	0.5	Amoxicillin-clavulanate	≤ 0.125 –2.0	0.25	1.0
Trovafoxacin	0.03–1.0	0.25	0.5	Piperacillin-tazobactam	≤ 0.125 –16.0	1.0	16.0
Amoxicillin-clavulanate	≤ 0.125 –32.0	≤ 0.125	0.5	Imipenem	0.06–4.0	0.25	2.0
Piperacillin-tazobactam	≤ 0.125 –16.0	≤ 0.125	0.5	Clindamycin	0.06–>32.0	2.0	16.0
Imipenem	≤ 0.016 –1.0	0.03	0.125	Metronidazole	0.25–2.0	1.0	2.0
Clindamycin	≤ 0.016 –>32.0	0.25	4.0	All strains (133/357)			
Metronidazole	0.25–>16.0	1.0	2.0	BMS 284756	0.016–>32.0	0.5	2.0
Propionibacteria (0/19)				Ciprofloxacin	0.25–>32.0	2.0	16.0
BMS 284756	0.25–0.5	0.5	0.5	Levofloxacin	≤ 0.125 –>32.0	1.0	8.0
Ciprofloxacin	0.5–1.0	0.5	1.0	Moxifloxacin	0.03–>8.0	0.5	4.0
Levofloxacin	0.25–0.5	0.5	0.5	Trovafoxacin	0.03–8.0	0.5	2.0
Moxifloxacin	0.125–0.25	0.25	0.25	Amoxicillin-clavulanate	≤ 0.125 –128.0	0.5	2.0
Trovafoxacin	0.5–1.0	0.5	1.0	Piperacillin-tazobactam	≤ 0.125 –>128.0	0.25	8.0
Amoxicillin-clavulanate	≤ 0.125 –0.25	≤ 0.125	0.25	Imipenem	≤ 0.016 –>8.0	0.06	1.0
Piperacillin-tazobactam	0.25–1.0	0.5	1.0	Clindamycin	≤ 0.016 –>32.0	0.25	8.0
Imipenem	≤ 0.016 –0.03	0.03	0.03	Metronidazole	≤ 0.125 –>16.0	1.0	>16.0
Clindamycin	0.06–0.06	0.06	0.06				
Metronidazole	>16.0–>16.0	>16.0	>16.0				

^a Numbers in parentheses indicate number strains β -lactamase-positive/number of strains tested.

^b *Prevotella oralis*, 2; *Prevotella buccae*, 8; *Prevotella disiens*, 8; *Porphyromonas asaccharolytica*, 4; *Porphyromonas gingivalis*, 1.

^c *Peptostreptococcus asaccharolyticus*, 11; *Peptostreptococcus magnus*, 12; *Peptostreptococcus micros*, 8; *Peptostreptococcus anaerobius*, 10; *Peptostreptococcus tetradicus*, 7; *Peptostreptococcus prevotii*, 1.

^d *Actinomyces* sp., 6; *Eubacterium* sp., 8; *Bifidobacterium* sp., 4.

^e *Clostridium tertium*, 6; *Clostridium bifementans*, 3; *Clostridium cadaveris*, 1; *Clostridium sordellii*, 5; *Clostridium hastiforme*, 1; *Clostridium baratii*, 1; *Clostridium innocuum*, 2; *Clostridium ramosum*, 1.

strain (MIC, 16.0 µg/ml), one *Bacteroides distasonis* strain (MIC, 8.0 µg/ml), two *Prevotella bivia* strains (MICs, 4.0 µg/ml), eight *Fusobacterium varium* strains (six MICs of 4.0 µg/ml, one MIC of 8.0 µg/ml, and one MIC of >32.0 µg/ml), and one *Clostridium difficile* strain (MIC, 4.0 µg/ml).

Addition of clavulanate and tazobactam enhanced activity of amoxicillin and piperacillin, respectively, against β-lactamase-producing anaerobic gram-negative bacilli. Although most strains tested were susceptible to clindamycin (MICs of ≤2 µg/ml), resistance was seen in some gram-negative anaerobic rods and some clostridia. The only anaerobes resistant to metronidazole were the anaerobic gram-positive bacilli as well as a few peptostreptococci.

BMS 284756 (15) (K. Hayashi, Y. Todo, S. Hamamoto, K. Ojima, M. Yamada, T. Kito, M. Takahata, Y. Watanabe, and H. Narita, Abstr. 37th Intersci. Conf. Antimicrob. Agents Chemother., abstr. F-158, 1997) is a novel des-F(6) quinolone with a broad spectrum of activity against gram-positive organisms (including pneumococci and quinolone-susceptible and -resistant staphylococci), *Enterobacteriaceae* (with the exception of *Serratia marcescens*), acinetobacters, legionellae, chlamydiae, and mycoplasmas. The drug is less active against *Pseudomonas aeruginosa* (MIC₅₀ and MIC₉₀, 1.56 and >100 µg/ml, respectively) (R. Hori, M. Takahata, M. Shimakura, H. Sugiyama, M. Yonezawa, Y. Todo, S. Ninami, Y. Watanabe, and H. Narita, Abstr. 38th Intersci. Conf. Antimicrob. Agents Chemother., abstr. F-78, 1998; M. Takahata, M. Shimakura, R. Hori, M. Yonezawa, Y. Todo, S. Minami, Y. Watanabe, and H. Narita, Abstr. 39th Intersci. Conf. Antimicrob. Agents Chemother., abstr. 556, 1999). Takahata and coworkers (15) have reported BMS 284756 MIC₉₀s of 0.78 µg/ml against *B. fragilis*, 0.2 µg/ml against *Peptostreptococcus asaccharolyticus*, and 0.78 µg/ml against *C. difficile*.

BMS 284756 and trovafloxacin had the lowest MICs of all strains tested, with results for *B. fragilis*, peptostreptococci, and *C. difficile* similar to those reported by Takahata and coworkers (15) and lower than those of all other quinolones tested. MICs of ciprofloxacin, levofloxacin, trovafloxacin, and moxifloxacin are similar to those reported by us and other workers, while MICs of nonquinolone agents also reflect previous findings, with low MICs of all β-lactams against β-lactamase-positive and -negative strains, good activity of clindamycin except for a few gram-negative rods and clostridia, and good activity of metronidazole (except for gram-positive non-spore-forming rods). The few strains requiring high quinolone MICs were predominantly *Fusobacterium varium*, a rare human pathogen which has previously been reported to be intrinsically resistant to quinolones and other antimicrobials (6–9, 11, 13, 16).

The results of this first published in vitro anaerobe study suggest a potential place for BMS 284756 in treatment of anaerobic infections. The drug is also active against organisms requiring raised metronidazole and clindamycin MICs. The excellent antianaerobic activity of BMS 284756, together with its broad spectrum of activity against *Enterobacteriaceae* (15), makes it a promising alternative for empiric therapy of

mixed aerobic-anaerobic infections. Recent studies (R. Cisneros, R. J. Penzo, and A. B. Onderdonk, Abstr. 40th Intersci. Conf. Antimicrob. Agents Chemother., abstr. 996, 2000) have shown BMS 284756 to be as effective as standard treatment with clindamycin and gentamicin in an animal model. Oral as well as intravenous forms of this compound are under development. Clinical studies to validate these hypotheses are under way.

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