ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Aug. 1997, p. 1818–1824 Vol. 41, No. 8
0066-4804/97/$04.00+0

In Vitro Activity of Bay 12-8039, a New 8-Methoxyquinolone

ROBERT J. FASS*

Division of Infectious Diseases, Department of Internal Medicine, Ohio State University College of Medicine, Columbus, Ohio 43210

Received 21 January 1997/Returned for modification 16 April 1997/Accepted 14 May 1997

MICs of Bay 12-8039 and comparative antimicrobials were determined for 820 recent clinical isolates. Ciprofloxacin was ≈2-fold more active than Bay 12-8039 and ofloxacin against *Enterobacteriaceae* and ≈8-fold more active against *Pseudomonas aeruginosa*. Bay 12-8039 was ≈2- to 16-fold more active than ciprofloxacin and ofloxacin against nonfermenters (except *P. aeruginosa*), staphylococci, streptococci, enterococci, and anaerobes. As determined by regression analysis, there was a high degree of correlation among quinolone MICs.

Bay 12-8039 is a new 8-methoxyquinolone with a broad antibacterial spectrum (11). In this study, the MICs of Bay 12-8039, ciprofloxacin, ofloxacin, amoxicillin-clavulanate, cefuroxime, loracarbef, ceftriaxone, and clarithromycin were determined for 820 recent clinical isolates from Columbus, Ohio. Frequency distribution curves and regression analyses were used to compare quinolone MICs.

Organisms. The organisms studied included 820 bacterial strains arbitrarily selected from among fresh clinical isolates at the Ohio State University Medical Center during the course of the study, April to December 1996. Duplicate isolates from individual patients were excluded.

Antimicrobial agents. Bay 12-8039 and ciprofloxacin were obtained from Bayer Corp., West Haven, Conn., ofloxacin was obtained from R. W. Johnson Pharmaceutical Research Institute, Raritan, N.J., amoxicillin-clavulanate was obtained from Beecham Laboratories, Bristol, Tenn., cefuroxime and loracarbef were obtained from Eli Lilly and Co., Indianapolis, Ind., ceftriaxone was obtained from Hoffmann-La Roche Inc., Nutley, N.J., and clarithromycin was obtained from Abbott Laboratories, Abbott Park, Ill.

Laboratory standard powders were diluted in accordance with manufacturers' recommendations and were then dispensed into microdilution plates in $\log_2$ dilution steps with various ranges with a Quick Spense II dispensing machine (Dynatech Laboratories, Inc., Chantilly, Va.). Plates were stored at −70°C until they were used.

Susceptibility tests. MICs for nonfastidious organisms and *Haemophilus influenzae* were determined by a standardized microdilution method (7) in 0.1-ml volumes of cation-adjusted Mueller-Hinton broth (Difco Laboratories, Detroit, Mich.) and Haemophilus Test Medium, respectively. For *Streptococcus pneumoniae*, cation-adjusted Mueller-Hinton broth with 5% lysed horse blood was used. Incubation was in room air for approximately 20 h. For anaerobes, the medium was Schaedler broth (Difco) supplemented with 1% heat-inactivated horse serum and 0.5 μg of vitamin K_1 per ml; incubation was in 85% N_2–10% H_2–5% CO_2 for approximately 48 h (8). Microdilution plates were inoculated with disposable inoculators (Dynatech) so that the final inoculum was approximately 5×10^5 CFU/ml. Recommended control strains (7–9) were used. MIC breakpoints for defining susceptibility, intermediate susceptibility, and resistance were those recommended by manufacturers and the National Committee for Clinical Laboratory Standards (9).

The MICs of the eight study drugs and the percentages of strains susceptible to the bacterial species studied are shown in Table 1. Control strains and their Bay 12-8039 MICs were as follows: *Escherichia coli* ATCC 25922, 0.03 to 0.06 μg/ml (n = 9); *Pseudomonas aeruginosa* ATCC 27853, 2 μg/ml (n = 9); *Staphylococcus aureus* ATCC 29213, 0.03 to 0.06 μg/ml (n = 9); *Enterococcus faecalis* ATCC 29212, 0.12 to 0.25 μg/ml (n = 8); *Bacteroides fragilis* ATCC 25285, 0.12 μg/ml (n = 3); and *Bacteroides thetaiotaomicron* ATCC 29741, 0.5 to 1 μg/ml (n = 4).

The results of this study, which used strains from the United States, were similar to those recently reported from the United Kingdom (11), although the nonfermenters from the United States were more resistant to quinolones than those from the United Kingdom. Bay 12-8093, like all quinolones, had marked activity against *H. influenzae* and *Moraxella catarrhalis*. It was less active than ciprofloxacin and comparable in activity to ofloxacin against *Enterobacteriaceae* and *P. aeruginosa*. It was more active than both ciprofloxacin and ofloxacin against common nonfermenters (other than *P. aeruginosa*), staphylococci, streptococci, enterococci, and anaerobes. The in vitro activity of Bay 12-8039 was quite similar to that of another new quinolone, trovafloxacin (5, 11). The activities of the nonquinolone antibiotics were better than those of the quinolones against some species; ceftriaxone was better against *Morganella morganii*, *Providencia stuartii*, and *Acinetobacter baumannii*, and amoxicillin-clavulanate was better against *Enterococcus faecalis* and anaerobes.

Organisms which have been problematic in the United States, including *Providencia stuartii*, methicillin-resistant coagulase-negative staphylococci, pneumococci with reduced penicillin susceptibility, and vancomycin-resistant enterococci,

* Phone: (614) 293-8732. Fax: (614) 293-5240. E-mail: fass.1@osu.edu.

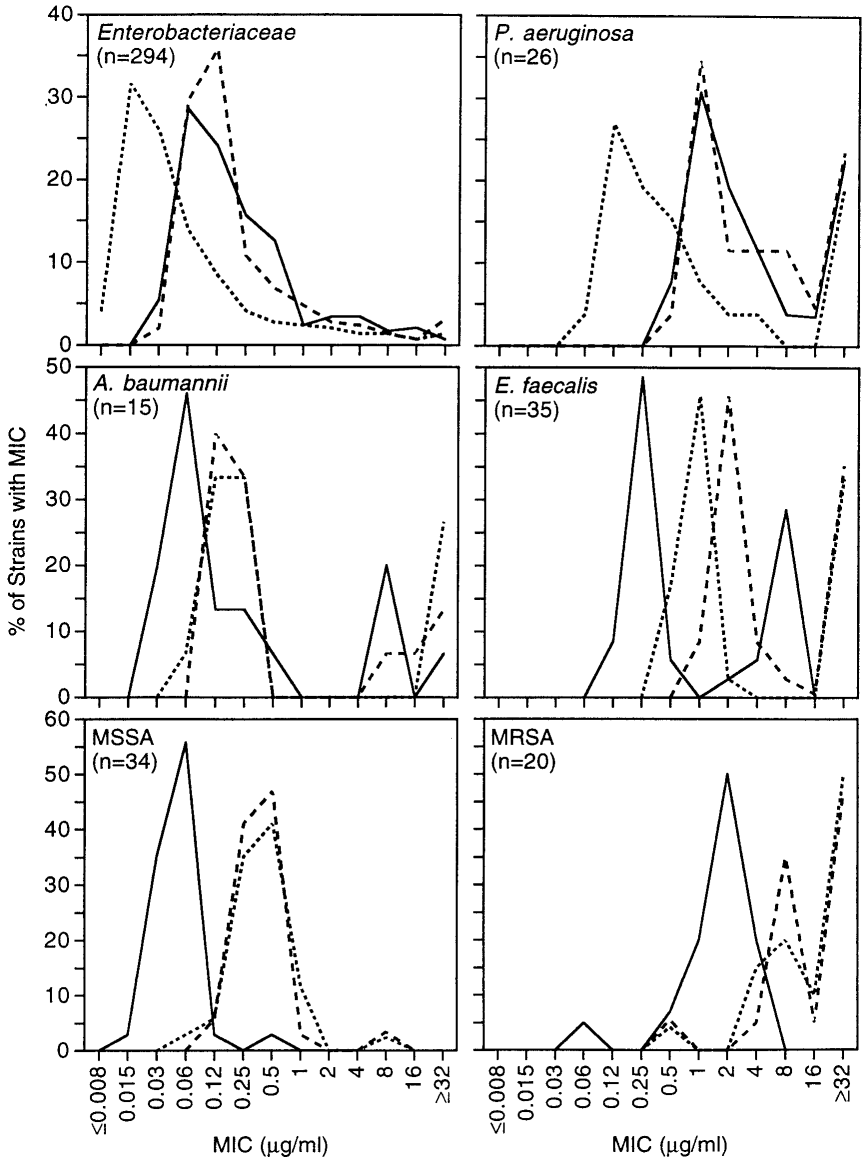

FIG. 1. Quinolone MIC frequency distribution curves for *Enterobacteriaceae*, *P. aeruginosa*, *A. baumannii*, *Enterococcus faecalis*, methicillin-susceptible *S. aureus* (MSSA), and methicillin-resistant *S. aureus* (MRSA). Solid line, Bay 12-8039; short-dashed line, ciprofloxacin; long-dashed line, ofloxacin.

were not included in the United Kingdom study (11). Bay 12-8039 was more active than ciprofloxacin and ofloxacin against all of these organisms, but most (except the pneumococci) were relatively quinolone resistant. The pneumococci were uniformly susceptible to all three quinolones regardless of penicillin susceptibility.

MIC frequency distribution curves and regression analyses. MICs were entered into a Macintosh model 7500/100 computer with File Maker Pro software. Quinolone MICs were converted to $\log_2$ values and then exported to Cricket Graph III. MIC frequency distribution curves were drawn, and regression lines of best fit were calculated for selected species and groups of similar species. The formula for the latter was $y = ax + b$, where x is the ciprofloxacin MIC ($\log_2$), a is the slope, b is the y-intercept, and y is the Bay 12-8039 or ofloxacin MIC ($\log_2$). r^2, the coefficient of determination, indicated the proportion of the total variance in y which could be explained by the variance in x. For example, if $r^2 = 0.85$, 85% of the total variance in the MIC of Bay 12-8039 or ofloxacin was determined by the MIC of ciprofloxacin.

There was a bimodal distribution of quinolone MICs for many of the species studied. Frequency distribution curves for selected species or groups of similar species are shown in Fig. 1.

In Table 2, regression analyses are used to compare Bay 12-8039 and ofloxacin MICs to ciprofloxacin MICs. Despite differences in activities against various species, there were high degrees of correlation among quinolone MICs; slopes of regression lines comparing MICs ($\log_2$) were close to unity, and coefficients of determination were usually >0.85. This has been the case with other quinolones (1–4, 6, 10). The relative differences in activities against various spe-

TABLE 1. In vitro activities of Bay 12-8039 and comparative antimicrobials

Organism(s) (no. of strains)[a]	Drug	MIC (μg/ml)[b]			Cum %[c]	
		Range	50%	90%	S	I
BLN *Haemophilus influenzae* (14)	Bay 12-8039	≤0.008–0.03	0.03	0.03		
	Ciprofloxacin	≤0.008–0.03	0.015	0.015	100	100
	Ofloxacin	0.03–0.06	0.06	0.06	100	100
	Amox-Clav[d]	0.25–1	0.25	0.5	100	100
	Cefuroxime	0.25–2	0.5	1	100	100
	Loracarbef	0.25–4	1	1	100	100
	Ceftriaxone	≤0.03	≤0.03	≤0.03	100	100
	Clarithromycin	0.5–8	4	8	100	100
BLP *Haemophilus influenzae* (12)	Bay 12-8039	≤0.008–0.06	0.03	0.03		
	Ciprofloxacin	≤0.008–0.015	0.015	0.015	100	100
	Ofloxacin	0.03–0.06	0.06	0.06	100	100
	Amox-Clav	0.25–1	0.5	1	100	100
	Cefuroxime	0.5–1	0.5	1	100	100
	Loracarbef	1–2	1	2	100	100
	Ceftriaxone	≤0.03–0.06	≤0.03	≤0.03	100	100
	Clarithromycin	0.5–≥32	4	4	92	92
BLP *Moraxella catarrhalis* (19)	Bay 12-8039	0.06	0.06	0.06		
	Ciprofloxacin	0.03–0.06	0.06	0.06	100	100
	Ofloxacin	0.06–0.25	0.06	0.12	100	100
	Amox-Clav	≤0.03–0.25	0.12	0.25	100	100
	Cefuroxime	0.5–4	1	4	100	100
	Loracarbef	0.5–4	1	2	100	100
	Ceftriaxone	≤0.03–1	0.5	1	100	100
	Clarithromycin	≤0.03–0.25	0.12	0.25	100	100
Escherichia coli (31)	Bay 12-8039	0.03–0.5	0.06	0.06		
	Ciprofloxacin	≤0.008–0.5	0.015	0.03	100	100
	Ofloxacin	0.03–0.5	0.06	0.12	100	100
	Amox-Clav	0.5–16	8	16	81	100
	Cefuroxime	0.5–16	4	8	61	100
	Loracarbef	0.5–4	1	2	100	100
	Ceftriaxone	≤0.03–0.25	0.06	0.12	100	100
Klebsiella pneumoniae (35)	Bay 12-8039	0.06–4	0.12	1		
	Ciprofloxacin	0.03–2	0.06	0.5	97	100
	Ofloxacin	0.12–4	0.12	1	94	100
	Amox-Clav	1–≥128	4	8	91	97
	Cefuroxime	1–≥128	4	16	71	91
	Loracarbef	0.5–≥128	1	2	94	97
	Ceftriaxone	≤0.03–4	0.06	0.25	100	100
Klebsiella oxytoca (25)	Bay 12-8039	0.06–0.12	0.12	0.12		
	Ciprofloxacin	0.015–0.06	0.015	0.06	100	100
	Ofloxacin	0.06–0.12	0.12	0.12	100	100
	Amox-Clav	1–32	2	4	92	96
	Cefuroxime	1–≥128	2	8	84	92
	Loracarbef	0.5–≥128	1	8	92	92
	Ceftriaxone	≤0.03–16	0.12	0.5	96	100
Citrobacter (*diversus*) *koseri* (20)	Bay 12-8039	0.03–4	0.06	0.06		
	Ciprofloxacin	≤0.008–1	0.015	0.015	100	100
	Ofloxacin	0.06–2	0.06	0.06	100	100
	Amox-Clav	2–64	2	4	90	95
	Cefuroxime	2–≥128	4	8	65	90
	Loracarbef	0.5–≥128	1	1	90	95
	Ceftriaxone	≤0.03–≥128	0.06	0.25	95	95
Citrobacter freundii (28)	Bay 12-8039	0.06–8	0.12	2		
	Ciprofloxacin	≤0.008–4	0.03	0.25	96	96
	Ofloxacin	0.06–8	0.12	2	96	96
	Cefuroxime	2–≥128	4	≥128	64	86
	Ceftriaxone	0.06–≥128	0.25	64	86	89
Enterobacter aerogenes (27)	Bay 12-8039	0.03–0.5	0.12	0.5		
	Ciprofloxacin	0.015–0.25	0.03	0.12	100	100

Continued on following page

TABLE 1—*Continued*

Organism(s) (no. of strains)[a]	Drug	MIC (μg/ml)[b]			Cum %[c]	
		Range	50%	90%	S	I
	Ofloxacin	0.06–1	0.12	1	100	100
	Cefuroxime	2–≥128	4	≥128	59	70
	Ceftriaxone	≤0.03–≥128	0.12	64	85	89
Enterobacter cloacae (29)	Bay 12-8039	0.03–≥32	0.06	0.5		
	Ciprofloxacin	≤0.008–≥32	0.015	0.25	93	93
	Ofloxacin	0.06–≥32	0.12	1	93	93
	Cefuroxime	4–≥128	16	≥128	24	59
	Ceftriaxone	0.06–≥128	0.5	≥128	72	76
Serratia marcescens (33)	Bay 12-8039	0.12–8	0.25	2		
	Ciprofloxacin	0.03–4	0.12	1	97	97
	Ofloxacin	0.12–8	0.25	2	97	97
	Ceftriaxone	0.12–16	0.5	2	97	100
Proteus mirabilis (33)	Bay 12-8039	0.12–≥32	0.25	2		
	Ciprofloxacin	0.015–≥32	0.03	0.25	97	97
	Ofloxacin	0.06–≥32	0.12	1	97	97
	Amox-Clav	0.5–8	0.5	1	100	100
	Cefuroxime	0.5–2	1	2	100	100
	Loracarbef	1–4	1	2	100	100
	Ceftriaxone	≤0.03	≤0.03	≤0.03	100	100
Proteus vulgaris (7)	Bay 12-8039	0.06–0.25				
	Ciprofloxacin	0.015–0.03				
	Ofloxacin	0.06–0.12				
	Amox-Clav	4–8				
	Ceftriaxone	≤0.03–≥128				
Morganella morganii (16)	Bay 12-8039	0.12–16	0.25	16		
	Ciprofloxacin	0.015–16	0.03	16	56	75
	Ofloxacin	0.06–≥32	0.12	≥32	56	69
	Ceftriaxone	≤0.03–4	≤0.03	2	100	100
Providencia stuartii (10)	Bay 12-8039	0.25–16	4	16		
	Ciprofloxacin	0.25–≥32	2	≥32	20	40
	Ofloxacin	1–≥32	4	≥32	20	50
	Cefuroxime	1–32	16	32	40	80
	Ceftriaxone	≤0.03–0.25	≤0.03	0.25	100	100
Pseudomonas aeruginosa (26)	Bay 12-8039	0.5–≥32	2	≥32		
	Ciprofloxacin	0.06–≥32	0.25	≥32	73	77
	Ofloxacin	0.5–≥32	4	≥32	46	58
	Ceftriaxone	4–≥128	16	≥128	19	62
Stenotrophomonas maltophilia (10)	Bay 12-8039	0.06–16	0.5	4		
	Ciprofloxacin	0.25–≥32	4	16	30	30
	Ofloxacin	0.25–≥32	4	16	30	60
Acinetobacter baumannii (15)	Bay 12-8039	0.03–≥32	0.06	8		
	Ciprofloxacin	0.06–≥32	0.25	≥32	73	73
	Ofloxacin	0.12–≥32	0.25	≥32	73	73
	Amox-Clav	4–32	8	16	80	93
	Ceftriaxone	4–32	16	32	33	100
Burkholderia cepacia (7)	Bay 12-8039	1–2				
	Ciprofloxacin	1				
	Ofloxacin	2–4				
	Ceftriaxone	2				
MS *Staphylococcus aureus* (34)	Bay 12-8039	0.015–0.5	0.06	0.06		
	Ciprofloxacin	0.06–8	0.5	1	97	97
	Ofloxacin	0.12–8	0.25	1	97	97
	Amox-Clav	0.25–2	0.5	1	100	100
	Cefuroxime	1–4	2	2	100	100
	Loracarbef	1–8	4	8	100	100

Continued on following page

TABLE 1—*Continued*

Organism(s) (no. of strains)[a]	Drug	MIC (μg/ml)[b]			Cum %[c]	
		Range	50%	90%	S	I
	Ceftriaxone	2–8	4	4	100	100
	Clarithromycin	0.12–≥32	0.25	0.5	91	91
MR *Staphylococcus aureus* (20)	Bay 12-8039	0.06–4	2	4		
	Ciprofloxacin	0.5–≥32	≥32	≥32	5	5
	Ofloxacin	0.5–≥32	≥32	≥32	5	10
	Clarithromycin	0.5–≥32	≥32	≥32	5	5
MS *Staphylococcus epidermidis* (23)	Bay 12-8039	0.03–0.12	0.06	0.12		
	Ciprofloxacin	0.12–1	0.25	0.5	100	100
	Ofloxacin	0.25–1	0.5	0.5	100	100
	Amox-Clav	0.06–0.5	0.25	0.25	100	100
	Cefuroxime	0.25–1	0.5	1	100	100
	Loracarbef	1–4	1	1	100	100
	Ceftriaxone	1–4	1	2	100	100
	Clarithromycin	0.12–≥32	0.25	≥32	65	65
MR *Staphylococcus epidermidis* (29)	Bay 12-8039	0.06–8	1	2		
	Ciprofloxacin	0.12–≥32	8	≥32	31	34
	Ofloxacin	0.25–≥32	8	16	31	38
	Clarithromycin	0.25–≥32	≥32	≥32	3	3
MR *Staphylococcus haemolyticus* (22)	Bay 12-8039	0.03–8	4	4		
	Ciprofloxacin	0.12–≥32	≥32	≥32	27	27
	Ofloxacin	0.12–≥32	≥32	≥32	27	27
	Clarithromycin	0.25–≥32	≥32	≥32	9	9
Staphylococcus hominis (10)	Bay 12-8039	0.03–0.5	0.06	0.5		
	Ciprofloxacin	0.12–4	0.12	0.5	90	90
	Ofloxacin	0.25–4	0.25	1	90	100
	Clarithromycin	0.25–≥32	≥32	≥32	30	30
Staphylococcus saprophyticus (16)	Bay 12-8039	0.12–0.25	0.12	0.25		
	Ciprofloxacin	0.25	0.25	0.25	100	100
	Ofloxacin	1	1	1	100	100
	Amox-Clav	0.5–1	0.5	1	100	100
	Cefuroxime	2–8	4	8	75	100
	Loracarbef	4–8	4	8	100	100
	Ceftriaxone	8–32	16	32	13	100
	Clarithromycin	0.25–0.5	0.25	0.5	100	100
Streptococcus pyogenes (14)	Bay 12-8039	0.06–0.12	0.12	0.12		
	Ciprofloxacin	0.12–0.5	0.25	0.25	100	100
	Ofloxacin	0.12–1	1	1	100	100
	Amox-Clav	≤0.03–0.06	≤0.03	≤0.03	100	100
	Cefuroxime	≤0.03	≤0.03	≤0.03	100	100
	Loracarbef	≤0.03–1	0.12	0.5	100	100
	Ceftriaxone	≤0.03–0.12	≤0.03	0.06	100	100
	Clarithromycin	≤0.03–2	≤0.03	0.06	93	93
PS *Streptococcus pneumoniae* (15)	Bay 12-8039	0.12–0.25	0.25	0.25		
	Ciprofloxacin	0.5–1	1	1	100	100
	Ofloxacin	1–2	2	2	100	100
	Amox-Clav	≤0.03–0.06	≤0.03	0.06	100	100
	Cefuroxime	≤0.03–0.06	0.06	0.06	100	100
	Loracarbef	0.5–2	1	1	100	100
	Ceftriaxone	≤0.03–0.12	≤0.03	0.12	100	100
	Clarithromycin	≤0.03–0.06	0.06	0.06	100	100
PI *Streptococcus pneumoniae* (20)	Bay 12-8039	0.12–0.25	0.12	0.25		
	Ciprofloxacin	0.5–2	1	1	95	100
	Ofloxacin	1–2	2	2	100	100
	Amox-Clav	0.12–4	1	1	40	90
	Cefuroxime	0.12–8	2	8	30	40
	Ceftriaxone	0.12–2	0.5	0.5	90	95
	Clarithromycin	0.06–≥32	0.12	16	59	59

Continued on following page

TABLE 1—*Continued*

Organism(s) (no. of strains)[a]	Drug	MIC (μg/ml)[b]			Cum %[c]	
		Range	50%	90%	S	I
PR *Streptococcus pneumoniae* (15)	Bay 12-8039	0.12–0.25	0.12	0.25		
	Ciprofloxacin	0.5–1	1	1	100	100
	Ofloxacin	1–2	2	2	100	100
	Amox-Clav	1–8	2	4	0	33
	Cefuroxime	8–16	8	16	0	0
	Ceftriaxone	0.5–8	1	4	13	60
	Clarithromycin	≤0.03–≥32	1	≥32	27	40
Streptococcus agalactiae (12)	Bay 12-8039	0.06–0.25	0.12	0.25		
	Ciprofloxacin	0.25–1	0.5	1	100	100
	Ofloxacin	1–2	1	2	100	100
	Amox-Clav	≤0.03–0.06	0.06	0.06	100	100
	Cefuroxime	≤0.03–0.06	0.06	0.06	100	100
	Loracarbef	1–2	1	2	100	100
	Ceftriaxone	0.06–0.12	0.06	0.12	100	100
	Clarithromycin	0.06–8	0.06	1	75	83
Viridans group streptococci (16)	Bay 12-8039	0.06–2	0.12	0.25		
	Ciprofloxacin	0.5–≥32	1	4	69	88
	Ofloxacin	1–≥32	1	4	88	94
	Amox-Clav	≤0.03–16	0.12	2	69	81
	Cefuroxime	≤0.03–8	0.12	2	69	81
	Loracarbef	0.12–≥128	4	≥128	81	81
	Ceftriaxone	0.06–4	0.12	1	100	100
	Clarithromycin	≤0.03–1	≤0.03	1	88	88
Enterococcus faecalis (35)	Bay 12-8039	0.12–8	0.25	8		
	Ciprofloxacin	0.5–≥32	1	≥32	63	63
	Ofloxacin	1–≥32	2	≥32	54	63
	Amox-Clav	0.25–1	0.5	0.5	100	100
	Clarithromycin	0.12–≥32	2	≥32	60	60
VS *Enterococcus faecium* (21)	Bay 12-8039	0.12–≥32	2	16		
	Ciprofloxacin	0.5–≥32	≥32	≥32	19	24
	Ofloxacin	1–≥32	≥32	≥32	14	24
	Amox-Clav	0.5–32	16	32	38	52
	Clarithromycin	0.12–≥32	≥32	≥32	19	24
VR *Enterococcus faecium* (17)	Bay 12-8039	2–≥32	4	≥32		
	Ciprofloxacin	4–≥32	≥32	≥32	0	0
	Ofloxacin	8–≥32	≥32	≥32	0	0
Bacteroides fragilis (24)	Bay 12-8039	0.06–4	0.25	4		
	Ciprofloxacin	1–≥32	4	≥32	4	42
	Ofloxacin	1–≥32	2	≥32	58	63
	Amox-Clav	0.12–2	0.25	2	100	100
	Ceftriaxone	2–≥128	4	≥128	67	67
	Clarithromycin	0.12–≥32	0.5	4	88	92
Bacteroides thetaiotaomicron (14)	Bay 12-8039	0.5–1	0.5	1		
	Ciprofloxacin	4–16	8	16	0	0
	Ofloxacin	4–16	8	8	0	29
	Amox-Clav	0.12–1	0.5	1	100	100
	Clarithromycin	0.5–≥32	1	≥32	86	86
Peptostreptococcus species (28)	Bay 12-8039	0.015–0.5	0.06	0.25		
	Ciprofloxacin	0.06–2	0.25	1	96	100
	Ofloxacin	0.06–8	0.5	4	89	93
	Amox-Clav	≤0.03–0.5	0.06	0.12	100	100
	Cefuroxime	≤0.03–4	0.5	2	100	100
	Loracarbef	≤0.03–8	1	4	100	100
	Ceftriaxone	≤0.03–8	0.25	8	100	100
	Clarithromycin	≤0.03–≥32	0.25	4	86	93
Clostridium perfringens (25)	Bay 12-8039	0.03–0.25	0.25	0.25		
	Ciprofloxacin	0.06–0.25	0.25	0.25	100	100
	Ofloxacin	0.06–0.5	0.5	0.5	100	100

Continued on following page

TABLE 1—*Continued*

Organism(s) (no. of strains)[a]	Drug	MIC (μg/ml)[b]			Cum %[c]	
		Range	50%	90%	S	I
	Amox-Clav	≤0.03–0.06	≤0.03	≤0.03	100	100
	Cefuroxime	0.06–2	0.5	1	100	100
	Loracarbef	≤0.03–1	0.25	1	100	100
	Ceftriaxone	≤0.03–1	≤0.03	0.25	100	100
	Clarithromycin	0.06–≥32	0.25	0.5	92	92
Fusobacterium species (13)	Bay 12-8039	0.03–0.12	0.06	0.12		
	Ciprofloxacin	0.06–1	0.5	1	100	100
	Ofloxacin	0.06–1	1	1	100	100
	Amox-Clav	≤0.03–0.25	≤0.03	≤0.03	100	100
	Cefuroxime	≤0.03–64	≤0.03	0.5	92	92
	Loracarbef	≤0.03–8	0.06	0.25	100	100
	Ceftriaxone	≤0.03–≥128	≤0.03	0.12	92	92
	Clarithromycin	0.12–16	4	8	46	69

[a] BLN, β-lactamase-negative; BLP, β-lactamase-positive; MS, methicillin-susceptible; MR, methicillin-resistant; PS, penicillin-susceptible; PI, penicillin-intermediate; PR, penicillin-resistant; VS, vancomycin-susceptible; VR, vancomycin-resistant.
[b] 50% and 90%, MICs at which 50 and 90% of the isolates are inhibited, respectively.
[c] Cum %, cumulative percentage of susceptibility relative to MIC breakpoints for defining susceptibility (S) and intermediate susceptibility (I). No breakpoints have been established for Bay 12-8039.
[d] Amox-Clav, amoxicillin-clavulanate.

cies (which were up to 16-fold) would likely be clinically significant, however, if achievable concentrations of the drugs in serum and tissue are comparable. Pending the acquisition of pharmacokinetic and safety data for Bay 12-8039, there is anticipation that Bay 12-8039 may realistically broaden the clinical utility of the quinolone class of antimicrobials.

TABLE 2. Comparison of Bay 12-8039 and ofloxacin MICs to ciprofloxacin MICs by regression analyses[a]

Organism(s)	Bay 12-8039			Ofloxacin		
	a	*b*	r^2	*a*	*b*	r^2
Enterobacteriaceae[b]	0.79	+1.00	0.84	0.84	+1.21	0.93
Pseudomonas aeruginosa	0.90	+2.52	0.89	0.94	+2.73	0.88
Acinetobacter baumannii	1.00	−1.54	0.97	0.89	−0.20	0.98
Stenotrophomonas maltophilia	1.00	−2.10	0.91	1.00	0.00	1.00
Staphylococcus spp.[c]	0.84	−2.60	0.93	0.93	+0.08	0.97
Enterococcus faecalis	0.92	−1.76	0.97	0.76	+1.22	0.97
Bacteroides spp.[d]	1.03	−3.69	0.85	1.02	−0.41	0.89

[a] $y = ax + b$, where x is the ciprofloxacin MIC ($\log_2$), a is the slope, b is the y-intersect, and y is the Bay 12-8039 or ofloxacin MIC ($\log_2$).
[b] Includes the 12 species in Table 1.
[c] Includes methicillin-susceptible and methicillin-resistant *S. aureus*, *Staphylococcus epidermidis*, and *Staphylococcus haemolyticus*.
[d] Includes *B. fragilis* and *B. thetaiotaomicron.*

This work was supported by a grant from Bayer Corp.

REFERENCES

1. **Barry, A. L., and P. C. Fuchs.** 1991. Cross-resistance and cross-susceptibility between fluoroquinolone agents. Eur. J. Clin. Microbiol. Infect. Dis. **10:**1013–1018.
2. **Fass, R. J.** 1983. In vitro activity of ciprofloxacin (Bay o 9867). Antimicrob. Agents Chemother. **24:**568–574.
3. **Fass, R. J.** 1993. In vitro activity of Bay y 3118, a new quinolone. Antimicrob. Agents Chemother. **37:**2348–2357.
4. **Fass, R. J.** 1994. Use of frequency distribution curves, scattergrams and regression analyses to compare in vitro activities and describe cross-susceptibility and cross-resistance among four quinolones. J. Chemother. **6:**368–376.
5. **Fass, R. J., J. Barnishan, M. C. Solomon, and L. W. Ayers.** 1996. In vitro activities of quinolones, β-lactams, tobramycin, and trimethoprim-sulfamethoxazole against nonfermentative gram-negative bacilli. Antimicrob. Agents Chemother. **40:**1412–1418.
6. **King, A., L. Bethune, and I. Phillips.** 1991. The in-vitro activity of tosufloxacin, a new fluorinated quinolone, compared with that of ciprofloxacin and temafloxacin. J. Antimicrob. Chemother. **28:**719–725.
7. **National Committee for Clinical Laboratory Standards.** 1993. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically, 3rd ed. Approved standard M7-A3. National Committee for Clinical Laboratory Standards, Villanova, Pa.
8. **National Committee for Clinical Laboratory Standards.** 1993. Methods for antimicrobial susceptibility testing of anaerobic bacteria, 3rd ed. Approved standard M11-A3. National Committee for Clinical Laboratory Standards, Villanova, Pa.
9. **National Committee for Clinical Laboratory Standards.** 1995. Performance standards for antimicrobial susceptibility testing. Sixth informational supplement M100-S6. National Committee for Clinical Laboratory Standards, Wayne, Pa.
10. **Thomson, K. S., C. C. Sanders, and M. E. Hayden.** 1991. In vitro studies with five quinolones: evidence for changes in relative potency as quinolone resistance rises. Antimicrob. Agents Chemother. **35:**2329–2334.
11. **Woodcock, J. M., J. M. Andrews, F. J. Boswell, N. P. Brenwald, and R. Wise.** 1997. The in vitro activity of Bay 12-8039, a new fluoroquinolone. Antimicrob. Agents Chemother. **41:**101–106.