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Comparative In Vitro Activities of ABT-773 against 362 Clinical Isolates of Anaerobic Bacteria

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The activity of ABT-773, a novel ketolide antibiotic, against clinical isolates of anaerobic bacteria was determined and compared to the activities of other antimicrobial agents. MICs at which 90% of isolates were inhibited (MIC_{90}s) were ≤0.06 μg/ml for *Actinomyces* spp., *Clostridium perfringens*, *Peptostreptococcus* spp., *Propionibacterium* spp., and *Porphyromonas* spp. The MIC_{50}s and MIC_{90}s were ≤0.06 and >32 μg/ml, respectively, for *Eubacterium* spp., *Lactobacillus* spp., *Clostridium difficile*, and *Clostridium ramosum*. The MIC_{90} for *Bilophila wadsworthia*, *Bacteroides ureolyticus*, and *Campylobacter gracilis* was 1 μg/ml, and that for *Prevotella bivia* and other *Prevotella* spp. was 0.5 μg/ml. The MIC_{90} for *Fusobacterium nucleatum* was 8 μg/ml, and that for *Fusobacterium mortiferum* and *Fusobacterium varium* was >32 μg/ml. The MIC_{90}s for the *Bacteroides fragilis* group were as follows: for *B. fragilis*, 8 μg/ml; for *Bacteroides thetaiotaomicron*, *Bacteroides ovatus*, *Bacteroides distasonis*, and *Bacteroides uniformis*, >32 μg/ml; and for *Bacteroides vulgatus*, 4 μg/ml. Telithromycin MICs for the *B. fragilis* group were usually 1 to 2 dilutions higher than ABT-773 MICs. For all strains, ABT-773 was more active than erythromycin by 4 or more dilutions, and for some strains this drug was more active than clindamycin.

ABT-773 is a novel ketolide with reported in vitro activity against macrolide-susceptible and -resistant respiratory pathogens, including *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Staphylococcus aureus*, and other organisms (E. J. C. Goldstein, D. M. Citron, C. V. Merriam, Y. Warren, and K. Tyrrell, Abstr. 5th Int. Conf. Macrolides, Azalides, Streptogramins, Ketolides and Oxazolidinones, abstr. 2.31, 2000; S. L. Hillier, M. Holloway, and L. Rabe, Abstr. 39th Intersci. Conf. Antimicrob. Agents Chemother., abstr. 2276, p. 271, 1999; D. Shortridge, N. C. Ramer, J. Beyer, Z. Ma, Y. Or, and R. K. Flamm, Abstr. 39th Intersci. Conf. Antimicrob. Agents Chemother., abstr. 2136, p. 346, 1999). The enhanced activity of ABT-773 is likely due to stronger binding affinities than those of erythromycin at the peptidyl transferase loop in domain V of 23S rRNA. The existence of additional binding sites of ABT-773 on ribosomes is suggested by the evidence that translocation reactions using highly methylated ribosomes could be inhibited by ABT-773 but not by erythromycin in *erm*-containing resistant *S. pneumoniae* (Z. Cao, R. Hammond, S. Pratt, A. Saike, C. Lerner, R. Flamm, and P. Zhong, Abstr. 5th Int. Conf. Macrolides, Azalides, Streptogramins, Ketolides and Oxazolidinones, abstr. 2.04, 2000).

Few data about the in vitro activities of ABT-773 and other ketolides against clinical isolates of anaerobic bacteria are available (S. M. Finegold, P. Summanen, D. Molitoris, M. L. Vaisanen, and H. M. Wexler, Abstr. 5th Int. Conf. Macrolides, Azalides, Streptogramins, Ketolides and Oxazolidinones, abstr. 2.30, 2000; Goldstein et al., 5th Int. Conf. Macrolides, Azalides, Streptogramins, Ketolides and Oxazolidinones). We determined the in vitro activity of ABT-773 using an agar dilution method and compared it to the activities of telithromycin, clarithromycin, erythromycin, azithromycin, roxithromycin, clindamycin, penicillin G, ampicillin-sulbactam, levofloxacin, and metronidazole against 362 clinical isolates of anaerobic bacteria.

(This study was presented at the 5th International Conference on the Macrolides, Azalides, Streptogramins, Ketolides and Oxazolidinones, 2000.)

The anaerobic bacteria were cultured from clinical specimens of patients hospitalized at Los Angeles County–University of Southern California Medical Center and stored at −70°C in 20% skim milk. Most of the organisms were isolated within 4 years of this study. They were taken from the freezer and transferred at least twice on brucella agar supplemented with vitamin K_1, hemin, and 5% sheep blood (Hardy Diagnostics, Santa Maria, Calif.) to ensure purity and good growth. The genera and species tested are listed in Table 1.

Laboratory reference standard powders were obtained as follows: ABT-773 and clarithromycin were from Abbott Laboratories, Abbott Park, Ill.; telithromycin and roxithromycin were from Hoechst-Marion-Roussel, Romainville, France; azithromycin, ampicillin, and sulbactam were from Pfizer, Groton, Conn.; levofloxacin was from R.W. Johnson PRI, Raritan, N.J.; erythromycin and penicillin G were from Eli Lilly and Company, Indianapolis, Ind.; clindamycin was from Pharmacia Upjohn, Kalamazoo, Mich.; and metronidazole was from Searle, Skokie, Ill.

The reference agar dilution method recommended by NCCLS (5) was followed. The antimicrobials were reconstituted according to the manufacturers' instructions. Serial twofold dilutions were prepared and added to molten supplemented brucella agar for plate preparation. The plates were used within 24 h of preparation. Inocula were prepared from 48-h cultures by suspending cell paste in brucella broth to equal the turbidity of the 0.5 McFarland standard. The inocula

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TABLE 1. Comparative in vitro activities of ABT-773 against 362 strains of anaerobic bacteria

Organism (no. tested)	Antimicrobial agent	MIC (μg/ml)		
		Range	50%	90%[a]
Actinomyces spp. (8)[b]	ABT-773	≤0.06–≤0.06	≤0.06	
	Telithromycin	≤0.06–≤0.06	≤0.06	
	Clarithromycin	≤0.06–0.125	≤0.06	
	Azithromycin	≤0.06–0.5	0.125	
	Erythromycin	≤0.06–0.25	0.125	
	Roxithromycin	≤0.06–0.25	0.25	
	Clindamycin	≤0.06–0.25	≤0.06	
	Penicillin G	≤0.06–0.5	0.125	
	Ampicillin-sulbactam	≤0.06–0.5	≤0.06	
	Levofloxacin	0.25–4	4	
	Metronidazole	0.25–>32	2	
Eubacterium spp. (18)[c]	ABT-773	≤0.06–>32	≤0.06	>32
	Telithromycin	≤0.06–>32	≤0.06	>32
	Clarithromycin	≤0.06–>32	0.5	>32
	Azithromycin	≤0.06–>32	4	>32
	Erythromycin	≤0.06–>32	4	>32
	Roxithromycin	≤0.06–>32	8	>32
	Clindamycin	≤0.06–4	0.25	4
	Penicillin G	≤0.06–2	0.5	2
	Ampicillin-sulbactam	≤0.06–2	≤0.06	1
	Levofloxacin	0.5–4	0.5	4
	Metronidazole	≤0.06–4	1	2
Lactobacillus spp. (22)[d]	ABT-773	≤0.06–>32	≤0.06	>32
	Telithromycin	≤0.06–>32	≤0.06	>32
	Clarithromycin	≤0.06–>32	0.5	>32
	Azithromycin	≤0.06–>32	2	>32
	Erythromycin	≤0.06–>32	1	>32
	Roxithromycin	≤0.06–>32	2	>32
	Clindamycin	≤0.06–>32	0.5	8
	Penicillin G	≤0.06–1	0.125	0.5
	Ampicillin-sulbactam	≤0.06–0.125	≤0.06	≤0.06
	Levofloxacin	0.125–8	2	4
	Metronidazole	0.25–>32	2	32
Propionibacterium spp. (16)[e]	ABT-773	≤0.06–0.125	≤0.06	≤0.06
	Telithromycin	≤0.06–0.25	≤0.06	≤0.06
	Clarithromycin	≤0.06–0.5	≤0.06	≤0.06
	Azithromycin	≤0.06–16	0.125	2
	Erythromycin	≤0.06–1	≤0.06	0.5
	Roxithromycin	≤0.06–2	≤0.06	0.125
	Clindamycin	≤0.06–0.5	≤0.06	0.25
	Penicillin G	≤0.06–1	≤0.06	1
	Ampicillin-sulbactam	≤0.06–0.5	0.25	1
	Levofloxacin	0.125–0.5	0.25	0.5
	Metronidazole	0.5–>32	0.5	>32
C. difficile (14)	ABT-773	≤0.06–>32	0.125	>32
	Telithromycin	≤0.06–>32	0.125	>32
	Clarithromycin	0.125–>32	0.5	>32
	Azithromycin	0.5–>32	2	>32
	Erythromycin	0.125–>32	1	>32
	Roxithromycin	0.25–>32	2	>32
	Clindamycin	0.125–>32	2	>32
	Penicillin G	0.5–4	2	4
	Ampicillin-sulbactam	0.125–>32	1	2
	Levofloxacin	4–>32	4	>32
	Metronidazole	0.25–>32	0.25	0.5
C. innocuum (11)	ABT-773	≤0.06–>32	4	>32
	Telithromycin	≤0.06–>32	0.5	>32
	Clarithromycin	0.25–>32	>32	>32
	Azithromycin	0.25–>32	>32	>32
	Erythromycin	0.5–>32	>32	>32
	Roxithromycin	0.5–>32	>32	>32
	Clindamycin	0.25–>32	0.5	1
	Penicillin G	0.25–0.5	0.25	0.5
	Ampicillin-sulbactam	0.125–0.25	0.125	0.25
	Levofloxacin	2–8	4	4
	Metronidazole	0.25–2	1	2
C. perfringens (16)	ABT-773	≤0.06–≤0.06	≤0.06	≤0.06
	Telithromycin	≤0.06–0.25	0.25	0.25
	Clarithromycin	0.125–1	0.125	0.125
	Azithromycin	2–4	4	4
	Erythromycin	0.25–2	2	2
	Roxithromycin	0.25–4	4	4
	Clindamycin	≤0.06–4	1	4
	Penicillin G	≤0.06–0.25	≤0.06	≤0.06
	Ampicillin-sulbactam	≤0.06–0.125	≤0.06	0.125
	Levofloxacin	0.25–2	0.25	0.5
	Metronidazole	0.25–2	1	2
Clostridium spp. (16)[f]	ABT-773	≤0.06–>32	1	>32
	Telithromycin	≤0.06–>32	1	>32
	Clarithromycin	0.25–>32	32	>32
	Azithromycin	0.5–>32	>32	>32
	Erythromycin	1–>32	>32	>32
	Roxithromycin	1–>32	>32	>32
	Clindamycin	0.125–>32	4	8
	Penicillin G	≤0.06–2	0.25	2
	Ampicillin-sulbactam	≤0.06–2	0.125	1
	Levofloxacin	0.15–16	4	8
	Metronidazole	0.25–8	0.5	1
Peptostreptococcus spp. (39)[g]	ABT-773	≤0.06–>32	≤0.06	≤0.06
	Telithromycin	≤0.06–>32	≤0.06	≤0.06
	Clarithromycin	≤0.06–>32	0.5	0.5
	Azithromycin	≤0.06–>32	0.5	4
	Erythromycin	≤0.06–>32	0.5	2
	Roxithromycin	≤0.06–>32	1	4
	Clindamycin	≤0.06–32	0.125	0.5
	Penicillin G	≤0.06–1	≤0.06	0.125
	Ampicillin-sulbactam	≤0.06–0.5	≤0.06	0.25
	Levofloxacin	0.125–0.5	0.25	1
	Metronidazole	0.25–>32	0.5	>32
B. distasonis (15)	ABT-773	0.125–>32	2	>32
	Telithromycin	1–>32	8	>32
	Clarithromycin	0.5–>32	4	>32
	Azithromycin	32–>32	>32	>32
	Erythromycin	4–>32	32	>32
	Roxithromycin	0.5–>32	32	>32
	Clindamycin	0.5–>32	8	>32
	Penicillin G	8–>32	16	>32
	Ampicillin-sulbactam	2–>32	4	16
	Levofloxacin	0.5–4	1	4
	Metronidazole	0.5–2	1	2
B. fragilis (20)	ABT-773	2–16	8	8
	Telithromycin	8–>32	16	32
	Clarithromycin	1–8	4	8
	Azithromycin	32–>32	>32	>32
	Erythromycin	8–>32	32	>32
	Roxithromycin	4–>32	>32	>32
	Clindamycin	0.25–16	1	2
	Penicillin G	4–>32	8	16
	Ampicillin-sulbactam	0.5–8	1	4
	Levofloxacin	0.5–4	1	2
	Metronidazole	0.25–1	0.5	1
B. ovatus (15)	ABT-773	0.5–>32	4	>32
	Telithromycin	1–>32	16	>32
	Clarithromycin	0.5–>32	8	>32
	Azithromycin	32–>32	>32	>32
	Erythromycin	2–>32	32	>32
	Roxithromycin	4–>32	>32	>32
	Clindamycin	0.5–>32	4	>32
	Penicillin G	1–>32	8	>32
	Ampicillin-sulbactam	0.5–16	1	16
	Levofloxacin	1–16	4	8
	Metronidazole	0.5–2	1	2
B. thetaiotaomicron (16)	ABT-773	1–>32	4	>32
	Telithromycin	2–>32	8	>32
	Clarithromycin	2–>32	8	>32
	Azithromycin	32–>32	>32	>32
	Erythromycin	2–>32	8	>32

Continued on following page

TABLE 1—*Continued*

Organism (no. tested)	Antimicrobial agent	MIC (μg/ml)		
		Range	50%	90%[a]
	Roxithromycin	16–>32	>32	>32
	Clindamycin	1–>32	4	>32
	Penicillin G	8–>32	16	>32
	Ampicillin-sulbactam	1–16	1	4
	Levofloxacin	1–4	4	4
	Metronidazole	0.5–1	0.5	1
B. uniformis (17)	ABT-773	0.5–>32	4	>32
	Telithromycin	1–>32	8	>32
	Clarithromycin	0.5–>32	4	>32
	Azithromycin	4–>32	>32	>32
	Erythromycin	2–>32	16	>32
	Roxithromycin	4–>32	>32	>32
	Clindamycin	1–>32	2	>32
	Penicillin G	4–>32	16	>32
	Ampicillin-sulbactam	1–4	2	4
	Levofloxacin	1–8	4	8
	Metronidazole	0.25–2	1	2
B. vulgatus (16)	ABT-773	0.125–8	0.25	4
	Telithromycin	0.5–>32	1	>32
	Clarithromycin	0.5–>32	1	>32
	Azithromycin	8–>32	32	>32
	Erythromycin	2–>32	4	>32
	Roxithromycin	2–>32	4	>32
	Clindamycin	≤0.06–>32	0.25	>32
	Penicillin G	0.5–>32	8	>32
	Ampicillin-sulbactam	0.5–0.16	1	16
	Levofloxacin	1–2	1	2
	Metronidazole	0.25–2	1	2
Bilophila wadsworthia (17)	ABT-773	0.25–2	0.5	2
	Telithromycin	≤0.06–2	1	2
	Clarithromycin	1–8	4	8
	Azithromycin	1–8	2	4
	Erythromycin	2–32	8	16
	Roxithromycin	1–32	4	32
	Clindamycin	≤0.06–4	0.5	2
	Penicillin G	0.5–>32	4	>32
	Ampicillin-sulbactam	0.25–8	2	4
	Levofloxacin	≤0.06–0.5	0.5	0.5
	Metronidazole	≤0.06–0.125	≤0.06	≤0.06
B. ureolyticus-C. gracilis group (22)[h]	ABT-773	0.25–8	0.5	1
	Telithromycin	≤0.06–8	1	2
	Clarithromycin	0.25–>32	2	4
	Azithromycin	≤0.06–8	0.125	2
	Erythromycin	0.125–>32	1	16
	Roxithromycin	1–32	4	16
	Clindamycin	0.125–16	2	8
	Penicillin G	≤0.06–>32	16	>32
	Ampicillin-sulbactam	≤0.06–>32	4	32
	Levofloxacin	0.25–32	0.25	0.5
	Metronidazole	≤0.06–>32	2	>32
F. nucleatum (13)	ABT-773	0.5–16	2	8
	Telithromycin	0.25–32	4	32
	Clarithromycin	4–>32	16	>32
	Azithromycin	0.25–8	1	8
	Erythromycin	4–>32	16	>32
	Roxithromycin	1–>32	>32	>32
	Clindamycin	≤0.06–≤0.06	≤0.06	≤0.06
	Penicillin G	≤0.06–0.125	≤0.06	≤0.06
	Ampicillin-sulbactam	≤0.06–0.5	≤0.06	0.25
	Levofloxacin	≤0.06–1	0.5	1
	Metronidazole	≤0.06–0.5	0.125	0.125
F. mortiferum-F. varium group (10)[i]	ABT-773	32–>32	>32	>32
	Telithromycin	32–>32	>32	>32
	Clarithromycin	>32–>32	>32	>32
	Azithromycin	16–>32	32	>32
	Erythromycin	>32–>32	>32	>32
	Roxithromycin	>32–>32	>32	>32
	Clindamycin	≤0.06–16	0.125	8
	Penicillin G	≤0.06–>32	0.125	0.5
	Ampicillin-sulbactam	≤0.06–32	1	2
	Levofloxacin	0.5–8	1	4
	Metronidazole	≤0.06–0.125	0.5	1
Fusobacterium spp. (5)[j]	ABT-773	0.125–1	0.5	
	Telithromycin	0.5–2	1	
	Clarithromycin	2–8	4	
	Azithromycin	0.125–16	2	
	Erythromycin	1–16	8	
	Roxithromycin	1–32	8	
	Clindamycin	0.5–2	1	
	Penicillin G	0.5–16	4	
	Ampicillin-sulbactam	0.5–4	2	
	Levofloxacin	0.25–1	0.5	
	Metronidazole	≤0.06–2	≤0.06	
P. asaccharolytica (7)	ABT-773	≤0.06–≤0.06	≤0.06	
	Telithromycin	≤0.06–≤0.06	≤0.06	
	Clarithromycin	≤0.06–4	≤0.06	
	Azithromycin	0.25–8	0.5	
	Erythromycin	≤0.06–2	0.25	
	Roxithromycin	≤0.06–8	0.125	
	Clindamycin	≤0.06–≤0.06	≤0.06	
	Penicillin G	≤0.06–≤0.06	≤0.06	
	Ampicillin-sulbactam	≤0.06–≤0.06	≤0.06	
	Levofloxacin	≤0.06–0.5	0.5	
	Metronidazole	≤0.06–0.25	≤0.06	
P. bivia (10)	ABT-773	≤0.06–0.125	≤0.06	0.125
	Telithromycin	≤0.06–2	0.25	2
	Clarithromycin	≤0.06–2	0.125	2
	Azithromycin	≤0.06–>32	1	2
	Erythromycin	≤0.06–>32	2	4
	Roxithromycin	≤0.06–>32	0.5	2
	Clindamycin	≤0.06–2	≤0.06	≤0.06
	Penicillin G	≤0.06–16	8	16
	Ampicillin-sulbactam	≤0.06–2	0.25	1
	Levofloxacin	0.5–4	2	2
	Metronidazole	0.25–4	2	4
Prevotella spp. (19)[k]	ABT-773	≤0.06–0.5	≤0.06	0.5
	Telithromycin	≤0.06–8	0.5	1
	Clarithromycin	≤0.06–8	0.25	1
	Azithromycin	≤0.125–>32	1	8
	Erythromycin	≤0.125–32	1	8
	Roxithromycin	≤0.06–8	1	4
	Clindamycin	≤0.06–0.5	≤0.06	0.25
	Penicillin G	≤0.06–32	≤0.06	8
	Ampicillin-sulbactam	≤0.06–2	0.125	1
	Levofloxacin	0.25–4	0.5	1
	Metronidazole	0.5–2	1	2

[a] MIC_{90}s were calculated for a minimum of 10 strains.

[b] *Actinomyces gerencseriae* (1 isolate), *A. israelii* (2), *A. meyeri* (3), *A. odontolyticus* (1), and one isolate not identified to species level.

[c] *Eubacterium lentum*; some of these strains may be *Eggerthella lenta* (15 isolates), *Eubacterium aerofaciens* (1), or *Eubacterium limosum* (1). One isolate was not identified to species level.

[d] *Lactobacillus acidophilus* (4 isolates), *L. brevis* (2), *L. casei* (2), *L. fermentum* (7), *L. jensenii* (1), *L. minutus* (*Atopobium minutum*) (1), *L. plantarum* (3), *L. rhamnosus* (1), and *L. uli* (1).

[e] *Propionibacterium acnes* (12 isolates) and 4 isolates not identified to species level.

[f] *Clostridium bifermentans* (1 isolate), *C. clostridioforme* (1), *C. hastiforme* (1), *C. novyi* (1), *C. paraputrificum* (1), *C. ramosum* (9), *C. subterminale* (1), and 1 isolate not identified to species level.

[g] *Peptostreptococcus anaerobius* (7 isolates), *P. magnus* (1), *P. micros* (24), *P. prevotii* (3), anaerobic *Streptococcus intermedius* (1), anaerobic *S. constellatus* (1), and 2 *Pepstreptococcus* isolates not identified to species level.

[h] *B. ureolyticus* (4 isolates) and *Campylobacter gracilis* (18).

[i] *F. mortiferum* (4 isolates) and *F. varium* (6).

[j] *Fusobacterium russii* (1 isolate) and 4 isolates not identified to species level.

[k] *Prevotella buccae* (7 isolates), *P. heparinolytica* (1), *P. intermedia* (6), *P. melaninogenica* (4), and *P. oris* (1).

were applied to the plates with a Steers replicator that delivered a final concentration of approximately 10^5 CFU/spot. Antimicrobial-free plates were stamped before and after each of the drug-containing-plate series. The plates were incubated at 37°C for 48 h in anaerobe jars using AnaeroGen envelopes (Oxoid Ltd., Basingstoke, Hampshire, England) to generate an anaerobic atmosphere containing 5 to 7% CO_2. The MIC was defined as the concentration of drug that resulted in a major change in the appearance of growth of a spot compared to that on the growth control plates.

The MICs are presented in Table 1. ABT-773 was most active against *Peptostreptococcus* spp., *Actinomyces* spp., *Propionibacterium* spp., *Clostridium perfringens*, and *Porphyromonas asaccharolytica*, with the MIC at which 90% of isolates were inhibited (MIC_{90}) being ≤0.06 μg/ml. ABT-773 activity against other anaerobic gram-positive bacilli showed a bimodal distribution. ABT-773 MICs for 7 of 14 strains of *Clostridium difficile* were greater than 32 μg/ml, and 6 of these strains were also highly resistant to the macrolides and clindamycin. ABT-773 MICs for 6 of 11 *Clostridium innocuum* strains and 4 of 9 *Clostridium ramosum* strains were greater than 32 μg/ml, and these strains were also highly resistant to the macrolides and clindamycin. The remaining five strains of *Clostridium ramosum* were moderately susceptible to clindamycin (MIC = 2 to 8 μg/ml), but they were very susceptible to ABT-773 (MIC ≤ 0.06 μg/ml). Five of 15 strains of *Eubacterium lentum* were resistant to all macrolides (MIC > 32 μg/ml) but were inhibited by ≤1 μg of ABT-773 and clindamycin/ml. ABT-773 MICs for 9 of 22 *Lactobacillus* strains were >32 μg/ml, and these strains were also highly resistant to all of the macrolides. Susceptibility to clindamycin among these strains was variable (MICs, 0.5 to >32 μg/ml).

Among the gram-negative strains, ABT-773 was most active against *Prevotella* spp., *Bilophila wadsworthia*, and the *Bacteroides ureolyticus-Campylobacter gracilis* group, with the MIC_{90} being ≤1 μg/ml. The MIC_{90} for *Bacteroides fragilis* was 8 μg/ml, and that for *Bacteroides vulgatus* was 4 μg/ml. For the other members of the *B. fragilis* group, the MIC_{90} was greater than 32 μg/ml. ABT-773 MICs were generally 2 to 4 dilutions lower than those of erythromycin. The members of the *Fusobacterium mortiferum-Fusobacterium varium* group were uniformly resistant to ABT-773 and the macrolides and had variable susceptibility to clindamycin (MIC range of ≤0.06 to 16 μg/ml). *Fusobacterium nucleatum* and other bile-sensitive *Fusobacterium* spp. were generally three- to fourfold more susceptible to ABT-773 than to erythromycin.

Since breakpoint interpretive criteria for ABT-773 (and other macrolides) have not been established for anaerobic bacteria, our study reports only the quantitative MICs of ABT-773. The drug's activity is similar to that of telithromycin, but it is slightly more active than telithromycin against some strains of *B. fragilis*, *B. vulgatus*, *Prevotella bivia*, and *F. nucleatum* (2, 3). Our results with *Bacteroides*, *Fusobacterium*, and clostridia are similar to those of Finegold et al. (5th Int. Conf. Macrolides, Azalides, Streptogramins, Ketolides and Oxazolidinones). Our results for *Prevotella* and *Porphyromonas* are similar to those reported by Goldstein et al. (5th International Conf. Macrolides, Azalides, Streptogramins, Ketolides and Oxazolidinones). Macrolide MICs for 10 of 22 of our lactobacillus strains were greater than 32 μg/ml. For nine of these, MICs of ABT-773 and telithromycin were also greater than 32 μg/ml. This is in contrast to a report by Hillier et al. (39th ICAAC), who found that erythromycin MIC_{90}s for vaginal species of lactobacilli were ≤0.25 μg/ml, using an agar dilution method with anaerobic incubation. The site of isolation for our strains was peritoneal fluid from patients with various types of intra-abdominal infections, which likely accounts for the difference.

Incubation of agar dilution plates in a CO_2-containing atmosphere has been shown to decrease the activity of erythromycin and other macrolides primarily by decreasing the pH of the agar medium (1, 4). The MICs of macrolides are affected to different degrees within the various genera of anaerobic bacteria, with MICs for fusobacteria exhibiting the greatest relative increase (1). Brown et al. reported that the MICs of ABT-773 are 1 doubling dilution higher for facultative respiratory pathogens when agar dilution tests are incubated in an atmosphere containing 5 to 7% CO_2 (S. D. Brown, A. L. Barry, and P. C. Fuchs, Abstr. 5th Int. Conf. Macrolides, Azalides, Streptogramins, Ketolides and Oxazolidinones, abstr. 2.07, 2000). When and if macrolide and ketolide breakpoints for anaerobes are defined, the effects of CO_2 on the MICs will have to be considered.

ABT-773 is a new ketolide with excellent in vitro activity against many species of anaerobes. Although ABT-773 is less active against members of the *B. fragilis* group and some strains of other *Clostridium* species, our study suggests potential clinical use against non-life-threatening infections caused by *Prevotella* spp., *Porphyromonas* spp., the *B. ureolyticus-C. gracilis* group, *Peptostreptococcus* spp. *Actinomyces* spp., *Propionibacterium* spp., and *C. perfringens.*

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