ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2002, p. 1136–1140 Vol. 46, No. 4
0066-4804/02/$04.00+0 DOI: 10.1128/AAC.46.4.1136–1140.2002

Comparative In Vitro Activities of Ertapenem (MK-0826) against 469 Less Frequently Identified Anaerobes Isolated from Human Infections

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Received 16 May 2001/Returned for modification 25 November 2001/Accepted 26 December 2001

We studied the in vitro activity of ertapenem against 469 less frequently identified anaerobes from 11 genera and 52 species isolated from human infections. Ertapenem was uniformly active against 460 of 469 (98%) strains at concentrations of ≤4 μg/ml. Only 4 of 14 *Clostridium difficile*, 1 of 11 *Clostridium innocuum*, and 4 of 6 *Lactobacillus* sp. strains required ertapenem concentrations of ≥8 μg/ml for inhibition.

Ertapenem (MK-0826) is a new parenteral carbapenem that is highly resistant to inactivation by a wide variety of beta-lactamases and that has a broad spectrum of antimicrobial activity (2, 3, 8, 9), a half-life of ~4.5 h, and a pharmacokinetic profile which allows once-a-day dosing (3, 14). Its activity against the more commonly isolated anaerobic pathogens, such as the *Bacteroides fragilis* group and *Clostridium perfringens*, has already been noted (2–4, 16; M. D. Appleman, D. M. Citron, P. N. R. Heseltine, H. Belzberg, A. E. Yellin, J. Murray, and T. V. Berne, Abstr. 38th Intersci. Conf. Antimicrob. Agents Chemother., abstr. F-43, p. 244, 1998). However, scant data exist on this agent's activity against the more recondite anaerobic pathogens that are less frequently identified in clinical specimens. In order to further evaluate ertapenem's full spectrum of anaerobic activity, we determined its comparative in vitro activities against a plethora of anaerobic pathogenic species encountered in human clinical infections.

We studied 469 less frequently identified human clinical anaerobic strains representing 11 genera and 52 species. Isolates were identified by standard criteria (7, 13) and stored in skim milk at −70°C. Isolates were taken from frozen stocks and subcultured twice on brucella agar supplemented with hemin, vitamin K_1, and 5% sheep blood. Susceptibility testing was performed by the reference agar dilution method with supplemented brucella agar according to NCCLS standards (11).

Antimicrobial agents were reconstituted according to the manufacturers' instructions. Serial twofold dilutions were prepared on the day of the test and added to the agar medium. Piperacillin was combined with tazobactam, and this combination was tested with tazobactam at a constant concentration of 4 μg/ml.

The agar plates were inoculated with an inoculum of 10^5 CFU per spot by use of a Steers replicator (Craft Machine Inc., Chester, Pa.). The plates were incubated in an anaerobic chamber for 44 h at 37°C prior to examination. The MIC was defined as the lowest concentration of an agent that yielded no growth or a marked change in appearance compared to that of the growth on a control plate. Control strains *Bacteroides fragilis* ATCC 25285 and *Bacteroides thetaiotaomicron* ATCC 29741 were included for each drug tested. The numbers and species of isolates tested are given in Table 1.

Standard laboratory powders were supplied as follows: ertapenem, imipenem, and cefoxitin by Merck & Co., West Point, Pa.; piperacillin and tazobactam by Wyeth-Ayerst, Philadelphia, Pa.; clindamycin by Pharmacia Inc., Kalamazoo, Mich.; metronidazole by Searle Research & Development, Skokie, Ill.; meropenem by Zeneca Pharmaceuticals, Wilmington, Del.; and penicillin G by Sigma Chemical Co., St. Louis, Mo.

The comparative in vitro activities of ertapenem and the seven other agents tested are presented in Table 1. Overall, ertapenem showed excellent activity against the full spectrum of the less frequently identified anaerobic pathogens that we tested. Provisional NCCLS-approved interpretive breakpoints for ertapenem against anaerobes are ≤4 μg/ml for susceptible, 8 μg/ml for intermediate, and ≥16 μg/ml for resistant (4). Overall, the in vitro activity of ertapenem was the same as, or within 3 dilutions of, those of piperacillin-tazobactam, imipenem, and meropenem, although some species and strain variabilities were observed. Ertapenem was more active than metronidazole against *Actinomyces* species, *Bacteroides ureolyticus*, *Campylobacter gracilis*, and *Anaerobiospirillum* species and was highly active against the clindamycin-resistant isolates of various species.

Bacteroides species, including *B. capillosus*, *B. putredinis*, *B. splanchnicus*, and *B. tectus*, were susceptible to ertapenem, but many were resistant to penicillin G and often required 2 to 8 μg of cefoxitin per ml for inhibition. The MICs at which 90% of organisms were inhibited (MIC_{90}s) by ertapenem were ≤0.015 μg/ml for *Bacteroides ureolyticus* and 0.06 μg/ml for *Campylobacter gracilis* isolates. Similarly, Wexler et al. (16), using the same methodology, found an ertapenem MIC_{90} of 0.12 μg/ml for 14 isolates of *Campylobacter gracilis*.

Prevotella species were susceptible to ertapenem, but many of the *Prevotella* sp. isolates (40 of 77 [52%]) were beta-lactamase producers and were resistant to penicillin G and 5 of 77 (6%) isolates were resistant to clindamycin.

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TABLE 1. Comparative in vitro activities of ertapenem and seven other agents against 469 unusual anaerobes

Organism (no. of isolates) and agent	MIC (μg/ml)		
	Range	50%	90%
Actinomyces spp. (19)[a]			
Ertapenem	0.06–2	0.125	1
Imipenem	≤0.015–0.5	0.06	0.5
Meropenem	≤0.015–1	0.06	0.5
Cefoxitin	≤0.03–2	0.25	0.5
Penicillin G	≤0.015–0.5	0.06	0.5
Piperacillin-tazobactam	≤0.03–4	0.25	2
Clindamycin	≤0.03–>32	0.06	0.5
Metronidazole	1–>16	>16	>16
Actinomyces odontolyticus (16)			
Ertapenem	0.06–0.5	0.5	0.5
Imipenem	0.06–0.5	0.06	0.125
Meropenem	0.06–0.25	0.125	0.25
Cefoxitin	0.06–0.25	0.125	0.25
Penicillin G	0.03–0.125	0.125	0.125
Piperacillin-tazobactam	0.125–2	0.5	2
Clindamycin	≤0.03–0.5	0.125	0.25
Metronidazole	8–>16	>16	>16
Actinomyces viscosus (14)			
Ertapenem	0.06–1	0.125	0.5
Imipenem	≤0.015–0.06	0.06	0.06
Meropenem	≤0.015–0.25	0.03	0.25
Cefoxitin	≤0.03–4	0.25	0.25
Penicillin G	≤0.015–0.5	0.06	0.25
Piperacillin-tazobactam	≤0.03–8	0.25	1
Clindamycin	≤0.03–>32	0.25	0.5
Metronidazole	16–>16	>16	>16
Anaerobiospirillum spp. (18)[b]			
Ertapenem	≤0.015–0.03	≤0.015	≤0.015
Imipenem	0.06–0.125	0.06	0.125
Meropenem	≤0.015–0.03	0.03	0.03
Cefoxitin	0.25–0.5	0.5	0.5
Penicillin G	≤0.015–0.5	0.125	0.25
Piperacillin-tazobactam	≤0.03–4	0.125	4
Clindamycin	2–32	8	16
Metronidazole	2–8	4	8
Bacteroides capillosus (12)			
Ertapenem	0.03–0.25	0.125	0.25
Imipenem	≤0.015–0.06	0.03	0.06
Meropenem	≤0.015–0.125	0.06	0.125
Cefoxitin	0.5–4	2	4
Penicillin G	0.03–32	8	16
Piperacillin-tazobactam	≤0.03	≤0.03	≤0.03
Clindamycin	≤0.03–>32	≤0.03	≤0.03
Metronidazole	0.25–1	1	1
Bacteroides putredinis (11)			
Ertapenem	≤0.015–1	0.125	0.5
Imipenem	≤0.015–1	0.5	1
Meropenem	≤0.015–0.5	0.25	0.5
Cefoxitin	≤0.03–8	2	8
Penicillin G	0.25–8	4	8
Piperacillin-tazobactam	≤0.03	≤0.03	≤0.03
Clindamycin	≤0.03–>32	≤0.03	0.5
Metronidazole	0.06–0.25	0.125	0.25
Bacteroides splanchnicus (10)			
Ertapenem	≤0.015–0.25	0.03	0.125
Imipenem	≤0.015–0.06	0.03	0.06
Meropenem	≤0.015–0.125	0.03	0.125
Cefoxitin	0.125–2	0.5	1
Penicillin G	4–>32	4	>32
Piperacillin-tazobactam	≤0.03	≤0.03	≤0.03
Clindamycin	≤0.03–>32	≤0.03	≤0.03
Metronidazole	≤0.03–0.125	0.06	0.125
Bacteroides tectus (16)			
Ertapenem	≤0.015–0.25	0.03	0.125
Imipenem	≤0.015–0.125	0.06	0.125
Meropenem	≤0.015–0.125	0.03	0.125
Cefoxitin	0.5–4	1	4
Penicillin G	≤0.015–>32	0.03	4
Piperacillin-tazobactam	≤0.03–0.25	≤0.03	0.25
Clindamycin	≤0.03–2	≤0.03	0.06
Metronidazole	0.125–1	0.5	1
Bacteroides ureolyticus (10)			
Ertapenem	≤0.015	≤0.015	≤0.015
Imipenem	0.03–0.06	0.03	0.03
Meropenem	≤0.015	≤0.015	≤0.015
Cefoxitin	0.125–4	0.25	2
Penicillin G	≤0.015–0.5	≤0.015	0.125
Piperacillin-tazobactam	≤0.03	≤0.03	≤0.03
Clindamycin	0.125–0.5	0.125	0.5
Metronidazole	0.125–4	1	4
Campylobacter gracilis (10)			
Ertapenem	≤0.015–0.25	0.06	0.06
Imipenem	≤0.015–0.25	0.125	0.125
Meropenem	≤0.015–0.06	0.03	0.03
Cefoxitin	0.25–>64	1	4
Penicillin G	0.03–8	0.25	0.5
Piperacillin-tazobactam	≤0.03–32	0.125	8
Clindamycin	0.06–>32	0.125	1
Metronidazole	0.125–4	1	4
Clostridium bifermentans (11)			
Ertapenem	≤0.015–0.125	0.06	0.06
Imipenem	0.06–0.25	0.125	0.25
Meropenem	0.06–0.125	0.06	0.125
Cefoxitin	0.125–4	2	4
Penicillin G	≤0.015–0.25	0.125	0.25
Piperacillin-tazobactam	0.125–0.5	0.5	0.5
Clindamycin	≤0.03–16	≤0.03	0.25
Metronidazole	0.25–8	1	2
Clostridium butyricum (11)			
Ertapenem	0.125–1	0.125	0.25
Imipenem	0.125–1	0.25	1
Meropenem	0.06–1	0.125	0.5
Cefoxitin	4–8	4	8
Penicillin G	0.25–>32	0.25	32
Piperacillin-tazobactam	0.25–2	0.25	2
Clindamycin	≤0.03–0.5	0.25	0.25
Metronidazole	1–2	1	2
Clostridium cadaveris (10)			
Ertapenem	≤0.015	≤0.015	≤0.015
Imipenem	0.06–0.125	0.06	0.06
Meropenem	≤0.015–0.03	≤0.015	≤0.015
Cefoxitin	0.5–1	0.5	0.5
Penicillin G	0.125–0.125	0.125	0.125
Piperacillin-tazobactam	≤0.03–0.25	≤0.03	≤0.03
Clindamycin	≤0.03–2	≤0.03	0.25
Metronidazole	0.06–0.125	0.125	0.125
Clostridium clostridioforme (10)			
Ertapenem	0.125–2	1	2
Imipenem	0.25–2	1	2
Meropenem	0.125–2	1	2
Cefoxitin	2–16	4	8
Penicillin G	0.25–>32	1	16
Piperacillin-tazobactam	0.125–64	8	8
Clindamycin	≤0.03–1	0.5	1
Metronidazole	≤0.03–1	0.125	0.25

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TABLE 1—*Continued*

Organism (no. of isolates) and agent	MIC (μg/ml)		
	Range	50%	90%
Clostridium difficile (14)			
Ertapenem	4–8	4	8
Imipenem	4–8	4	8
Meropenem	1–4	1	2
Cefoxitin	64–>64	>64	>64
Penicillin G	0.5–4	1	4
Piperacillin-tazobactam	4–16	8	16
Clindamycin	2–>32	2	>32
Metronidazole	0.25–1	0.5	1
Clostridium innocuum (11)			
Ertapenem	2–8	2	4
Imipenem	1–4	2	4
Meropenem	1–2	1	2
Cefoxitin	8–>64	64	>64
Penicillin G	0.125–1	0.5	0.5
Piperacillin-tazobactam	0.06–2	1	2
Clindamycin	0.25–>32	0.5	>32
Metronidazole	0.5–2	0.5	2
Clostridium ramosum (10)			
Ertapenem	0.5–2	1	2
Imipenem	0.125–0.5	0.25	0.5
Meropenem	1	1	1
Cefoxitin	2–64	8	64
Penicillin G	0.03–1	0.125	0.5
Piperacillin-tazobactam	0.06–1	0.125	1
Clindamycin	1–>32	2	>32
Metronidazole	0.5–2	1	2
Clostridium symbiosum (9)			
Ertapenem	≤0.015–0.125	0.125	NA[f]
Imipenem	0.125–0.25	0.125	NA
Meropenem	0.06–0.125	0.125	NA
Cefoxitin	0.5–1	1	NA
Penicillin G	≤0.015–1	0.5	NA
Piperacillin-tazobactam	0.25–1	1	NA
Clindamycin	0.06–0.5	0.25	NA
Metronidazole	0.06–0.125	0.125	NA
Clostridium tertium (10)			
Ertapenem	0.25–0.5	0.5	0.5
Imipenem	0.125–0.25	0.25	0.25
Meropenem	0.25	0.25	0.25
Cefoxitin	1–2	1	2
Penicillin G	0.5–2	1	2
Piperacillin-tazobactam	4–16	16	16
Clindamycin	1–8	8	8
Metronidazole	0.5–4	1	2
Fusobacterium mortiferum (11)			
Ertapenem	0.06–0.125	0.06	0.125
Imipenem	0.06–0.5	0.5	0.5
Meropenem	≤0.03–0.5	0.25	0.5
Cefoxitin	1–4	1	4
Penicillin G	0.25–1	0.25	1
Piperacillin-tazobactam	0.125–0.5	0.25	0.5
Clindamycin	0.06–4	0.06	0.125
Metronidazole	0.25–1	0.5	0.5
Fusobacterium naviforme (10)			
Ertapenem	≤0.015	≤0.015	≤0.015
Imipenem	≤0.015	≤0.015	≤0.015
Meropenem	≤0.015–0.03	≤0.015	≤0.015
Cefoxitin	≤0.03–0.25	0.06	0.125
Penicillin G	≤0.015–0.06	≤0.015	≤0.015
Piperacillin-tazobactam	≤0.03–0.5	≤0.03	0.125
Clindamycin	≤0.03–0.06	≤0.03	0.06
Metronidazole	≤0.03–0.5	0.06	0.5
Fusobacterium russii (12)			
Ertapenem	≤0.015–0.03	≤0.015	≤0.015
Imipenem	≤0.015–0.06	0.03	0.06
Meropenem	≤0.015	≤0.015	≤0.015
Cefoxitin	0.06–0.125	0.06	0.125
Penicillin G	≤0.015	≤0.015	≤0.015
Piperacillin-tazobactam	≤0.03–0.125	≤0.03	≤0.03
Clindamycin	≤0.03–0.06	0.06	0.06
Metronidazole	0.06–1	0.25	0.5
Fusobacterium varium (15)			
Ertapenem	≤0.015–0.06	0.06	0.06
Imipenem	≤0.015–1	0.5	1
Meropenem	≤0.015–0.125	0.06	0.125
Cefoxitin	0.5–4	2	4
Penicillin G	0.125–1	0.25	0.5
Piperacillin-tazobactam	≤0.03–4	2	2
Clindamycin	0.06–32	4	32
Metronidazole	0.125–1	0.5	0.5
Gardnerella vaginalis (10)			
Ertapenem	0.03–2	0.06	0.25
Imipenem	0.06–0.5	0.06	0.125
Meropenem	≤0.015–0.5	0.03	0.125
Cefoxitin	0.125–16	0.5	8
Penicillin G	0.06–2	0.125	0.25
Piperacillin-tazobactam	≤0.03–2	0.25	1
Clindamycin	≤0.03–0.06	≤0.03	≤0.03
Metronidazole	4–>16	>16	>16
Lactobacillus spp. (16)[c]			
Ertapenem	0.03–>16	2	>16
Imipenem	≤0.015–8	0.125	8
Meropenem	0.03–>16	0.25	>16
Cefoxitin	0.5–>64	>64	>64
Penicillin G	≤0.015–16	1	4
Piperacillin-tazobactam	≤0.03–>32	1	16
Clindamycin	≤0.03–>16	0.125	16
Metronidazole	1–>16	>16	>16
Peptostreptococcus spp. (21)[d]			
Ertapenem	≤0.015–1	0.06	0.125
Imipenem	≤0.015–0.5	0.03	0.06
Meropenem	≤0.015–0.5	0.03	0.125
Cefoxitin	≤0.03–2	0.5	0.5
Penicillin G	≤0.015–1	1	1
Piperacillin-tazobactam	≤0.03–0.5	≤0.03	0.25
Clindamycin	≤0.03–32	0.125	1
Metronidazole	0.06–8	0.5	1
Porphyromonas canoris (10)			
Ertapenem	≤0.015	≤0.015	≤0.015
Imipenem	≤0.015–0.06	0.03	0.06
Meropenem	≤0.015–0.03	≤0.015	≤0.015
Cefoxitin	≤0.03–1	0.06	0.125
Penicillin G	≤0.015–0.25	≤0.015	≤0.015
Piperacillin-tazobactam	≤0.03–≤0.03	≤0.03	≤0.03
Clindamycin	≤0.03–≤0.03	≤0.03	≤0.03
Metronidazole	≤0.03–1	0.5	0.5
Porphyromonas gingivalis (15)			
Ertapenem	≤0.015	≤0.015	≤0.015
Imipenem	≤0.015–0.03	≤0.015	≤0.015
Meropenem	≤0.015–0.03	≤0.015	≤0.015
Cefoxitin	0.06–1	0.25	0.5
Penicillin G	≤0.015–0.06	≤0.015	0.03
Piperacillin-tazobactam	≤0.03	≤0.03	≤0.03
Clindamycin	≤0.03	≤0.03	≤0.03
Metronidazole	≤0.03–0.25	≤0.03	0.06

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TABLE 1—*Continued*

Organism (no. of isolates) and agent	MIC (μg/ml)		
	Range	50%	90%
Porphyromonas levii (10)			
Ertapenem	≤0.015–0.06	≤0.015	≤0.015
Imipenem	≤0.015–0.03	≤0.015	≤0.015
Meropenem	≤0.015–0.06	≤0.015	0.03
Cefoxitin	≤0.03–2	0.125	0.5
Penicillin G	≤0.015–8	1	2
Piperacillin-tazobactam	≤0.03	≤0.03	≤0.03
Clindamycin	≤0.03–>32	≤0.03	≤0.03
Metronidazole	0.125–1	0.25	1
Porphyromonas macacae (15)			
Ertapenem	≤0.015–0.03	≤0.015	0.03
Imipenem	≤0.015–0.125	0.03	0.125
Meropenem	≤0.015–0.03	≤0.015	0.03
Cefoxitin	0.06–1	0.5	1
Penicillin G	≤0.015–0.5	0.125	0.5
Piperacillin-tazobactam	≤0.03	≤0.03	≤0.03
Clindamycin	≤0.03	≤0.03	≤0.03
Metronidazole	≤0.03–0.5	0.25	0.25
Prevotella buccae (10)			
Ertapenem	0.125–1	0.125	1
Imipenem	0.03–0.25	0.03	0.125
Meropenem	0.06–0.5	0.06	0.25
Cefoxitin	1–16	1	16
Penicillin G	0.125–>32	0.125	16
Piperacillin-tazobactam	≤0.03–2	≤0.03	0.125
Clindamycin	≤0.03–>32	≤0.03	>32
Metronidazole	0.5–2	1	2
Prevotella disiens (10)			
Ertapenem	≤0.015–0.125	0.06	0.125
Imipenem	≤0.015–0.06	0.03	0.06
Meropenem	≤0.015–0.06	0.03	0.06
Cefoxitin	0.125–2	0.5	2
Penicillin G	≤0.015–32	2	16
Piperacillin-tazobactam	≤0.03	≤0.03	≤0.03
Clindamycin	≤0.03	≤0.03	≤0.03
Metronidazole	0.25–2	1	2
Prevotella heparinolytica (14)			
Ertapenem	0.06–0.25	0.125	0.125
Imipenem	0.06–0.125	0.125	0.125
Meropenem	0.06–0.125	0.125	0.125
Cefoxitin	1–4	1	1
Penicillin G	0.125–32	0.125	0.25
Piperacillin-tazobactam	≤0.03–0.25	0.125	0.25
Clindamycin	≤0.03	≤0.03	≤0.03
Metronidazole	0.125–1	0.25	0.5
Prevotella loescheii and *Prevotella melaninogenica* (21)[e]			
Ertapenem	≤0.015–1	0.125	0.5
Imipenem	≤0.015–1	0.03	0.06
Meropenem	≤0.015–0.25	0.06	0.125
Cefoxitin	0.125–32	1	4
Penicillin G	≤0.015–32	4	16
Piperacillin-tazobactam	≤0.03–4	≤0.03	0.25
Clindamycin	≤0.03–>32	≤0.03	16
Metronidazole	0.125–2	0.5	1
Prevotella oralis (11)			
Ertapenem	0.06–1	0.25	1
Imipenem	≤0.015–0.25	0.125	0.25
Meropenem	0.03–0.25	0.125	0.25
Cefoxitin	0.25–16	4	16
Penicillin G	0.06–>32	16	>32
Piperacillin-tazobactam	≤0.03–8	0.06	2
Clindamycin	≤0.03–>32	≤0.03	2
Metronidazole	0.25–2	1	2
Prevotella oris (11)			
Ertapenem	0.03–0.5	0.125	0.25
Imipenem	≤0.015–0.25	0.03	0.125
Meropenem	≤0.015–0.125	0.06	0.125
Cefoxitin	0.25–16	1	8
Penicillin G	≤0.015–>32	0.06	16
Piperacillin-tazobactam	≤0.03–0.25	≤0.03	0.25
Clindamycin	≤0.03–0.5	≤0.03	0.25
Metronidazole	0.25–2	1	2
Veillonella spp. (15)			
Ertapenem	≤0.015–4	0.125	1
Imipenem	0.03–0.5	0.125	0.5
Meropenem	≤0.015–0.125	0.03	0.125
Cefoxitin	0.5–8	4	8
Penicillin G	0.125–4	2	4
Piperacillin-tazobactam	0.5–>64	8	64
Clindamycin	0.06–1	0.125	0.25
Metronidazole	2–8	4	4

[a] *Actinomyces israelii* ($n = 9$), *A. meyeri* ($n = 3$), *A. naeslundii* ($n = 6$), and *A. neuii* ($n = 1$).
[b] *Anaerobiospirillum succiniciproducens* ($n = 3$) and *A. thomasii* ($n = 15$).
[c] *Lactobacillus acidophilus* ($n = 3$), *L. brevis* ($n = 2$), *L. casei* ($n = 3$), *L. catenaformis* ($n = 3$), *L. confusus* ($n = 1$), *L. delbrueckii* ($n = 1$), *L. jensenii* ($n = 1$), and *L. lactis* ($n = 2$).
[d] *Peptostreptococcus asaccharolyticus* ($n = 6$), *P. magnus* ($n = 5$), *P. micros* ($n = 6$), and *P. prevotii* ($n = 4$).
[e] *Prevotella loescheii* ($n = 9$) and *Prevotella melaninogenica* ($n = 12$).
[f] NA, not applicable.

Nine different *Clostridium* species comprising 96 isolates showed species variation in their susceptibilities to ertapenem. *Clostridium innocuum* strains required 2 to 8 μg of ertapenem per ml for inhibition, and all 14 *Clostridium difficile* isolates required 4 to 8 μg/ml for inhibition. Wexler et al. (16) also found ertapenem MIC_{90}s of 8 μg/ml for *Clostridium difficile* and 1 μg/ml for *Clostridium ramosum*. In our study, cefoxitin resistance was commonly seen in *Clostridium clostridioforme*, *Clostridium difficile*, *Clostridium innocuum*, and *Clostridium ramosum* isolates.

Peptostreptococcus spp. were susceptible to ertapenem and all other agents tested. Many of the *Lactobacillus* strains were less susceptible than the *Peptostreptococcus* spp. to all agents tested, with an ertapenem MIC_{90} of >16 μg/ml. Piperacillin-tazobactam and penicillin G were less active against *Veillonella* spp. than were the three carbapenems and clindamycin (MIC_{90}, 0.25 μg/ml).

In assessing its overall activity against anaerobes, we found that ertapenem appears to inhibit the growth of the majority of both typical and less frequently identified anaerobic pathogens. We previously reported ertapenem's activity against 1,001 anaerobes isolated from human intra-abdominal infections in 17 countries worldwide and found it to be uniformly active against all isolates, including all *Bacteroides fragilis* group species isolates, with the exception of 12 of 61 (20%) strains of *Bilophila wadsworthia*, three strains of lactobacilli, and one isolate of *Acidaminococcus fermentans* (4). Appleman et al. (38th ICAAC) studied the comparative activities of ertapenem

against 88 anaerobic isolates obtained from 60 patients with serious intra-abdominal infections and found that ertapenem had "excellent activity" against the 41 *Bacteroides fragilis* group strains (MIC_{90}, ≤4 μg/ml). Using the same agar dilution method that we employed, Appleman et al. found 99% of the isolates to be susceptible to both ertapenem and imipenem at MICs of ≤4μg/ml. Wexler et al. (16) tested ertapenem against 363 anaerobic isolates and found that 98% of the strains were susceptible to ertapenem.

Clinicians must rely on published studies to help guide both empirical therapy as well as specific therapy in situations that involve anaerobes in mixed infections (5, 6). The increasing resistance of many anaerobes to widely used antimicrobial agents (1, 10, 12, 15) underlies a growing need for consistently active antianaerobe agents. Our study, coupled with data from prior studies (4, 16; Appleman et al., 38th ICAAC), suggests that ertapenem offers in vitro activity against a complete spectrum of anaerobic bacterial pathogens that is comparable to or better than that of piperacillin-tazobactam or metronidazole; it was more active than cefoxitin and was active against clindamycin-resistant isolates. Ertapenem is a valuable addition to the armamentarium of antianaerobe drugs.

We thank Judee H. Knight and Alice E. Goldstein for various forms of assistance.

This study was funded in part by an educational grant from Merck & Co.

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