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SUSCEPTIBILITY

Comparative *In Vitro* Activities of Relebactam, Imipenem, the Combination of the Two, and Six Comparator Antimicrobial Agents against 432 Strains of Anaerobic Organisms, Including Imipenem-Resistant Strains

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ABSTRACT Relebactam is an important beta-lactamase inhibitor for certain aerobic organisms, but alone it has no antianaerobic activity, with most anaerobes having MICs of ≥32 μg/ml with the exception of a very few strains. There was no enhancement or antagonism of imipenem activity with the addition of relebactam, including activity against imipenem-resistant strains. The relebactam-imipenem combination had excellent overall activity against the anaerobes tested.

KEYWORDS *Bacteroides fragilis*, *Bacteroides thetaiotaomicron*, *Bilophila wadsworthia*, *Desulfovibrio* spp., *Eggerthella lenta*, *F. necrophorum*, *Parabacteroides goldsteinii*, anaerobes, imipenem resistance, relebactam

Relebactam is a novel diazobicyclooctane inhibitor that has activity in combination with imipenem against a broad range of beta-lactamases, including class A (extended-spectrum beta-lactamases [ESBLs] and KPCs) and class C enzymes, as well as carbapenemases most commonly found in *Klebsiella pneumoniae* (1, 2). Anaerobes are important pathogens in a variety of human infections for which carbapenems are important therapeutic choices. In a previous study, the combination of imipenem-relebactam's *in vitro* activity against 453 *Bacteroides fragilis* group species strains reported resistance rates of 0.7% (MIC_{90}s, 1 μg/ml). The authors concluded that relebactam does not add activity to that of imipenem, but did not study relebactam alone as a comparator (3). They also suggested that imipenem-relebactam does not inhibit the *B. fragilis* metalloenzyme (*cfiA* gene) and that any resistance might be due to other mechanisms, such as outer membrane proteins (Opr proteins and porins) and/or efflux (3, 4).

In order to further define the antianaerobic activity of imipenem-relebactam against a broader range of anaerobic pathogens involved in human clinical infections, we assessed its activity on a broad spectrum of clinical anaerobic isolates, many of which are beta-lactamase producers. We studied relebactam and imipenem alone as well as in combination, and other comparator agents, including ampicillin-sulbactam, piperacillin-tazobactam, moxifloxacin, clindamycin, metronidazole, and tigecycline. Clinical isolates were recovered from a variety of infections and included 131 recent isolates of *Bacteroides* spp., plus 17 selected strains of *Bacteroides* spp. with imipenem MICs ranging from 4 to >32 μg/ml. Other Gram-negative genera included *Parabacteroides*, *Prevotella*, *Fusobacterium*, *Porphyromonas*, *Veillonella*, *Bilophila*, and *Desulfovibrio*. Gram-positive genera included *Eggerthella*, *Actinomyces*, *Eubacterium*, *Flavonifractor*, *Mogibacterium*, *Slackia*, *Solobacterium*, and *Clostridium*. Isolates were identified by standard criteria (4, 5), and MICs were determined using the agar dilution method according to CLSI M11-A8 procedures (6). Serial 2-fold dilutions of comparators were

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TABLE 1 Comparative *in vitro* activity and percentage resistance against anaerobic bacterial strains[a]

Organism (no. of strains) or agent	Range	MIC_{50}	MIC_{90}	% R
Anaerobic Gram-negative strains				
Bacteroides fragilis (38)				
Relebactam	>32–>32	>32	>32	
Imipenem	0.06–2	0.125	1	0
Imipenem-relebactam	≤0.03–2	0.125	2	
Ampicillin-sulbactam	0.5–32	2	16	5.2
Piperacillin-tazobactam	0.06–4	0.5	4	0
Moxifloxacin	0.125–8	0.25	4	5.2
Clindamycin	0.125–>32	1	>32	13.1
Metronidazole	0.25–2	1	2	0
Tigecycline	0.06–8	0.5	4	0
Bacteroides caccae (10)				
Relebactam	>32–>32	>32	>32	
Imipenem	≤0.03–>32	0.125	0.5	10
Imipenem-relebactam	≤0.03–>32	0.25	0.5	
Ampicillin-sulbactam	0.5–8	1	8	0
Piperacillin-tazobactam	0.06–8	4	8	0
Moxifloxacin	1–>32	4	>32	40
Clindamycin	0.25–>32	1	>32	30
Metronidazole	0.25–2	0.5	1	0
Tigecycline	0.125–>8	0.5	8	10
Bacteroides ovatus (24)				
Relebactam	>32–>32	>32	>32	
Imipenem	0.125–8	0.25	4	0
Imipenem-relebactam	0.125–2	0.25	2	
Ampicillin-sulbactam	1–32	8	16	8.3
Piperacillin-tazobactam	1–>64	4	32	4.2
Moxifloxacin	1–>16	2	16	0.25
Clindamycin	0.125–>32	>32	>32	54.2
Metronidazole	0.25–2	1	1	0
Tigecycline	0.06–>8	2	8	4.2
Bacteroides thetaiotaomicron (24)				
Relebactam	>32–>32	>32	>32	
Imipenem	0.125–4	0.25	2	0
Imipenem-relebactam	0.125–4	0.25	1	
Ampicillin-sulbactam	0.5–32	2	32	12.5
Piperacillin-tazobactam	4–>64	8	64	8.3
Moxifloxacin	1–>16	1	>16	33.3
Clindamycin	0.125–>32	2	>32	0.25
Metronidazole	0.25–2	1	2	0
Tigecycline	0.125–>8	0.5	>8	12.5
Bacteroides uniformis (10)				
Relebactam	>32–>32	>32	>32	
Imipenem	0.125–0.5	0.25	0.25	0
Imipenem-relebactam	0.125–0.5	0.25	0.25	
Ampicillin-sulbactam	1–16	1	4	0
Piperacillin-tazobactam	0.5–2	1	2	0
Moxifloxacin	1–>16	>16	>16	60
Clindamycin	≤0.03–>32	32	>32	60
Metronidazole	0.5–1	0.5	1	0
Tigecycline	≤0.03–1	0.125	0.25	0
Bacteroides vulgatus (12)				
Relebactam	>32–>32	>32	>32	
Imipenem	0.06–1	0.5	1	0
Imipenem-relebactam	0.06–1	0.5	1	
Ampicillin-sulbactam	1–16	4	8	0
Piperacillin-tazobactam	1–32	4	8	0
Moxifloxacin	0.25–>16	16	>16	58.3
Clindamycin	≤0.03–>32	0.125	>32	41.7
Metronidazole	0.25–4	0.5	1	0
Tigecycline	0.125–1	0.25	1	0
Bacteroides spp. (13)[b]				
Relebactam	>32–>32	>32	>32	
Imipenem	0.125–2	0.5	2	0
Imipenem-relebactam	0.125–2	0.25	2	

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TABLE 1 (Continued)

Organism (no. of strains) or agent	Range	MIC_{50}	MIC_{90}	% R
Ampicillin-sulbactam	0.25–32	4	16	15.4
Piperacillin-tazobactam	1–64	4	32	0
Moxifloxacin	0.25–>16	2	>16	38.5
Clindamycin	0.25–>32	1	>32	30.8
Metronidazole	0.25–2	1	2	0
Tigecycline	0.125–4	0.25	4	0
Bacteroides spp. (15)[c]				
Relebactam	>32–>32	>32	>32	
Imipenem	4–>32	8	>32	46.7
Imipenem-relebactam	0.5–>32	8	>32	
Ampicillin-sulbactam	4–>32	>32	>32	80
Piperacillin-tazobactam	0.125–>64	64	>64	40
Moxifloxacin	0.25–8	1	8	26.7
Clindamycin	0.125–>32	>32	>32	53.3
Metronidazole	0.25–>32	1	1	13.3
Tigecycline	0.125–>8	1	8	6.7
Parabacteroides distasonis (11)				
Relebactam	>32–>32	>32	>32	
Imipenem	0.25–8	0.5	5	0
Imipenem-relebactam	0.25–4	0.5	2	
Ampicillin-sulbactam	2–32	8	32	18.1
Piperacillin-tazobactam	2–8	4	8	0
Moxifloxacin	0.25–16	0.5	16	36.4
Clindamycin	0.5–>32	2	>32	45.4
Metronidazole	0.5–2	1	2	0
Tigecycline	0.5–4	1	4	0
Parabacteroides goldsteinii (10)				
Relebactam	>32–>32	>32	>32	
Imipenem	0.5–4	1	2	0
Imipenem-relebactam	0.25–4	1	2	
Ampicillin-sulbactam	2–16	8	16	0
Piperacillin-tazobactam	2–8	4	4	0
Moxifloxacin	0.25–16	0.5	8	30
Clindamycin	≤0.03–>32	2	>32	30
Metronidazole	1–2	1	1	0
Tigecycline	0.25–4	0.5	4	0
Parabacteroides merdae (10)				
Relebactam	>32–>32	>32	>32	
Imipenem	0.5–16	1	8	10
Imipenem-relebactam	0.5–16	1	4	
Ampicillin-sulbactam	2–>32	8	32	20
Piperacillin-tazobactam	1–>64	4	8	10
Moxifloxacin	0.125–16	0.5	8	50
Clindamycin	0.125–>32	0.25	>32	30
Metronidazole	0.5–2	1	2	0
Tigecycline	0.125–4	0.25	1	0
Prevotella bivia (11)				
Relebactam	>32–>32	>32	>32	
Imipenem	≤0.03–0.125	0.06	0.125	0
Imipenem-relebactam	≤0.03–0.125	0.06	0.125	
Ampicillin-sulbactam	0.06–4	2	4	0
Piperacillin-tazobactam	≤0.03–0.06	≤0.03	0.06	0
Moxifloxacin	0.125–>16	4	8	18.2
Clindamycin	≤0.03–>32	≤0.03	>32	18.2
Metronidazole	0.5–8	2	2	0
Tigecycline	0.125–2	0.5	1	0
Prevotella buccae (10)				
Relebactam	>32–>32	>32	>32	
Imipenem	0.06–0.25	0.125	0.125	0
Imipenem-relebactam	0.06–0.25	0.125	0.125	
Ampicillin-sulbactam	0.125–2	0.125	1	0
Piperacillin-tazobactam	≤0.03–≤0.03	≤0.03	≤0.03	0
Moxifloxacin	0.5–16	1	8	20
Clindamycin	≤0.03–>32	32	>32	60
Metronidazole	0.125–1	0.5	0.5	0
Tigecycline	0.06–0.125	0.06	0.125	0

(Continued on next page)

TABLE 1 (Continued)

Organism (no. of strains) or agent	Range	MIC_{50}	MIC_{90}	% R
Prevotella melaninogenica (10)				
Relebactam	16–>32	>32	>32	
Imipenem	≤0.03–0.06	≤0.03	0.06	0
Imipenem-relebactam	≤0.03–≤0.03	≤0.03	≤0.03	
Ampicillin-sulbactam	0.125–4	0.5	2	0
Piperacillin-tazobactam	≤0.03–≤0.03	≤0.03	≤0.03	0
Moxifloxacin	0.25–16	1	16	40
Clindamycin	≤0.03–>32	16	>32	60
Metronidazole	0.06–0.5	0.25	0.5	0
Tigecycline	0.06–0.25	0.125	0.25	0
Prevotella spp. (10)[d]				
Relebactam	32–>32	>32	>32	
Imipenem	≤0.03–0.125	0.06	0.125	0
Imipenem-relebactam	≤0.03–0.125	0.06	0.125	
Ampicillin-sulbactam	≤0.03–2	0.5	1	0
Piperacillin-tazobactam	≤0.03–0.25	≤0.03	≤0.03	0
Moxifloxacin	0.25–4	2	4	0
Clindamycin	≤0.03–>32	≤0.03	>32	50
Metronidazole	0.25–2	0.5	1	0
Tigecycline	≤0.03–1	0.5	0.5	0
Porphyromonas spp. (10)[e]				
Relebactam	8–>32	32	>32	
Imipenem	≤0.03–0.06	≤0.03	0.06	0
Imipenem-relebactam	≤0.03–≤0.03	≤0.03	≤0.03	
Ampicillin-sulbactam	≤0.03–0.5	≤0.03	0.125	0
Piperacillin-tazobactam	≤0.03–0.125	≤0.03	≤0.03	0
Moxifloxacin	≤0.03–2	0.25	0.5	0
Clindamycin	≤0.03–>32	≤0.03	>32	20
Metronidazole	≤0.03–4	0.25	0.5	0
Tigecycline	≤0.03–0.06	≤0.03	0.06	0
Fusobacterium nucleatum (10)				
Relebactam	>32–>32	>32	>32	
Imipenem	0.06–0.125	0.06	0.06	0
Imipenem-relebactam	≤0.03–0.06	≤0.03	0.06	
Ampicillin-sulbactam	≤0.03–0.125	0.06	0.06	0
Piperacillin-tazobactam	≤0.03–≤0.03	≤0.03	≤0.03	0
Moxifloxacin	0.125–2	0.25	2	0
Clindamycin	≤0.03–>32	≤0.03	1	10
Metronidazole	≤0.03–0.25	≤0.03	0.25	0
Tigecycline	≤0.03–0.06	0.06	0.06	0
Fusobacterium necrophorum (10)				
Relebactam	>32–>32	>32	>32	
Imipenem	0.06–2	0.5	2	0
Imipenem-relebactam	≤0.03–0.5	0.125	0.5	
Ampicillin-sulbactam	≤0.03–0.125	0.125	0.125	0
Piperacillin-tazobactam	≤0.03–≤0.03	≤0.03	≤0.03	0
Moxifloxacin	1–2	1	2	0
Clindamycin	≤0.03–>32	≤0.03	>32	20
Metronidazole	0.125–0.5	0.25	0.5	0
Tigecycline	≤0.03–0.06	≤0.03	0.06	0
Fusobacterium mortiferum (10)				
Relebactam	>32–>32	>32	>32	
Imipenem	1–4	2	2	0
Imipenem-relebactam	1–2	2	2	
Ampicillin-sulbactam	1–16	2	8	0
Piperacillin-tazobactam	0.25–4	0.25	4	0
Moxifloxacin	0.5–>16	0.5	>16	30
Clindamycin	≤0.03–0.125	≤0.03	0.125	0
Metronidazole	0.5–1	0.5	1	0
Tigecycline	≤0.03–0.25	0.125	0.25	0
Fusobacterium varium (10)				
Relebactam	>32–>32	>32	>32	
Imipenem	2–16	16	16	60
Imipenem-relebactam	2–4	4	4	
Ampicillin-sulbactam	0.5–1	1	1	0
Piperacillin-tazobactam	1–4	2	4	0

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TABLE 1 (Continued)

Organism (no. of strains) or agent	Range	MIC_{50}	MIC_{90}	% R
Moxifloxacin	1–>16	4	>16	50
Clindamycin	0.125–32	2	32	40
Metronidazole	0.5–2	1	2	0
Tigecycline	≤0.03–0.125	≤0.03	0.125	0
Bilophila wadsworthia (10)				
Relebactam	>32–>32	>32	>32	
Imipenem	0.5–>32	8	16	50
Imipenem-relebactam	0.125–>32	0.25	4	
Ampicillin-sulbactam	2–>32	32	>32	60
Piperacillin-tazobactam	16–>64	>64	>64	80
Moxifloxacin	0.25–8	1	1	10
Clindamycin	0.25–>32	1	4	10
Metronidazole	0.06–>32	0.125	0.25	10
Tigecycline	0.125–0.5	0.25	0.5	0
Desulfovibrio spp. (10)[f]				
Relebactam	8–>32	>32	>32	
Imipenem	0.25–0.5	0.5	0.5	0
Imipenem-relebactam	0.125–0.5	0.25	0.5	
Ampicillin-sulbactam	2–4	2	4	0
Piperacillin-tazobactam	64–>64	64	>64	40
Moxifloxacin	0.25–>16	0.25	8	20
Clindamycin	0.25–>32	0.25	1	10
Metronidazole	0.125–0.25	0.25	0.25	0
Tigecycline	0.125–0.5	0.125	0.5	0
Veillonella spp. (10)[g]				
Relebactam	>32–>32	>32	>32	
Imipenem	0.06–1	0.5	1	0
Imipenem-relebactam	0.06–0.5	0.5	0.5	
Ampicillin-sulbactam	0.125–32	2	32	30
Piperacillin-tazobactam	8–>64	64	>64	30
Moxifloxacin	0.06–>16	4	8	30
Clindamycin	≤0.03–>32	0.06	>32	20
Metronidazole	1–4	2	4	0
Tigecycline	0.125–0.5	0.25	0.5	0
Anaerobic Gram-positive strains				
Clostridium clostridioforme group (20)[h]				
Relebactam	>32–>32	>32	>32	
Imipenem	1–4	2	4	0
Imipenem-relebactam	1–4	2	4	
Ampicillin-sulbactam	0.5–8	1	2	10
Piperacillin-tazobactam	0.5–64	8	16	0
Moxifloxacin	4–16	8	16	10
Clindamycin	0.06–32	0.5	4	25
Metronidazole	≤0.03–0.5	0.25	0.5	0
Tigecycline	≤0.03–0.125	≤0.03	0.06	0
Clostridium innocuum (15)				
Relebactam	>32–>32	>32	>32	
Imipenem	0.25–4	1	2	6.7
Imipenem-relebactam	0.5–4	2	2	
Ampicillin-sulbactam	0.125–0.5	0.25	0.5	0
Piperacillin-tazobactam	0.25–1	0.5	1	0
Moxifloxacin	1–>16	2	16	26.7
Clindamycin	0.25–>32	0.5	>32	20
Metronidazole	0.5–2	1	1	0
Tigecycline	≤0.03–0.06	≤0.03	0.06	6.7
Clostridium perfringens (10)				
Relebactam	32–>32	32	>32	
Imipenem	0.06–0.25	0.125	0.125	0
Imipenem-relebactam	0.06–0.25	0.125	0.125	
Ampicillin-sulbactam	≤0.03–0.5	0.125	0.25	0
Piperacillin-tazobactam	≤0.03–0.5	0.25	0.5	0
Moxifloxacin	0.25–1	0.5	0.5	0
Clindamycin	≤0.03–>32	0.06	2	10
Metronidazole	1–4	2	4	0
Tigecycline	0.06–4	2	4	10

(Continued on next page)

TABLE 1 (Continued)

Organism (no. of strains) or agent	Range	MIC_{50}	MIC_{90}	% R
Clostridium spp. (15)[i]				
Relebactam	32–>32	>32	>32	
Imipenem	0.06–0.5	0.25	0.5	0
Imipenem-relebactam	0.06–0.5	0.25	0.5	
Ampicillin-sulbactam	≤0.03–1	0.25	1	0
Piperacillin-tazobactam	≤0.03–2	0.25	1	0
Moxifloxacin	0.25–>16	2	8	53.3
Clindamycin	≤0.03–>32	1	16	40
Metronidazole	0.06–2	0.5	1	0
Tigecycline	≤0.03–4	0.06	1	20
Clostridioides difficile (10)				
Relebactam	>32–>32	>32	>32	
Imipenem	4–8	4	8	0
Imipenem-relebactam	4–8	4	4	
Ampicillin-sulbactam	1–4	2	2	0
Piperacillin-tazobactam	4–8	4	8	0
Moxifloxacin	1–16	2	2	60
Clindamycin	4–>32	4	8	60
Metronidazole	0.5–2	1	2	0
Tigecycline	0.06–0.125	0.06	0.125	0
Eggerthella lenta (11)				
Relebactam	>32–>32	>32	>32	
Imipenem	≤0.03–0.5	0.5	0.5	0
Imipenem-relebactam	≤0.03–0.5	0.5	0.5	
Ampicillin-sulbactam	0.125–2	1	2	0
Piperacillin-tazobactam	≤0.03–16	16	16	0
Moxifloxacin	0.06–8	0.5	2	63.6
Clindamycin	≤0.03–>32	0.125	>32	18.1
Metronidazole	0.25–>32	0.5	0.5	9.0
Tigecycline	0.125–0.25	0.125	0.25	0
Anaerobic, non-sporeforming rod bacteria (10)[j]				
Relebactam	>32–>32	>32	>32	
Imipenem	≤0.03–2	0.06	0.5	0
Imipenem-relebactam	≤0.03–0.5	0.06	0.5	
Ampicillin-sulbactam	≤0.03–2	0.125	1	0
Piperacillin-tazobactam	≤0.03–1	0.125	0.5	0
Moxifloxacin	0.25–>16	2	>16	30
Clindamycin	≤0.03–1	0.06	1	0
Metronidazole	0.125–>32	1	>32	20
Tigecycline	0.06–0.5	0.125	0.5	0
Finegoldia magna (10)				
Relebactam	4–>32	>32	>32	
Imipenem	≤0.03–0.06	0.06	0.06	0
Imipenem-relebactam	≤0.03–0.06	0.06	0.06	
Ampicillin-sulbactam	0.06–0.25	0.25	0.25	0
Piperacillin-tazobactam	≤0.03–0.125	0.06	0.06	0
Moxifloxacin	0.125–>16	0.5	8	20
Clindamycin	0.125–8	0.25	4	10
Metronidazole	0.25–>32	0.5	1	10
Tigecycline	0.06–2	0.125	0.25	0
Parvimonas micra (11)				
Relebactam	>32–>32	>32	>32	
Imipenem	≤0.03–0.06	≤0.03	0.06	0
Imipenem-relebactam	≤0.03–0.06	≤0.03	0.06	
Ampicillin-sulbactam	≤0.03–0.125	0.06	0.125	0
Piperacillin-tazobactam	≤0.03–≤0.03	≤0.03	≤0.03	0
Moxifloxacin	0.25–2	0.25	2	0
Clindamycin	0.06–>32	0.125	0.25	10
Metronidazole	≤0.03–32	0.25	0.25	10
Tigecycline	≤0.03–0.125	≤0.03	0.06	0
Peptoniphilus harei (10)				
Relebactam	32–>32	>32	>32	
Imipenem	≤0.03–≤0.03	≤0.03	≤0.03	0
Imipenem-relebactam	≤0.03–≤0.03	≤0.03	≤0.03	
Ampicillin-sulbactam	≤0.03–0.06	0.06	0.06	0

(Continued on next page)

TABLE 1 (Continued)

Organism (no. of strains) or agent	Range	MIC_{50}	MIC_{90}	% R
Piperacillin-tazobactam	≤0.03–≤0.03	≤0.03	≤0.03	0
Moxifloxacin	0.25–>16	0.5	16	20
Clindamycin	0.06–>32	0.5	>32	30
Metronidazole	0.25–2	0.5	1	0
Tigecycline	0.06–0.125	0.06	0.125	0
Peptostreptococcus anaerobius (10)				
Relebactam	>32–>32	>32	>32	
Imipenem	≤0.03–0.25	0.06	0.06	0
Imipenem-relebactam	≤0.03–0.5	0.06	0.06	
Ampicillin-sulbactam	≤0.03–0.25	0.125	0.25	0
Piperacillin-tazobactam	≤0.03–0.25	0.125	0.125	0
Moxifloxacin	0.125–16	0.25	8	30
Clindamycin	≤0.03–32	0.125	0.5	10
Metronidazole	0.25–1	0.5	0.5	0
Tigecycline	≤0.03–0.25	0.06	0.06	0

[a]Antimicrobial agents tested consisted of relebactam, imipenem, and the combination of the two, plus six comparator antimicrobial agents (μg/ml). Percent resistance (% R) was against 432 strains of anaerobic bacteria, including imipenem-resistant organisms.
[b]*Bacteroides intestinalis* (1), *B. massiliensis* (3), *B. nordii* (3), and *B. xylanisolvens* (6).
[c]Species selected for decreased susceptibility to imipenem: *Bacteroides fragilis* (13) and *B. ovatus* (2).
[d]*Prevotella bergensis* (3), *P. baroniae* (1), and *P. nanceiensis* (6).
[e]*Porphyromonas asaccharolytica* (4), *P. gingivalis* (1), *P. pasteri* (1), *P. somerae* (2), *P. uenonis* (1), and *Porphyromonas* species (1).
[f]*Desulfovibrio desulfuricans* (5) and *D. fairfieldensis* (5).
[g]*Veillonella parvula* (6), *V. atypica* (2), and *V. dispar* (2).
[h]*Clostridium aldenense* (2), *C. bolteae* (2), *C. citroniae* (2), *C. clostridioforme* (2), and *C. hathewayi* (12).
[i]*Clostridium butyricum* (2), *C. cadaveris* (2), *C. scindens* (2), *C. sordellii* (2), *C. symbiosum* (2), and *C. ramosum* (5).
[j]*Actinomyces turicensis* (2), *Eubacterium limosum* (2), *Flavonifractor plautii* (2), *Mogibacterium timidum* (1), *Slackia exigua* (1), and *Solobacterium moorei* (2).

tested, as well as relebactam. Imipenem alone and in combination with relebactam held constant at 4 μg/ml was also tested.

The results of the comparative *in vitro* activities of relebactam, imipenem, and the combination are shown in Table 1. Relebactam alone had MICs of ≥32 μg/ml against all isolates, including against all *B. fragilis* group spp., with the exception of *Desulfovibrio desulfuricans* (1 strain) (MIC 8 μg/ml), *Porphyromonas asaccharolytica* (3) and *P. gingivalis* (1) (8 to 16 μg/ml), *Prevotella melaninogenica* (1) (16 μg/ml), and *Finegoldia magna* (1) (4 μg/ml). Results of the combination of imipenem-relebactam showed minimal difference from those of imipenem alone for most of the strains tested with the following exceptions: 7 of 10 *Bilophila wadsworthia* strains were imipenem-resistant (MIC ≥ 8 μg/ml), with 6 of the strains showing a 2- to 32-fold decrease in MIC with imipenem-relebactam (range 0.25 to 4 μg/ml), and 4 of 10 *F. varium* strains showed a 4-fold reduction in MIC (16 to 4 μg/ml). Of the strains that were imipenem susceptible, 4 of 10 *F. necrophorum* strains showed a 4-fold MIC decrease, as did 2 of 24 strains of *B. ovatus* that showed a 4- to 16-fold decrease. Among the 13 strains of *B. fragilis* selected because of decreased susceptibility or resistance to imipenem, there was no enhancement of activity with the addition of relebactam. MICs for the quality-control strains were all within acceptable ranges for all drugs.

Relebactam alone had no antianaerobic activity, with MICs of >32 μg/ml for most of the organisms, with the exceptions of a very few strains of *D. desulfuricans*, *P. asaccharolytica*, *P. gingivalis*, *P. melaninogenica*, and *F. magna*. Relebactam had limited impact on the activity of imipenem as far as overall results for the broad spectrum of anaerobes tested. Our results for the *B. fragilis* group spp. are in accord with those reported by Snydman et al. (3), with MIC_{90}s occasionally differing from reported results by only one doubling dilution. Among the 13 strains of *B. fragilis* selected because of decreased susceptibility or resistance to imipenem (MICs > 8 μg/ml), there was no enhancement of imipenem activity with the addition of relebactam. Still, the imipenem-relebactam combination had general excellent anaerobic activity and would cover organisms present in the typical mixed infections of anaerobes and facultative organisms.

The other comparator drugs showed various results. Resistance to moxifloxacin and clindamycin was common among many species. *Veillonella* species (7 of 10, 70%), *Desulfovibrio*, and *Bilophila* species showed a high percentage of resistance to piperacillin-tazobactam (≥64 μg/ml). *Bacteroides* species (19 of 58, 33%), but not *B. fragilis*, showed decreased susceptibility and resistance to tigecycline (MIC_{90} ≥8 μg/ml). Resistance to metronidazole remained infrequent among Gram-negative species. While relebactam is an important beta-lactamase inhibitor for certain aerobic organisms, its enhanced activity against beta-lactamase-producing anaerobes was limited to *Bilophila* sp., two strains of *B. ovatus*, and four of *F. varium*, although no antagonism was detected for any of the species tested. The relebactam-imipenem combination had excellent overall activity against the anaerobes tested.

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