

In Vitro Activities of the New Semisynthetic Glycopeptide Telavancin (TD-6424), Vancomycin, Daptomycin, Linezolid, and Four Comparator Agents against Anaerobic Gram-Positive Species and *Corynebacterium* spp.

Ellie J. C. Goldstein,^{1,2*} Diane M. Citron,¹ C. Vreni Merriam,¹ Yumi A. Warren,¹
Kerin L. Tyrrell,¹ and Helen T. Fernandez¹

R. M. Alden Research Laboratory, Santa Monica, California 90404,¹ and UCLA School of Medicine,
Los Angeles, California 90073²

Received 16 October 2003/Returned for modification 21 January 2004/Accepted 9 February 2004

Telavancin is a new semisynthetic glycopeptide anti-infective with multiple mechanisms of action, including inhibition of bacterial membrane phospholipid synthesis and inhibition of bacterial cell wall synthesis. We determined the in vitro activities of telavancin, vancomycin, daptomycin, linezolid, quinupristin-dalfopristin, imipenem, piperacillin-tazobactam, and ampicillin against 268 clinical isolates of anaerobic gram-positive organisms and 31 *Corynebacterium* strains using agar dilution methods according to National Committee for Clinical Laboratory Standards procedures. Plates with daptomycin were supplemented with Ca²⁺ to 50 mg/liter. The MICs at which 90% of isolates tested were inhibited (MIC₉₀s) for telavancin and vancomycin were as follows: *Actinomyces* spp. (*n* = 45), 0.25 and 1 µg/ml, respectively; *Clostridium difficile* (*n* = 14), 0.25 and 1 µg/ml, respectively; *Clostridium ramosum* (*n* = 16), 1 and 4 µg/ml, respectively; *Clostridium innocuum* (*n* = 15), 4 and 16 µg/ml, respectively; *Clostridium clostridioforme* (*n* = 15), 8 and 1 µg/ml, respectively; *Eubacterium* group (*n* = 33), 0.25 and 2 µg/ml, respectively; *Lactobacillus* spp. (*n* = 26), 0.5 and 4 µg/ml, respectively; *Propionibacterium* spp. (*n* = 34), 0.125 and 0.5 µg/ml, respectively; *Peptostreptococcus* spp. (*n* = 52), 0.125 and 0.5 µg/ml, respectively; and *Corynebacterium* spp. (*n* = 31), 0.03 and 0.5 µg/ml, respectively. The activity of TD-6424 was similar to that of quinupristin-dalfopristin for most strains except *C. clostridioforme* and *Lactobacillus casei*, where quinupristin-dalfopristin was three- to fivefold more active. Daptomycin had decreased activity (MIC > 4 µg/ml) against 14 strains of *Actinomyces* spp. and all *C. ramosum*, *Eubacterium lentum*, and *Lactobacillus plantarum* strains. Linezolid showed decreased activity (MIC > 4 µg/ml) against *C. ramosum*, two strains of *C. difficile*, and 15 strains of *Lactobacillus* spp. Imipenem and piperacillin-tazobactam were active against >98% of strains. The MICs of ampicillin for eight *Clostridium* spp. and three strains of *L. casei* were >1 µg/ml. The MIC₉₀ of TD-6424 for all strains tested was ≤2 µg/ml. TD-6424 has potential for use against infections with gram-positive anaerobes and deserves further clinical evaluation.

The development of resistance in gram-positive organisms—including *Staphylococcus aureus* resistant to oxacillin and vancomycin (10, 11, 13) and linezolid (12) and vancomycin-resistant enterococci also resistant to linezolid (4)—has accentuated the need for new antimicrobial agents. Telavancin is a novel glycopeptide that is bactericidal and shows concentration-dependent killing against gram-positive aerobes, including vancomycin-resistant strains (9). Unlike vancomycin, TD-6424 has multiple synergistic mechanisms of action resulting in TD-6424's enhanced activity against aerobic gram-positive species (5a, 9). At the MIC, it has exhibited postantibiotic effects of up to 6 h against *S. aureus*, compared to 2 h for vancomycin (9). TD-6424 is currently in phase 2 trials for serious gram-positive infections.

Little has been published regarding the activity of telavancin against either unusual aerobic bacteria or anaerobes. In order to evaluate the potential efficacy of TD-6424 against a broad spectrum of aerobic and anaerobic gram-positive species, we

determined its in vitro activities against 299 recent aerobic and anaerobic clinical isolates.

MATERIALS AND METHODS

Strains were isolated from clinical specimens obtained from adult patients between 1996 and 2002 and identified by standard criteria (5, 6). Strains were consecutive isolates, except when needed to make at least 10 isolates per species. *Staphylococcus aureus* ATCC 29213 and *Eubacterium lentum* ATCC 43055 were tested simultaneously with the appropriate plates and environments. The numbers and species of clinical isolates tested are given in Table 1.

The following standard laboratory powders were provided by suppliers as indicated: TD-6424, Theravance Inc., South San Francisco, Calif.; vancomycin, Eli Lilly & Co., Indianapolis, Ind.; daptomycin, Cubist Pharmaceuticals, Lexington, Mass.; linezolid, Pharmacia, Kalamazoo, Mich.; quinupristin-dalfopristin, Aventis Pharmaceuticals, Somerset, N.J.; imipenem, Merck & Co., West Point, Pa.; piperacillin-tazobactam, Wyeth-Ayerst, Philadelphia, Pa.; and ampicillin, Sigma, St. Louis, Mo.

Susceptibility testing was performed according to the standards established by the National Committee for Clinical Laboratory Standards (7, 8), using an agar dilution method with Mueller-Hinton agar and an inoculum of 10⁴ CFU per spot for corynebacteria and brucella agar supplemented with hemin, vitamin K₁, and 5% laked sheep blood and an inoculum of 10⁵ CFU per spot for anaerobic species. Daptomycin was supplemented with Ca²⁺ (50 mg/liter) as suggested by the manufacturer.

* Corresponding author. Mailing address: R. M. Alden Research Laboratory, 2021 Santa Monica Blvd., Suite 740 East, Santa Monica, CA 90404. Phone: (310) 315-1511. Fax: (310) 315-3662. E-mail: EJCGMD@aol.com.

TABLE 1. In vitro activities of telavancin (TD-6424) against 271 recent clinical isolates of gram-positive anaerobes and corynebacteria

Antimicrobial	MIC ($\mu\text{g/ml}$) ^a			Antimicrobial	MIC ($\mu\text{g/ml}$) ^a		
	Range	50%	90%		Range	50%	90%
<i>Actinomyces israelii</i> (n = 13)				Vancomycin	0.5–0.5	0.5	0.5
Telavancin	0.125–0.25	0.25	0.25	Linezolid	2–2	2	2
Daptomycin	0.5–>32	2	4	Quinupristin-dalfopristin	0.125–0.5	0.25	0.5
Vancomycin	0.5–1	0.5	1	Imipenem	≤0.03–0.25	0.06	0.125
Linezolid	0.25–16	0.5	16	Piperacillin-tazobactam	≤.03–2	0.06	0.5
Quinupristin-dalfopristin	0.125–0.5	0.25	0.25	Ampicillin	≤0.03–0.06	≤0.03	0.06
Imipenem	≤0.03–0.25	≤0.03	0.125	<i>Clostridium ramosum</i> (n = 16)			
Piperacillin-tazobactam	≤0.03–4	≤0.03	4	Telavancin	0.25–8	0.5	1
Ampicillin	≤0.03–0.5	≤0.03	0.5	Daptomycin	8–>32	32	32
<i>Actinomyces meyeri-A. turicensis</i> group ^b (n = 12)				Vancomycin	1–8	4	4
Telavancin	0.125–0.25	0.125	0.25	Linezolid	4–8	8	8
Daptomycin	0.5–16	2	8	Quinupristin-dalfopristin	0.125–2	0.25	2
Vancomycin	0.25–1	0.5	0.5	Imipenem	0.125–2	0.25	0.5
Linezolid	0.125–1	0.5	0.5	Piperacillin-tazobactam	≤0.03–1	0.06	0.5
Quinupristin-dalfopristin	0.06–0.5	0.125	0.125	Ampicillin	≤0.03–1	0.06	0.25
Imipenem	≤0.03–0.125	0.125	0.125	<i>Eubacterium lentum</i> (n = 10)			
Piperacillin-tazobactam	≤0.03–2	0.5	1	Telavancin	0.125–0.25	0.25	0.25
Ampicillin	0.125–0.5	0.25	0.5	Daptomycin	1–32	16	32
<i>Actinomyces odontolyticus</i> (n = 10)				Vancomycin	0.5–1	1	1
Telavancin	0.125–0.25	0.25	0.25	Linezolid	0.5–2	2	2
Daptomycin	16–>32	16	32	Quinupristin-dalfopristin	0.125–0.5	0.25	0.5
Vancomycin	0.5–1	1	1	Imipenem	≤0.03–0.25	0.25	0.25
Linezolid	0.5–1	0.5	0.5	Piperacillin-tazobactam	≤0.03–32	16	16
Quinupristin-dalfopristin	0.125–0.5	0.25	0.25	Ampicillin	≤0.03–0.5	0.25	0.5
Imipenem	0.06–0.25	0.125	0.125	<i>Eubacterium limosum</i> (n = 10)			
Piperacillin-tazobactam	0.25–4	1	4	Telavancin	0.06–0.25	0.125	0.25
Ampicillin	0.06–0.5	0.125	0.5	Daptomycin	0.06–0.5	0.25	0.25
<i>Actinomyces viscosus</i> (n = 10)				Vancomycin	0.25–2	2	2
Telavancin	0.125–0.25	0.125	0.25	Linezolid	1–4	2	4
Daptomycin	0.5–8	4	8	Quinupristin-dalfopristin	0.125–2	0.25	1
Vancomycin	0.5–0.5	0.5	0.5	Imipenem	≤0.03–≤0.03	≤0.03	≤0.03
Linezolid	0.5–0.5	0.5	0.5	Piperacillin-tazobactam	≤0.03–2	≤0.03	0.25
Quinupristin-dalfopristin	0.06–0.5	0.25	0.25	Ampicillin	≤0.03–0.125	≤0.03	0.06
Imipenem	≤0.03–≤0.03	≤0.03	≤0.03	<i>Eubacterium group^c</i> (n = 13)			
Piperacillin-tazobactam	≤0.03–0.5	0.125	0.5	Telavancin	0.03–1	0.25	0.25
Ampicillin	≤0.03–0.06	0.06	0.06	Daptomycin	0.06–8	0.5	0.5
<i>Clostridium clostridioforme</i> (n = 15)				Vancomycin	0.25–4	1	2
Telavancin	0.25–8	1	8	Linezolid	0.5–2	2	2
Daptomycin	0.25–8	1	4	Quinupristin-dalfopristin	≤0.03–1	0.5	1
Vancomycin	0.25–>32	0.5	1	Imipenem	≤0.03–0.125	≤0.03	≤0.03
Linezolid	2–4	2	4	Piperacillin-tazobactam	≤0.03–0.5	≤0.03	0.5
Quinupristin-dalfopristin	0.125–8	0.5	4	Ampicillin	≤0.03–0.125	≤0.03	0.06
Imipenem	0.5–2	1	2	<i>Lactobacillus plantarum</i> (n = 10)			
Piperacillin-tazobactam	0.25–64	4	8	Telavancin	0.125–0.25	0.25	0.25
Ampicillin	0.5–>32	1	1	Daptomycin	8–>32	32	>32
<i>Clostridium difficile</i> (n = 14)				Vancomycin	0.5–4	4	4
Telavancin	0.125–0.5	0.25	0.25	Linezolid	4–8	8	8
Daptomycin	0.5–2	0.5	2	Quinupristin-dalfopristin	0.5–2	0.5	2
Vancomycin	0.25–2	0.5	1	Imipenem	0.125–0.5	0.125	0.25
Linezolid	2–8	2	8	Piperacillin-tazobactam	≤0.03–1	0.06	0.5
Quinupristin-dalfopristin	0.25–2	0.25	1	Ampicillin	≤0.03–0.5	≤0.03	0.25
Imipenem	2–32	4	8	<i>Lactobacillus casei</i> (n = 6)			
Piperacillin-tazobactam	4–16	8	16	Telavancin	32–>64	32	
Ampicillin	0.5–2	1	2	Daptomycin	1–4	2	
<i>Clostridium innocuum</i> (n = 15)				Vancomycin	>32–>32	>32	
Telavancin	2–4	4	4	Linezolid	4	4	
Daptomycin	2–8	4	8	Quinupristin-dalfopristin	0.5–1	1	
Vancomycin	8–16	16	16	Imipenem	1–16	2	
Linezolid	2–4	2	2	Piperacillin-tazobactam	1–8	4	
Quinupristin-dalfopristin	0.125–1	0.25	0.25	Ampicillin	0.5–4	1	
Imipenem	1–2	2	2	<i>Lactobacillus sp.^d</i> (n = 16)			
Piperacillin-tazobactam	0.5–4	1	2	Telavancin	≤0.015–2	0.25	1.25
Ampicillin	0.125–0.25	0.125	0.25	Daptomycin	0.25–>32	4	>32
<i>Clostridium perfringens</i> (n = 12)				Vancomycin	0.25–8	1	4
Telavancin	0.06–0.125	0.06	0.125	Linezolid	1–8	4	8
Daptomycin	0.25–1	1	1	Quinupristin-dalfopristin	0.125–4	0.25	1
				Imipenem	≤0.03–1	0.06	0.25

Continued on following page

TABLE 1—Continued

Antimicrobial	MIC ($\mu\text{g/ml}$) ^a			Antimicrobial	MIG ($\mu\text{g/ml}$) ^a		
	Range	50%	90%		Range	50%	90%
Piperacillin-tazobactam	≤ 0.03 –1	0.25	1	Daptomycin	0.25–4	0.5	1
Ampicillin	≤ 0.03 –1	0.125	0.5	Vancomycin	0.25–1	0.25	0.5
<i>Propionibacterium acnes</i> (n = 12)				Linezolid	0.5–2	1	2
Telavancin	0.06–0.125	0.125	0.125	Quinupristin-dalfopristin	0.25–0.5	0.25	0.5
Daptomycin	0.125–1	0.5	1	Imipenem	≤ 0.03 –0.125	≤ 0.03	0.125
Vancomycin	0.25–0.5	0.5	0.5	Piperacillin-tazobactam	≤ 0.03 –0.5	0.125	0.5
Linezolid	0.25–0.5	0.5	0.5	Ampicillin	≤ 0.03 –0.25	0.125	0.25
Quinupristin-dalfopristin	≤ 0.03 –0.5	0.125	0.125	<i>Micromonas micros</i> ^e (n = 10)			
Imipenem	≤ 0.03 – ≤ 0.03	≤ 0.03	≤ 0.03	Telavancin	0.06–0.125	0.06	0.125
Piperacillin-tazobactam	≤ 0.03 –0.5	0.125	0.5	Daptomycin	0.25–1	0.5	0.5
Ampicillin	≤ 0.03 –0.125	0.06	0.06	Vancomycin	0.25–0.5	0.5	0.5
<i>Propionibacterium avidum</i> (n = 12)				Linezolid	0.5–1	0.5	1
Telavancin	0.125–0.25	0.125	0.125	Quinupristin-dalfopristin	0.5–1	0.5	1
Daptomycin	1–2	2	2	Imipenem	≤ 0.03 –0.125	≤ 0.03	≤ 0.03
Vancomycin	0.5–0.5	0.5	0.5	Piperacillin-tazobactam	≤ 0.03 –0.25	≤ 0.03	≤ 0.03
Linezolid	0.5–1	0.5	0.5	Ampicillin	≤ 0.03 – ≤ 0.03	≤ 0.03	≤ 0.03
Quinupristin-dalfopristin	0.125–0.125	0.125	0.125	<i>Anaerococcus prevotii</i> ^e (n = 11)			
Imipenem	≤ 0.03 – ≤ 0.03	≤ 0.03	≤ 0.03	Telavancin	≤ 0.015 –0.5	0.03	0.06
Piperacillin-tazobactam	≤ 0.03 –1	0.5	1	Daptomycin	≤ 0.03 –16	0.06	0.125
Ampicillin	≤ 0.03 –0.125	0.125	0.125	Vancomycin	0.125–1	0.5	0.5
<i>Propionibacterium granulosum</i> (n = 10)				Linezolid	≤ 0.03 –2	0.5	1
Telavancin	0.06–0.125	0.06	0.125	Quinupristin-dalfopristin	≤ 0.03 –1	0.25	0.5
Daptomycin	0.125–1	0.5	1	Imipenem	≤ 0.03 –0.06	≤ 0.03	≤ 0.03
Vancomycin	0.5–1	0.5	1	Piperacillin-tazobactam	≤ 0.03 –0.125	≤ 0.03	0.06
Linezolid	0.25–0.5	0.25	0.25	Ampicillin	≤ 0.03 –0.125	≤ 0.03	0.06
Quinupristin-dalfopristin	0.06–0.125	0.125	0.125	<i>Corynebacterium amycolatum</i> (n = 10)			
Imipenem	≤ 0.03 –0.06	≤ 0.03	≤ 0.03	Telavancin	0.03–0.06	0.03	0.06
Piperacillin-tazobactam	≤ 0.03 –1	≤ 0.03	≤ 0.03	Daptomycin	≤ 0.03 –0.125	0.06	0.06
Ampicillin	≤ 0.03 –0.5	0.06	0.06	Vancomycin	0.25–0.5	0.5	0.5
<i>Peptostreptococcus anaerobius</i> (n = 10)				Linezolid	0.25–0.5	0.5	0.5
Telavancin	0.06–0.25	0.06	0.25	Quinupristin-dalfopristin	0.125–0.25	0.25	0.25
Daptomycin	0.25–4	0.25	0.5	Imipenem	≤ 0.03 –>32	0.125	>32
Vancomycin	0.25–0.5	0.25	0.5	Piperacillin-tazobactam	≤ 0.03 –>128	4	>128
Linezolid	0.5–8	0.5	8	Ampicillin	0.06–>32	2	>32
Quinupristin-dalfopristin	0.06–0.5	0.125	0.25	<i>Corynebacterium jeikeium</i> (n = 11)			
Imipenem	≤ 0.03 –0.06	≤ 0.03	0.06	Telavancin	0.03–0.06	0.06	0.06
Piperacillin-tazobactam	≤ 0.03 –1	0.25	0.25	Daptomycin	0.125–0.5	0.25	0.5
Ampicillin	≤ 0.03 –0.125	0.06	0.125	Vancomycin	0.5–0.5	0.5	0.5
<i>Peptoniphilus asaccharolyticus</i> ^e (n = 10)				Linezolid	0.5–0.5	0.5	0.5
Telavancin	0.03–0.06	0.03	0.06	Quinupristin-dalfopristin	0.25–1	0.25	0.5
Daptomycin	≤ 0.03 –0.25	≤ 0.03	≤ 0.03	Imipenem	1–>32	>32	>32
Vancomycin	0.06–0.5	0.125	0.125	Piperacillin-tazobactam	64–>128	>128	>128
Linezolid	0.5–1	0.5	1	Ampicillin	>32–>32	>32	>32
Quinupristin-dalfopristin	0.25–0.5	0.5	0.5	<i>Corynebacterium group</i> ^f (n = 10)			
Imipenem	≤ 0.03 – ≤ 0.03	≤ 0.03	≤ 0.03	Telavancin	≤ 0.015 –0.03	≤ 0.015	0.03
Piperacillin-tazobactam	≤ 0.03 –0.06	≤ 0.03	≤ 0.03	Daptomycin	≤ 0.03 –0.125	0.06	0.06
Ampicillin	≤ 0.03 –0.125	≤ 0.03	0.06	Vancomycin	0.125–0.5	0.25	0.5
<i>Finegoldia magna</i> ^e (n = 11)				Linezolid	0.125–0.5	0.25	0.5
Telavancin	0.03–0.25	0.06	0.06	Quinupristin-dalfopristin	0.125–2	0.5	0.5
				Imipenem	≤ 0.03 –>32	0.04	32
				Piperacillin-tazobactam	≤ 0.03 –>128	4	32
				Ampicillin	≤ 0.03 –>32	0.5	32

^a 50% and 90%, MIC₅₀ and MIC₉₀, respectively.

^b *A. meyeri* (n = 5) and *A. turicensis* (n = 7).

^c *E. contortum* (n = 2), *E. moniliforme* (n = 1), *E. tenue* (n = 2), *Pseudoramibacter alactolyticus* (n = 7), and *Eubacterium* sp., no good fit (n = 1).

^d Includes *L. acidophilus* (n = 2), *L. catenaforme* (n = 8), *L. gasserii* (n = 1), *L. jensenii* (n = 2), *L. leichmannii* (n = 1), *L. rhamnusus* (n = 1), and *L. uli* (n = 1).

^e Formerly *Peptostreptococcus*.

^f *C. pseudodiphtheriticum* (n = 3), *C. striatum* (n = 6), and *Brevibacterium* sp. (n = 1).

RESULTS AND DISCUSSION

The results of the study are shown in Table 1. Overall, 240 of 268 (90%) of anaerobic isolates and 31 of 31 (100%) of the corynebacterium isolates tested were inhibited by telavancin at concentrations of ≤ 1 $\mu\text{g/ml}$. Telavancin was typically at least

two- to fourfold more active than vancomycin against most strains, with the exception of *Clostridium clostridioforme* and *Lactobacillus casei* isolates. The activity of telavancin was similar to that of quinupristin-dalfopristin for most strains except against *C. clostridioforme* and *L. casei*, where quinupristin-dalfopristin was three- to fivefold more active. Daptomycin

had decreased activity (MIC > 4 µg/ml) against 14 strains of *Actinomyces* spp. and all *Clostridium ramosum*, *E. lentum*, and *Lactobacillus plantarum* strains. Linezolid showed decreased activity (MIC > 4 µg/ml) against *C. ramosum*, two strains of *Clostridium difficile*, and 15 strains of *Lactobacillus* spp. Imipenem and piperacillin-tazobactam were active against >98% of strains, while the MICs of ampicillin for eight *Clostridium* spp. and three strains of *L. casei* were >1 µg/ml.

All *Actinomyces* and *Eubacterium* isolates, including *Actinomyces israelii*, *Actinomyces meyeri*, *Actinomyces turicensis*, *Actinomyces odontolyticus*, *Actinomyces viscosus*, *E. lentum*, and *Eubacterium limosum* strains, were susceptible to telavancin at concentrations of ≤0.25 µg/ml. Its activity against clostridia was variable by species, with excellent in vitro activity against *Clostridium perfringens* (MIC at which 90% of isolates tested were inhibited [MIC₉₀], 0.125 µg/ml), *C. difficile* (MIC₉₀, 0.25 µg/ml), and *C. ramosum* (MIC₉₀, 1 µg/ml). Telavancin had limited activity against *C. clostridioforme* (MIC₉₀, 8 µg/ml), a gram-negative appearing species, and *C. innocuum* (MIC₉₀, 4 µg/ml) but had MICs similar to those of daptomycin and linezolid. All other gram-positive strains tested with the exception of two *Lactobacillus* species (one of eight *Lactobacillus cateniforme* strains and one *Lactobacillus leichmannii* strain) were susceptible to telavancin at concentrations of ≤0.25 µg/ml.

The classification of the genus *Peptostreptococcus* has recently undergone taxonomic changes in nomenclature (2). New species names include *Peptoniphilus asaccharolyticus*, *Finegoldia magna*, *Micromonas micros*, and *Anaerococcus prevotii*. Telavancin at concentrations of <0.5 µg/ml inhibited all “peptostreptococci.” *Corynebacterium* species, *Corynebacterium amycolatum*, and *Corynebacterium jeikeium* were inhibited by telavancin, the most active agent tested, at concentrations of <0.06 µg/ml. Daptomycin had similar activities against corynebacteria. *A. israelii*, *A. meyeri*, *A. turicensis*, *A. odontolyticus*, and *A. viscosus* strains that were resistant to daptomycin were very susceptible to telavancin, which was two- to fourfold more active than vancomycin.

Some *Lactobacillus* spp. have been associated with bacteremia and endocarditis for which therapy may be problematic; others have been associated with vaginal health, while depletion has been associated with an increased risk of urinary tract infections and bacterial vaginosis (1, 12, 14). In our study, many *Lactobacillus* species that were resistant to vancomycin, linezolid, and daptomycin were generally susceptible to telavancin at concentrations of ≤0.25 µg/ml. *L. casei* isolates were resistant to telavancin and vancomycin (MIC₅₀, 32 µg/ml) but were generally susceptible to daptomycin at concentrations of ≤2 µg/ml, quinupristin-dalfopristin at concentrations of 1 µg/ml, and linezolid at concentrations of 4 µg/ml. Limited activity against *Lactobacillus acidophilus* and *L. casei* could be viewed as a positive health factor, allowing maintenance of the normal vaginal flora.

Telavancin demonstrated potent activity (<1 µg/ml) against a broad spectrum of gram-positive anaerobes and unusual aerobes, including *Actinomyces* species, *Propionibacterium* species, the *Peptostreptococcus* group, and *Clostridium* species such as *C. perfringens* and *C. difficile* (but excluding *C. clostridioforme*). Telavancin was typically two- to fourfold more active than van-

comycin against most strains. Telavancin was less active than vancomycin against *C. clostridioforme*, a gram-negative species, but the MICs of telavancin were similar to those of daptomycin and linezolid. Its overall activity compared favorably with that of the other agents tested.

Telavancin was described as “one of the most promising molecules” (3) on the basis of its aerobic gram-positive activity. We found that telavancin also exhibited excellent in vitro activities against most of the anaerobic gram-positive and *Corynebacterium* strains tested, with 271 of 299 (91%) of all strains inhibited by telavancin at concentrations of ≤1 µg/ml. Telavancin warrants clinical evaluation against infections caused by anaerobic gram-positive bacteria and corynebacteria.

ACKNOWLEDGMENTS

We thank Judee H. K. Knight, Alice E. Goldstein, Kone Koniga, and Stephen Barriere for various forms of assistance.

This study was supported, in part, by a grant from Theravance Inc., South San Francisco, Calif.

REFERENCES

- Cadieux, P., J. Burton, A. W. Bruce, C. Y. Kang, and G. Reid. 2002. *Lactobacillus* strains and vaginal ecology. *JAMA* 287:1940–1941.
- Finegold, S. M., Y. Song, and C. Liu. 2002. Taxonomy: general comments and an update on the taxonomy of clostridia and anaerobic cocci. *Anaerobe* 8:283–285.
- Gigliante, C., and T. Meinel. 2002. The situation on antimicrobial agents and chemotherapy in 2002: highlights of the 42nd ICAAC. *Expert Opin. Ther. Targets* 6:691–697.
- Gonzales, R. D., P. C. Schreckenberger, M. B. Graham, S. Kelkar, K. DenBesten, and J. Quinn. 2001. Infections due to vancomycin-resistant *Enterococcus faecium* resistant to linezolid. *Lancet* 357:1179.
- Jousimies-Somer, H. R., P. Summanen, D. M. Citron, E. J. Baron, H. M. Wexler, and S. M. Finegold. 2002. *Wadsworth anaerobic bacteriology manual*, 6th ed. Star Publishing Co., Belmont, Calif.
- King, A., I. Phillips, and K. Kaniga. 2004. Comparative in vitro activity of telavancin (TD-6424), a rapidly bactericidal, concentration dependent, anti-infective with multiple mechanisms of action against gram-positive bacteria. *J. Antimicrob. Chemother.*, in press.
- Murray, P. R., E. J. Baron, J. H. Jorgensen, M. A. Pfaller, and R. H. Tenover. 2003. *Manual of clinical microbiology*, 8th ed., American Society for Microbiology, Washington, D.C.
- National Committee for Clinical Laboratory Standards. 2000. Method for dilution antimicrobial susceptibility testing for bacteria that grow aerobically. Approved standard, 5th ed. NCCLS publication no. M7–A5. National Committee for Clinical Laboratory Standards, Wayne, Pa.
- National Committee for Clinical Laboratory Standards. 2001. Methods for antimicrobial susceptibility testing of anaerobic bacteria, 5th ed. Approved standard. NCCLS publication no. M11–A5. National Committee for Clinical Laboratory Standards, Wayne, Pa.
- Pace, J. L., K. Krause, D. Johnston, D. Debabov, T. Wu, L. Farrington, D. L. Lane Higgins, B. Christensen, J. K. Judice, and K. Koniga. 2003. In vitro activity of TD-6424 against *Staphylococcus aureus*. *Antimicrob. Agents Chemother.* 47:3602–3604.
- Sievert, D. M., M. L. Boulton, G. Stoltman, D. Johnson, M. G. Stobierski, F. P. Downes, P. A. Somsel, J. Y. Rudnick, W. Brown, W. Hafeez, T. Lundstrom, E. Flanagan, J. Mitchell, and S. Chang. 2002. *Staphylococcus aureus* resistant to vancomycin—United States, 2002. *Morbidity and Mortality Weekly Report* 51:565–567.
- Tenover, F. C., J. W. Biddle, and M. V. Lancaster. 2001. Increasing resistance to vancomycin and other glycopeptides in *Staphylococcus aureus*. *Emerg. Infect. Dis.* 7:327–332.
- Tsioupras, S., H. S. Gold, G. Sakoulas, G. M. Eliopoulos, C. Wennerstein, L. Venkataraman, R. C. Moellering, Jr., and M. J. Ferraro. 2001. Linezolid resistance in a clinical isolate of *Staphylococcus aureus*. *Lancet* 358:207–208.
- Van Griethuysen, S., A. Van 't Veen, A. Buiting, T. Walsh, and J. Kluytmans. 2003. High percentage of methicillin-resistant *Staphylococcus aureus* isolates with reduced susceptibility to glycopeptides in The Netherlands. *Antimicrob. Agents Chemother.* 41:2487–2491.
- Weeks, J. C., H. Nelson, S. Gelber, D. Sargent, and G. Schroeder. 2002. Short-term quality-of-life outcomes following laparoscopic-assisted colectomy vs. open colectomy for colon cancer: a randomized trial. *JAMA* 287:321–328.