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In Vitro Activity of RU 64004, a New Ketolide Antibiotic, against Gram-Positive Bacteria

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The comparative in vitro activity of RU 64004 (also known as HMR 3004), a new ketolide antibiotic, was tested by agar dilution against approximately 500 gram-positive organisms, including multiply resistant enterococci, streptococci, and staphylococci. All streptococci were inhibited by ≤1 μg of RU 64004 per ml. The ketolide was more potent than other macrolides against erythromycin A-susceptible staphylococci and was generally more potent than clindamycin against erythromycin A-resistant strains susceptible to this agent. Clindamycin-resistant staphylococci (MIC, >128 μg/ml) proved resistant to the ketolide, but some erythromycin A- and clindamycin-resistant enterococci remained susceptible to RU 64004.

RU 64004 (also known as HMR 3004) is a ketolide derivative, which is a new chemical entity of the macrolide antibiotic class. This class of semisynthetic 14-membered-ring macrolides differs from that of erythromycin A by having a 3-keto group instead of an L-cladinose at position 3 on the erythronolide A ring (1). RU 64004 has shown activity against a variety of gram-positive organisms, including erythromycin A-resistant strains (2, 4, 5). Our study examined the in vitro activity of the ketolide against almost 500 clinical isolates of gram-positive bacteria, including macrolide- and multiply resistant enterococci, staphylococci, and streptococci. The activity of the ketolide was compared with those of other antibiotics which are active against gram-positive organisms, including erythromycin A, clarithromycin, roxithromycin, clindamycin, vancomycin, and ampicillin or oxacillin.

Bacterial strains used in this study had been referred to our collection from numerous sources over several years and were selected for study based upon specific resistance patterns. Standard antimicrobial reference powders were gifts from the following sources: RU 64004, erythromycin A, clarithromycin, and roxithromycin, Roussel Uclaf, Romainville, France; vancomycin, Eli Lilly & Co., Indianapolis, Ind.; and quinupristin-dalfopristin, Rhône-Poulenc Rorer, Collegeville, Pa. Clindamycin, ampicillin, and oxacillin were purchased from Sigma Chemical Co., St. Louis, Mo.

(This work was presented in part at the 36th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, La., 1996 [10].)

MICs were determined by an agar dilution technique (7) with Mueller-Hinton II agar (BBL Microbiology Systems, Cockeysville, Md.). This agar was supplemented with 5% defibrinated sheep blood when streptococci and diphtheroids were tested.

Inocula were prepared by suspending several bacterial colonies from blood agar plates in Mueller-Hinton broth (BBL) to a density of ca. 10^7 CFU/ml. Final inocula of ca. 10^4 CFU/ml were applied to plates with a 32-prong replicating device. Plates were examined for growth after 18 to 20 h of incubation in room air at 35°C, except as follows: 5% CO_2 atmosphere was used for incubation of lactobacilli, *Leuconostoc* spp., *Pediococcus* spp., *Streptococcus pneumoniae*, and diphtheroids, and plates with lactobacilli, *Leuconostoc* spp., and *Pediococcus* spp. were examined for growth after 24 h.

Killing studies were performed with each of two RU 64004-susceptible (MIC, 0.06 μg/ml) strains of *Enterococcus faecalis* and *Enterococcus faecium* at concentrations 4 and 10 times the MIC. The final inoculum in brain heart infusion broth (Difco Laboratories, Detroit, Mich.) was 10^5 CFU/ml. Samples were removed at 0, 4, and 24 h for colony counts, which were done in duplicate.

Results are shown in Table 1. All streptococci, including strains resistant to other macrolides, were inhibited by RU 64004 at concentrations of ≤1 μg/ml. Three isolates (two penicillin-resistant viridans group streptococci and one penicillin-resistant *S. pneumoniae*) were highly resistant to clindamycin (MIC, ≥128 μg/ml) as well; RU 64004 inhibited these isolates at concentrations of 0.03, 0.25, and 0.25 μg/ml. MICs of the ketolide exceeded 0.25 μg/ml for only 2 (penicillin-resistant *S. pneumoniae*) of 95 strains; these were resistant to the other three macrolides (MICs, >128 μg/ml) and demonstrated lower levels of resistance to clindamycin (MICs, 8 and 32 μg/ml). Against erythromycin A-susceptible streptococci, MICs of RU 64004 were generally equal to or two- to fourfold lower than those of clarithromycin.

The new ketolide was substantially more potent than erythromycin A against enterococci that were susceptible or intermediately susceptible to erythromycin A. All isolates of *E. faecalis* and *E. faecium* inhibited by erythromycin A at concentrations of ≤4 μg/ml were inhibited by RU 64004 at concentrations of ≤0.008 to 0.12 μg/ml. Probably because of the intrinsic resistance of enterococci to clindamycin (6), moderate resistance to clindamycin did not predict resistance to the ketolide. All but one strain of these species with clindamycin MICs of 8 to 64 μg/ml were inhibited by RU 64004 at 0.12 μg/ml or less. Higher-level resistance to both erythromycin A and clindamycin (MICs, >128 μg/ml) was encountered in 107 isolates of *E. faecium* and *E. faecalis* (excluding β-lactamase-producing strains). Against these strains, MICs of RU 64004 were ≥8 μg/ml for 47 isolates, 1 to 4 μg/ml for 47 strains, and ≤0.5 μg/ml for 13 isolates. Thus, high-level macrolide and clindamycin resistance predicted reduced susceptibility to the ketolide in some, but not all, enterococci. RU 64004 was the most active of the agents tested against other enterococcal

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TABLE 1. Comparative in vitro activity of RU 64004

Organism(s), relevant characteristic (*n*)	Antimicrobial	MIC (μg/ml)		
		Range	MIC_{50}	MIC_{90}
E. faecalis (20)	RU 64004	0.06–64	0.12	8
	Quinupristin-dalfopristin	2.0–32	8	16
	Clarithromycin	0.12–>128	4	>128
	Erythromycin A	0.5–>128	4	>128
	Roxithromycin	0.5–>128	16	>128
	Ampicillin	1.0–4	1	2
	Clindamycin	16–>128	32	>128
	Vancomycin	1.0–4	1	4
E. faecalis, high-level resistance to gentamicin (20)	RU 64004	0.03–>128	2	8
	Quinupristin-dalfopristin	8.0–64	8	16
	Clarithromycin	0.06–>128	>128	>128
	Erythromycin A	0.12–>128	>128	>128
	Roxithromycin	0.25–>128	>128	>128
	Ampicillin	1.0–4	2	4
	Clindamycin	32–>128	>128	>128
	Vancomycin	1.0–4	2	4
E. faecalis, β-lactamase producing (10)	RU 64004	<0.008–16	0.03	4
	Quinupristin-dalfopristin	4.0–32	8	32
	Clarithromycin	2–>128	128	>128
	Erythromycin A	4–>128	>128	>128
	Roxithromycin	8–>128	128	>128
	Ampicillin	1.0–2	1	2
	Clindamycin	8–>128	>128	>128
	Vancomycin	0.5–1	0.5	1
E. faecalis, VanA (10)	RU 64004	0.015–0.5	0.25	0.5
	Quinupristin-dalfopristin	8	8	8
	Clarithromycin	2–>128	>128	>128
	Erythromycin A	8–>128	>128	>128
	Roxithromycin	16–>128	>128	>128
	Ampicillin	1.0–2	1	2
	Clindamycin	32–>128	>128	>128
	Vancomycin	128–>128	>128	>128
E. faecalis, VanB (21)	RU 64004	0.015–16	8	16
	Quinupristin-dalfopristin	4.0–32	16	32
	Clarithromycin	2.0–>128	>128	>128
	Erythromycin A	2–>128	>128	>128
	Roxithromycin	4–>128	>128	>128
	Ampicillin	1.0–32	1	2
	Clindamycin	8–>128	>128	>128
	Vancomycin	8–>128	>128	>128
E. faecium (30)	RU 64004	0.015–16	4	16
	Quinupristin-dalfopristin	0.25–4	1	2
	Clarithromycin	0.12–>128	>128	>128
	Erythromycin A	0.5–>128	>128	>128
	Roxithromycin	0.5–>128	>128	>128
	Ampicillin	0.5–>128	128	>128
	Clindamycin	0.06–>128	128	>128
	Vancomycin	0.5–8	1	1
E. faecium, high-level resistance to gentamicin (10)	RU 64004	4.0–8	8	8
	Quinupristin-dalfopristin	0.5–2	1	2
	Clarithromycin	>128	>128	>128
	Erythromycin A	>128	>128	>128
	Roxithromycin	>128	>128	>128
	Ampicillin	64–128	128	128
	Clindamycin	>128	>128	>128
	Vancomycin	0.5–2	0.5	1
E. faecium, VanA (21)	RU 64004	0.015–8	4	8
	Quinupristin-dalfopristin	0.5–8	1	2
	Clarithromycin	0.5–>128	>128	>128
	Erythromycin A	0.5–>128	>128	>128

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TABLE 1—*Continued*

Organism(s), relevant characteristic (*n*)	Antimicrobial	MIC (μg/ml)		
		Range	MIC_{50}	MIC_{90}
	Roxithromycin	1–>128	>128	>128
	Ampicillin	1–>128	128	>128
	Clindamycin	8–>128	>128	>128
	Vancomycin	>128	>128	>128
E. faecium, VanB (19)	RU 64004	<0.008–16	2	16
	Quinupristin-dalfopristin	0.25–4	0.5	1
	Clarithromycin	1–>128	>128	>128
	Erythromycin A	1–>128	>128	>128
	Roxithromycin	4–>128	>128	>128
	Ampicillin	32–128	64	128
	Clindamycin	0.12–>128	>128	>128
	Vancomycin	8–>128	64	>128
Enterococcus avium (12)	RU 64004	<0.008–0.5	0.03	0.06
	Quinupristin-dalfopristin	1.0–4	2	2
	Clarithromycin	0.03–>128	0.06	128
	Erythromycin A	0.03–>128	0.25	>128
	Roxithromycin	0.03–>128	0.25	128
	Ampicillin	0.5–1	0.5	1
	Clindamycin	1–>128	4	>128
	Vancomycin	0.25–1	0.5	0.5
Enterococcus casseliflavus (10)	RU 64004	0.03–0.06	0.06	0.06
	Quinupristin-dalfopristin	2.0–4	4	4
	Clarithromycin	2.0–16	4	8
	Erythromycin A	2.0–16	4	8
	Roxithromycin	8–>128	16	128
	Ampicillin	0.5–1	0.5	1
	Clindamycin	8.0–32	16	16
	Vancomycin	0.5–8	4	8
E. raffinosus (11)	RU 64004	<0.008–>128	0.03	32
	Quinupristin-dalfopristin	1–8.0	4	4
	Clarithromycin	0.03–>128	0.06	>128
	Erythromycin A	0.06–>128	0.25	>128
	Roxithromycin	0.015–>128	0.25	>128
	Ampicillin	2–>128	16	128
	Clindamycin	2–>128	8	>128
	Vancomycin	0.5–>128	0.5	>128
Enterococcus gallinarum (10)	RU 64004	<0.008	<0.008	<0.008
	Quinupristin-dalfopristin	1.0–2	1	2
	Clarithromycin	0.06–1	0.25	0.5
	Erythromycin A	0.12–2	0.5	1
	Roxithromycin	0.12–2	1	2
	Ampicillin	0.25–1	1	1
	Clindamycin	8.0–16	16	16
	Vancomycin	0.5–8	4	8
Erysipelothrix spp. (3)	RU 64004	0.06		
	Quinupristin-dalfopristin	1		
	Clarithromycin	0.12		
	Erythromycin A	0.25		
	Roxithromycin	0.5		
	Ampicillin	0.12		
	Clindamycin	0.25		
	Vancomycin	64		
Pediococcus spp. (5)	RU 64004	0.015–0.03		
	Quinupristin-dalfopristin	0.5–1		
	Clarithromycin	0.06		
	Erythromycin A	0.12–0.25		
	Roxithromycin	0.12–0.25		
	Ampicillin	2.0–4.0		
	Clindamycin	0.015–0.03		
	Vancomycin	>128		

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TABLE 1—*Continued*

Organism(s), relevant characteristic (*n*)	Antimicrobial	MIC (μg/ml)		
		Range	MIC_{50}	MIC_{90}
Leuconostoc spp. (15)	RU 64004	0.015–0.03	0.03	0.03
	Quinupristin-dalfopristin	0.25–1	1	1
	Clarithromycin	0.03–0.12	0.06	0.12
	Erythromycin A	0.12–1	0.25	0.25
	Roxithromycin	0.12–0.5	0.25	0.5
	Ampicillin	0.5–4	0.5	1
	Clindamycin	0.015–0.5	0.06	0.25
	Vancomycin	>128	>128	>128
Lactobacillus spp. (10)	RU 64004	0.015–0.03	0.015	0.03
	Quinupristin-dalfopristin	0.25–2	1	2
	Clarithromycin	0.03–0.06	0.06	0.06
	Erythromycin A	0.12–0.25	0.25	0.25
	Roxithromycin	0.12–0.5	0.25	0.25
	Ampicillin	0.25–8	1	4
	Clindamycin	0.03–0.25	0.12	0.25
	Vancomycin	>128	>128	>128
Streptococcus, group A (20)	RU 64004	0.015–0.25	0.03	0.03
	Quinupristin-dalfopristin	0.5–2	0.5	0.5
	Clarithromycin	0.03–8	0.06	0.06
	Erythromycin A	0.06–8	0.06	0.12
	Roxithromycin	0.03–16	0.06	0.06
	Ampicillin	0.015–0.06	0.03	0.06
	Clindamycin	0.03–0.12	0.12	0.12
	Vancomycin	0.5–2	0.5	2
Streptococcus, group B (10)	RU 64004	0.015–0.03	0.03	0.03
	Quinupristin-dalfopristin	1	1	1
	Clarithromycin	0.06	0.06	0.06
	Erythromycin A	0.03–0.06	0.06	0.06
	Roxithromycin	0.03–0.06	0.06	0.06
	Ampicillin	0.12–0.25	0.12	0.25
	Clindamycin	0.06–0.25	0.12	0.12
	Vancomycin	0.25–1	0.25	1
Streptococcus, groups C and G (10)	RU 64004	0.03–0.06	0.03	0.03
	Quinupristin-dalfopristin	1	2	2
	Clarithromycin	0.03–0.06	0.06	0.06
	Erythromycin A	0.06–0.12	0.12	0.12
	Roxithromycin	0.03–0.06	0.06	0.06
	Ampicillin	0.015–0.12	0.03	0.12
	Clindamycin	0.12–0.5	0.25	0.25
	Vancomycin	0.5–1	0.5	1
Viridans group streptococci, penicillin susceptible (10)	RU 64004	0.008–0.06	0.015	0.03
	Quinupristin-dalfopristin	0.5–4	2	4
	Clarithromycin	0.008–1	0.03	0.06
	Erythromycin A	0.008–2	0.03	0.06
	Roxithromycin	<0.004–2	0.03	0.06
	Ampicillin	0.06–0.25	0.12	0.25
	Clindamycin	0.008–0.12	0.06	0.06
	Vancomycin	0.5–1	1	1
Viridans group streptococci, penicillin resistant (10)	RU 64004	0.015–0.25	0.015	0.06
	Quinupristin-dalfopristin	1.0–4	2	2
	Clarithromycin	0.03–>128	1	64
	Erythromycin A	0.03–>128	4	64
	Roxithromycin	0.015–>128	1	128
	Ampicillin	0.25–32	8	16
	Clindamycin	0.03–>128	0.06	128
	Vancomycin	0.5–1	1	1
Corynebacteria, JK diphtheroids (20)	RU 64004	0.06–0.5	0.12	0.25
	Quinupristin-dalfopristin	0.5–2	0.5	2
	Clarithromycin	0.12–>128	4	16
	Erythromycin A	0.12–>128	8	>128

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TABLE 1—*Continued*

Organism(s), relevant characteristic (*n*)	Antimicrobial	MIC (μg/ml)		
		Range	MIC_{50}	MIC_{90}
	Roxithromycin	0.25–>128	32	>128
	Ampicillin	1–>128	>128	>128
	Clindamycin	1–>128	>128	>128
	Vancomycin	0.5–1	0.5	0.5
L. monocytogenes (20)	RU 64004	0.015–0.06	0.03	0.06
	Quinupristin-dalfopristin	0.5–2	1	1
	Clarithromycin	0.06–0.25	0.12	0.12
	Erythromycin A	0.12–0.5	0.25	0.25
	Roxithromycin	0.25–1	0.5	0.5
	Ampicillin	0.06–1	0.5	1
	Clindamycin	1.0–4	4	4
	Vancomycin	0.25–1	0.5	1
S. pneumoniae, penicillin susceptible (21)	RU 64004	0.03–0.06	0.06	0.06
	Quinupristin-dalfopristin	1.0–2	1	2
	Clarithromycin	0.06–0.12	0.12	0.12
	Erythromycin A	0.06–0.25	0.12	0.25
	Roxithromycin	0.12–0.5	0.25	0.5
	Ampicillin	0.03–0.12	0.06	0.06
	Clindamycin	0.03–0.25	0.12	0.12
	Vancomycin	0.25–0.5	0.25	0.5
S. pneumoniae, penicillin resistant (14)	RU 64004	0.03–1	0.06	1
	Quinupristin-dalfopristin	0.5–2	1	2
	Clarithromycin	0.06–>128	0.12	>128
	Erythromycin A	0.12–>128	0.25	>128
	Roxithromycin	0.25–>128	0.5	>128
	Ampicillin	0.12–4	4	4
	Clindamycin	0.06–>128	0.12	32
	Vancomycin	0.25–0.5	0.25	0.5
S. aureus, oxacillin susceptible (39)	RU 64004	<0.008–>128	0.03	0.06
	Quinupristin-dalfopristin	0.25–0.5	0.5	0.5
	Clarithromycin	0.06–>128	0.25	>128
	Erythromycin A	0.12–>128	0.5	>128
	Roxithromycin	0.25–>128	0.5	>128
	Oxacillin	0.12–1	0.5	1
	Clindamycin	0.03–>128	0.12	0.12
	Vancomycin	0.5–1	0.5	1
S. aureus, oxacillin resistant (25)	RU 64004	>128	>128	>128
	Quinupristin-dalfopristin	0.25–1	1	1
	Clarithromycin	>128	>128	>128
	Erythromycin A	>128	>128	>128
	Roxithromycin	>128	>128	>128
	Oxacillin	16–>128	>128	>128
	Clindamycin	>128	>128	>128
	Vancomycin	0.5–2	1	1
Coagulase-negative staphylococci, oxacillin susceptible (33)	RU 64004	0.015–>128	0.06	>128
	Quinupristin-dalfopristin	0.06–2	0.5	1
	Clarithromycin	0.06–>128	0.25	>128
	Erythromycin A	0.12–>128	0.5	>128
	Roxithromycin	0.25–>128	1	>128
	Oxacillin	0.12–2	0.25	2
	Clindamycin	0.06–>128	0.12	>128
	Vancomycin	0.5–2	1	2
Coagulase-negative staphylococci, oxacillin resistant (26)	RU 64004	0.03–>128	>128	>128
	Quinupristin-dalfopristin	0.12–1	0.5	1
	Clarithromycin	0.12–>128	>128	>128
	Erythromycin A	0.25–>128	>128	>128
	Roxithromycin	0.25–>128	>128	>128
	Oxacillin	8–>128	128	>128
	Clindamycin	0.03–>128	>128	>128
	Vancomycin	0.5–2	2	2

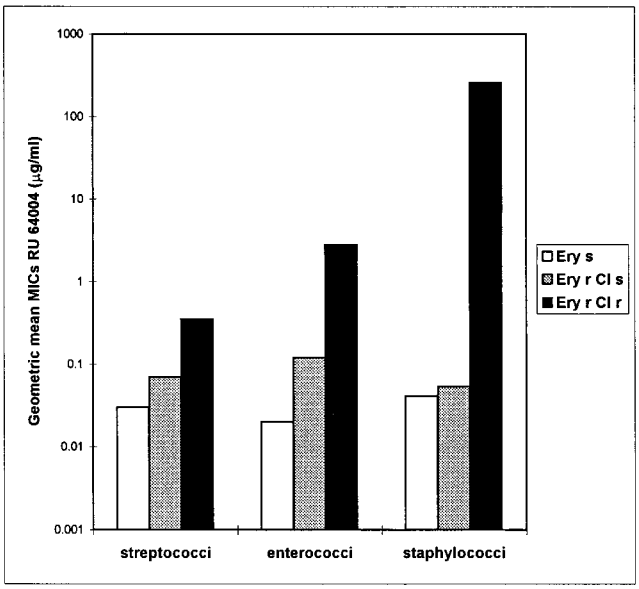

FIG. 1. Geometric mean MICs of RU 64004 for streptococci, enterococci, and staphylococci based upon patterns of resistance to erythromycin A (Ery) and clindamycin (Cl). r, resistant; s, sensitive.

species except *Enterococcus raffinosus*, against which quinupristin-dalfopristin was more active based on a comparison of MICs at which 90% of the isolates are inhibited (MIC_{90}s).

RU 64004 was the most active macrolide tested against staphylococci. All strains of *Staphylococcus aureus* that were susceptible to clindamycin were inhibited by the ketolide at ≤0.06 μg/ml, irrespective of resistance to the other macrolides. All but one strain of clindamycin-susceptible coagulase-negative staphylococci were inhibited by ≤0.25 μg of RU 64004 per ml. The single isolate inhibited by RU 64004 at 1 μg/ml was susceptible to clindamycin (1 μg/ml) and intermediately susceptible to erythromycin A (MIC, 2 μg/ml). Staphylococci that demonstrated resistance to both erythromycin A and clindamycin were also resistant to the ketolide (MIC, ≥128 μg/ml) as shown in Fig. 1.

Based on a comparison of MIC_{90}s, the new macrolide was the most potent agent tested against *Leuconostoc* spp., *Lactobacillus* spp., *Corynebacterium* spp., and *Listeria monocytogenes*, inhibiting all isolates of these species at concentrations of ≤0.5 μg/ml. MICs of RU 64004 and erythromycin A for control strains in these studies are shown in Table 2.

Time-kill studies demonstrated bacteriostatic activity of RU 64004 against both enterococcal strains, with killing at ≤1 $\log_{10}$ CFU/ml at 4 h and at ≤2 $\log_{10}$ CFU/ml at 24 h at both concentrations tested.

The results of this study support data presented in several recent abstracts which described activity of RU 64004 against erythromycin A-resistant as well as erythromycin A-susceptible streptococci (2, 4, 5). High levels of activity of the ketolide (MICs, ≤0.25 μg/ml) against the three isolates resistant to high levels of erythromycin A and clindamycin (MICs, >128 μg/ml) suggest not only that RU 64004 is a poor inducer of resistance in streptococci, as deduced from its activity against erythromycin A-resistant, clindamycin-susceptible strains, but also that the new agent is active against constitutively resistant strains as well. A murine septicemia model confirmed the generally comparable activities in vivo of RU 64004 against erythromycin A-susceptible *Streptococcus pyogenes* and against *S. pneumoniae* with inducible or constitutive resistance to erythromycin A (3).

In contrast, while RU 64004 was highly active against erythromycin A-susceptible staphylococci and against isolates with presumptive macrolide-lincosamide-streptogramin B-inducible resistance (erythromycin A resistant and clindamycin susceptible), the ketolide was inactive against erythromycin A- and clindamycin-resistant strains as described previously (2). RU 64004 has also been reported to be a poor inducer of *msrA*-mediated macrolide efflux in staphylococci (8). Although we did not investigate resistance mechanisms in this study, RU 64004 was highly active against several strains of coagulase-negative staphylococci which were susceptible to clindamycin and which showed resistance to erythromycin A, with MICs of 32 to 128 μg/ml, which is consistent with *msrA* resistance patterns (9).

The activity in vitro of RU 64004 against enterococci appeared to be more complex. While strains of *E. faecium* and *E. faecalis* that were susceptible or intermediately susceptible to erythromycin A were highly susceptible to the ketolide (MICs, ≤0.12 μg/ml), strains with high levels of resistance to clindamycin and erythromycin A were often but not always inhibited by ≤4 μg of the ketolide per ml. Because of the intrinsic resistance of most enterococci to lincosamides, it is possible that the macrolide resistance in some of these isolates was actually inducible rather than constitutive despite a phenotype that might suggest the latter resistance pattern. Studies with enterococcal strains with known mechanisms of resistance would be needed to further address this issue. Because almost half of the isolates of *E. faecium* and *E. faecalis* resistant to both erythromycin A and clindamycin at >128 μg/ml were

TABLE 2. MICs of RU 64004 and erythromycin A for ATCC control strains tested on Mueller-Hinton II agar alone or with supplementation

Organism	Medium supplement	CO_2	MIC (μg/ml)[a]	
			RU 64004	Erythromycin A[b]
S. aureus ATCC 29213	None	−	0.03_5, 0.06_7, and 0.12_1	0.12_1, 0.25_9, and 0.5_3
	5% sheep blood	−	0.06_2	0.12_1 and 0.25_1
	None	+	0.12_1	1_1
	5% sheep blood	+	0.12_2	0.25_1 and 0.5_1
Escherichia coli ATCC 25922	None	−	8_5, 16_6, and 32_2	64_{11}, 128_1, and $>128_1$
	5% sheep blood	−	16_2	64_2
	None	+	32_1	$>128_1$
	5% sheep blood	+	16_1 and 32_1	128_1 and $>128_1$
S. pneumoniae ATCC 49619	5% sheep blood	+	0.06_1	0.12_1

[a] Subscripts indicate the number of runs for which the MIC was observed.
[b] Reference ranges of erythromycin A are as follows: 0.12 to 0.5 μg/ml for *S. aureus* ATCC 29213 and 0.03 to 0.12 μg/ml for *S. pneumoniae* ATCC 49619 (by microdilution broth testing).

inhibited by 1 to 4 μg of RU 64004 per ml, concentrations falling into the intermediately susceptible range for erythromycin A (7), further studies with in vivo models would be useful to determine whether such isolates are truly susceptible to the new compound. This question is of special relevance given the high rates of macrolide resistance among current isolates of vancomycin-resistant enterococci and the limited therapeutic options available for treatment of infections due to such organisms.

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