Available online at www.sciencedirect.com

SCIENCE DIRECT

Diagnostic Microbiology and Infectious Disease 53 (2005) 307–310

DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE

www.elsevier.com/locate/diagmicrobio

Antimicrobial susceptibility studies

Dalbavancin activity against selected populations of antimicrobial-resistant Gram-positive pathogens

Jennifer M. Streit[a], Helio S. Sader[a,*], Thomas R. Fritsche[a], Ronald N. Jones[a,b]

[a]*The JONES Group/JMI Laboratories, North Liberty, IA 52317, USA*
[b]*Tufts University School of Medicine, Boston, MA 02111, USA*

Received 10 January 2005; accepted 6 March 2005

Abstract

Dalbavancin, a dimethylaminepropyl amide derivative of the lipoglycopeptide A40926, was tested against 375 antimicrobial-resistant Gram-positive pathogens collected worldwide during 2001–2003. The isolates were tested by reference and Clinical Laboratory Standards Institute broth microdilution susceptibility methods, and dalbavancin was compared with over 20 other antimicrobials. Vancomycin resistance determinants among enterococci were identified using PCR primer sets for *vanA* and *vanB*. Dalbavancin was generally more potent than vancomycin or teicoplanin. Dalbavancin was highly active against penicillin- and ceftriaxone-resistant *Streptococcus pneumoniae* strains (MIC_{90}, ≤ 0.016 μg/mL). Dalbavancin was also very active against teicoplanin-nonsusceptible coagulase-negative staphylococci (CoNS; MIC range, 0.03–0.25 μg/mL), but dalbavancin MIC results were slightly elevated compared with wild type strains. Dalbavancin inhibited *vanB* enterococci (MIC range, 0.03–0.12 μg/mL) and was active against other resistant, non-*vanA* enterococcal species. However, *vanA* enterococcal strains were not as susceptible to dalbavancin (MIC_{50}, 16 μg/mL). In summary, dalbavancin was very active against a wide spectrum of resistant Gram-positive isolates and demonstrated greater potency than vancomycin or teicoplanin.
© 2005 Elsevier Inc. All rights reserved.

Keywords: Dalbavancin; Gram-positive pathogens; Vancomycin resistance; *Staphylococcus aureus*; *Streptococcus pneumoniae*; Enterococcus; Coagulase-negative staphylococci

1. Introduction

Novel and increasing resistance mechanisms among Gram-positive pathogens are presenting challenges to existing antimicrobials (Chang et al., 2003; Meka and Gold, 2004). Oxacillin and glycopeptide resistance in staphylococci and glycopeptide resistance in enterococci have accelerated the need for the development of new antimicrobial agents to treat these Gram-positive infections. Dalbavancin is a second-generation lipoglycopeptide, synthesized by dimethylaminepropyl amide derivatization of the natural glycopeptide A40926, which recently completed phase III clinical trials in skin and skin structure infections. Results of Phase II studies in skin and skin structure infections and catheter-related bacteremia were recently published (Raad et al., 2005; Seltzer et al., 2003). Dalbavancin has exhibited a wide spectrum of activity against Gram-positive bacteria, including methicillin-resistant staphylococci and multidrug-resistant organisms (Candiani et al., 1999; Jones et al., 2001; Lefort et al., 2004).

Dalbavancin's mechanism of action consists of inhibiting cell-wall peptidoglycan cross-linking, similar to that of other glycopeptides, but the agent is not completely cross-resistant to vancomycin (Raad et al., 2005). Dalbavancin has been shown to be more potent than vancomycin and teicoplanin and is active against *vanB* and *vanC* vancomycin-resistant enterococcal strains (Candiani et al., 1999; Jones et al., 2001). Dalbavancin has also been reported to be active against *Staphylococcus* spp. strains with decreased susceptibility to glycopeptides (Lefort et al., 2004). The extended half-life of dalbavancin (approximately 8 days) (Leighton et al., 2004) permits once-weekly dosing, making it a more advantageous therapeutic option than other similar acting glycopeptides (Candiani et al., 1999; Lefort et al., 2004; Seltzer et al., 2003). In the present study, we expanded previous studies (Gales et al., 2005; Streit et al., 2004) by evaluating the in vitro activity of dalbavancin against a contemporary worldwide collection of multidrug-resistant Gram-positive strains displaying the most problematic resistance phenotypes.

* Corresponding author. Tel.: +1-319-665-3370; fax: +1-319-665-3371.
E-mail address: helio-sader@jmilabs.com (H.S. Sader).

0732-8893/$ – see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.diagmicrobio.2005.03.004

2. Materials and methods

2.1. Bacterial isolates

A total of 375 Gram-positive isolates with antimicrobial-resistant phenotypes were selected from a worldwide collection (2001–2003). The resistant subsets included *Staphylococcus aureus* (4 quinupristin/dalfopristin-resistant strains; 10 vancomycin-intermediate strains; 3 linezolid-resistant strains), coagulase-negative staphylococci (CoNS; 3 strains, vancomycin MIC at 4 μg/mL; 4 quinupristin/dalfopristin-resistant strains; 15 teicoplanin-nonsusceptible strains, 1 linezolid-resistant strain), *Enterococcus faecium* (49 strains vancomycin-resistant; 33 strains quinupristin/dalfopristin-resistant; 6 strains linezolid-resistant), *Enterococcus faecalis* (20 strains vancomycin-resistant; 3 strains linezolid-resistant), *Streptococcus pneumoniae* (202 strains penicillin-resistant; 16 strains ceftriaxone-resistant), and viridans-group streptococci (5 strains penicillin-resistant).

Table 1
Activity of dalbavancin and selected antimicrobial agents tested against resistant Gram-positive strains collected worldwide

Organism (no. tested)/ antimicrobial agent	MIC (μg/mL)			Percent susceptible
	Range	50%	90%	
Streptococcus pneumoniae, penicillin-resistant (202)				
Dalbavancin	≤0.016–0.03	≤0.016	≤0.016	–[a]
Amoxicillin/clavulanate	≤2–16	2	8	79.2
Ceftriaxone	≤0.25–8	1	1	91.6
Clindamycin	≤0.06–>8	≤0.06	>8	64.0
Erythromycin	≤0.25–>32	4	>32	25.6
Linezolid	≤0.25–2	1	1	100.0
Quinupristin/dalfopristin	0.12–1	0.25	0.5	100.0
Vancomycin	0.12–0.5	0.25	0.5	100.0
E. faecium, quinupristin/dalfopristin-resistant (vancomycin-susceptible; 29)				
Dalbavancin	≤0.016–0.12	0.06	0.12	–[a]
Ampicillin	≤2–>16	4	>16	44.8
Chloramphenicol	≤2–>16	8	16	82.8
Doxycycline	≤0.5–>4	50.5	>4	69.0
Linezolid	1–2	2	2	100.0
E. faecium, vancomycin-resistant (*vanA*-positive strains; 44)				
Dalbavancin	0.03–>32	16	32	–[a]
Ampicillin	2–>32	>32	>32	2.0
Chloramphenicol	≤2–>16	8	8	95.4
Quinupristin/dalfopristin	0.25–8	1	1	97.7
Linezolid	0.5–>16	2	2	97.7
Teicoplanin	>16	>16	>16	0.0
E. faecalis, vancomycin-resistant (*vanA*; 14)				
Dalbavancin	0.12–>32	32	32	–[a]
Ampicillin	4–32	8	16	71.4
Chloramphenicol	4–>16	8	>16	57.1
Quinupristin/dalfopristin	≥8	>8	>8	0.0
Linezolid	0.5–2	1	2	100.0
Teicoplanin	>16	>16	>16	0.0
Enterococci, vancomycin-resistant (*vanB*; 11)[b]				
Dalbavancin	0.03–0.12	0.03	0.12	–[a]
Ampicillin	2–>32	>32	>32	45.4
Chloramphenicol	4–>16	8	16	72.7
Quinupristin/dalfopristin	0.25–>8	4	8	45.5
Linezolid	1–2	1	2	100.0
Teicoplanin	≤2	≤2	≤2	100.0
Coagulase-negative staphylococci, teicoplanin-resistant (15)				
Dalbavancin	0.03–0.25	0.12	0.25	–[a]
Chloramphenicol	≤2–>16	4	>16	66.7
Linezolid	0.5–1	1	1	100.0
Oxacillin	0.12–>8	>8	>8	13.3
Quinupristin/dalfopristin	0.12–1	0.25	1	100.0
Vancomycin	1–4	2	2	100.0

[a] No interpretive breakpoint has been established by CLSI (2005).
[b] Includes *E. faecium* (5 strains) and *E. faecalis* (6 strains).

Table 2
Dalbavancin activity tested against other resistant subsets of Gram-positive cocci

Organism (no. tested)	MIC (μg/mL)		
	Range	50%	90%
Streptococcus pneumoniae, ceftriaxone-resistant (16)	≤0.016–0.03	≤0.016	≤0.016
viridans-group streptococci, penicillin-resistant (5)[a]	≤0.016–0.03	≤0.016	–
Enterococci, vancomycin-resistant (*vanA*; 58)[b]	0.03–>32	16	32
Enterococci, vancomycin-resistant (*vanB*; 11)[c]	0.03–0.12	0.03	0.12
Staphylococci, quinupristin/dalfopristin-resistant[d] (8)	0.03–0.06	0.06	–
Staphylococci, vancomycin-intermediate (10)	0.06–2	0.06	1
CoNS, vancomycin MIC at 4 μg/mL (3)	0.12–0.5	0.12	–
Gram-positive cocci, linezolid-resistant (14)[e]	≤0.016–>32	0.06	32

[a] Includes *Streptococcus mitis* (1 strain), *Streptococcus oralis* (1 strain), and *Streptococcus viridans* or α-hemolytic streptococci (3 strains were not identified to species level).
[b] Includes *E. faecalis* (14 strains) and *E. faecium* (44 strains).
[c] Includes *E. faecalis* (6 strains) and *E. faecium* (5 strains).
[d] Includes *Staphylococcus aureus* (4 strains), *Staphylococcus xylosis* (1 strain), *Staphylococcus epidermidis* (1 strain), *Staphylococcus sciuri* (1 strain), and CoNS (1 strain was not identified to species level).
[e] Includes *Staphylococcus aureus* (3 strains) and *E. faecalis* (3 strains), *Staphylococcus epidermidis* (1 strain), *Staphylococcus oralis* (1 strain), and *E. faecium* (6 strains).

2.2. Susceptibility testing

All tests were performed by reference Clinical and Laboratory Standards Institute (CLSI; formerly, National Committee for Clinical Laboratory Standards [NCCLS]) methods (M7-A6) using Mueller-Hinton broth, supplemented with 2–5% lysed horse blood for testing streptococci (CLSI, 2005; NCCLS, 2003). Validated dry-form Sensititre® panels for susceptibility testing were manufactured by TREK Diagnostics (Cleveland, OH) (Jones et al., 2004). Dalbavancin (Vicuron Pharmaceuticals, King of Prussia, PA) was compared with over 20 other antimicrobial agents, including the 13 drugs reported here: vancomycin, teicoplanin, linezolid, ampicillin, oxacillin, amoxicillin/clavulanate, ceftriaxone, clindamycin, erythromycin, quinupristin/dalfopristin, penicillin, chloramphenicol, and doxy-

Download English Version:

https://daneshyari.com/en/article/9263272

Download Persian Version:

https://daneshyari.com/article/9263272

Daneshyari.com