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Antimicrobial Activity of Dalbavancin against Gram-Positive Bacteria Isolated from Patients with Bone and Joint Infections from the United States (US) and Europe (2016–2020): Results from the International Dalbavancin Evaluation of Activity (IDEA) Program

Helio S. Sader, Leonard R. Duncan, Mariana Castanheira, Rodrigo E. Mendes

JMI Laboratories, North Liberty, Iowa, USA

CONCLUSIONS

S. aureus isolates were the most frequent pathogens responsible for BJI in this study population; a total of 35.5% of the US *S. aureus* isolates were methicillin-resistant, which precludes administering commonly used antimicrobial therapies, cefazolin and oxacillin, for such cases.

Dalbavancin demonstrated potent *in vitro* activity against common Gram-positive isolates causing BJI in US and EU medical centers (2016–2020).

This *in vitro* characteristic, along with prolonged half-life and convenient administration, make dalbavancin a promising candidate for treating BJI, including osteomyelitis, caused by Gram-positive cocci.

RESULTS

- *S. aureus* (n=503; 63.0%) was the most common pathogen associated with BJI, followed by β-hemolytic steptococci (BHS; n=140; 17.5%), coagulase-negative staphylococci (CoNS; n=71; 8.9%), *Enterococcus* spp. (n=57; 7.1%), viridans group streptococci (VHS; n=22; 2.8%), and *S. pneumoniae* (n=5; 0.6%; Figure 1).
- All *S. aureus* isolates were susceptible to dalbavancin ($MIC_{50/90}$, 0.03/0.03 mg/L), linezolid ($MIC_{50/90}$, 1/2 mg/L), teicoplanin ($MIC_{50/90}$, ≤0.5/1 mg/L), vancomycin ($MIC_{50/90}$, 1/1 mg/L), and daptomycin (DAPTO; $MIC_{50/90}$, 0.25/0.0.5 mg/L; Table 1 and Figure 2).
- Dalbavancin was 8- to 16-fold more potent than daptomycin and 32- to 64-fold more potent than linezolid, vancomycin, and teicoplanin against *S. aureus* (Table 1).
- Oxacillin resistance (MRSA) rates among *S. aureus* were 35.5% and 15.4% in the US and EU, respectively (Table 1).
- Ceftaroline was active against 98.6% of *S. aureus* ($MIC_{50/90}$, 0.25/1 mg/L; Table 1) and 94.7% of MRSA ($MIC_{50/90}$, 1/1 mg/L) isolates (data not shown).
- Doxycycline and levofloxacin were active against 97.0% and 76.5% of *S. aureus*, respectively (Table 1).
- Among CoNS, (54.9% oxacillin-resistant), dalbavancin ($MIC_{50/90}$, 0.03/0.03 mg/L; highest MIC, 0.12 mg/L) was the most potent agent, followed by daptomycin ($MIC_{50/90}$, 0.25/0.5 mg/L), ceftaroline ($MIC_{50/90}$, 0.25/0.5 mg/L), and linezolid ($MIC_{50/90}$, 0.5/1 mg/L; Table 1).
- The highest dalbavancin MIC value among BHS and VGS was 0.12 mg/L (MIC_{90}, 0.03 mg/L for both groups; Table 1 and Figure 2).
- Vancomycin was active against 82.5% of *Enterococcus* spp. (Table 1) and dalbavancin inhibited all vancomycin-susceptible isolates at ≤0.06 mg/L (data not shown).

Table 1. Activity of dalbavancin and comparator antimicrobial agents when tested against Gram-positive organisms isolated from patients with bone and joint infections from US medical centers (2016–2020)

Organism / Antimicrobial agent (no.)	All regions combined				% Susceptible [a] (no.)	
	MIC_{50}	MIC_{90}	%S[a]	%R[a]	US	EU
S. aureus (503)					(276)	(227)
Dalbavancin	0.03	0.03	100.0		100.0	100.0
Daptomycin	0.25	0.5	100.0		100.0	100.0
Teicoplanin	≤0.5	1	100.0	0.0	100.0	100.0
Vancomycin	1	1	100.0	0.0	100.0	100.0
Linezolid	1	2	100.0	0.0	100.0	100.0
Oxacillin	0.5	>2	73.6	23.4	64.5	84.6
Ceftaroline	0.25	1	98.4	0.0	98.9	97.8
Clindamycin	≤0.25	≤0.25	91.7	8.2	87.7	96.5
Levofloxacin	0.25	>4	76.3	23.3	69.6	84.6
Doxycycline	≤0.06	≤0.5	97.0	0.6	95.7	98.7
TMP-SMX[e]	≤0.5	≤0.5	98.6	1.4	97.8	99.6
CoNS (71)					(51)	(20)
Dalbavancin	0.03	0.03	[100.0][b]		[100.0][b]	[100.0][b]
Daptomycin	0.25	0.5	100.0		100.0	100.0
Teicoplanin	1	4	100.0	0.0	100.0	100.0
Vancomycin	1	2	100.0	0.0	100.0	100.0
Linezolid	0.5	1	98.6	1.4	100.0	95.0
Oxacillin	2	>2	26.8	73.2	29.4	20.0
Clindamycin	≤0.25	>2	77.5	19.7	78.4	75.0
Levofloxacin	0.25	>4	56.3	39.4	54.9	60.0
Doxycycline	≤0.5	1	100.0	0.0	100.0	100.0
TMP-SMX[e]	≤0.5	4	76.1	23.9	70.6	90.0
Enterococcus spp. (57)					(46)	(11)
Dalbavancin	0.06	>2	[82.5][c]		[78.3][c]	[100.0][c]
Daptomycin	1	2	[100.0][d]		[100.0][d]	[100.0][d]
Teicoplanin	≤0.5	>16	82.5	15.8	78.3	100.0
Vancomycin	1	>16	82.5	17.5	78.3	100.0
Linezolid	1	2	100.0	0.0	100.0	100.0
Ampicillin	1	>16	84.2	15.8	82.6	90.9
Levofloxacin	1	>4	64.9	35.1	60.9	81.8
Doxycycline	4	8	63.6	0.0	60.0	100.0
β-haemolytic streptococci (140)					(86)	(54)
Dalbavancin	0.015	≤0.03	100.0		100.0	100.0
Daptomycin	≤0.06	0.25	100.0		100.0	100.0
Vancomycin	0.25	0.5	100.0		100.0	100.0
Linezolid	1	2	100.0		100.0	100.0
Penicillin	0.015	0.06	100.0		100.0	100.0
Ceftriaxone	0.03	0.06	100.0		100.0	100.0
Clindamycin	≤0.25	>2	76.4	23.6	72.1	83.3
Levofloxacin	0.5	1	97.9	0.7	98.8	96.3
Tetracycline	4	>4	46.4	50.0	39.5	57.4
Viridans group streptococci (22)					(14)	(8)
Dalbavancin	0.008	0.03	[100.0][b]		[100.0]	[100.0]
Daptomycin	0.25	0.5	100.0		100.0	100.0
Vancomycin	0.5	1	100.0		100.0	100.0
Linezolid	1	2	100.0		100.0	100.0
Penicillin	0.03	1	72.7	4.6	64.3	87.5
Ceftriaxone	0.12	1	95.5	0.0	92.9	100.0
Clindamycin	≤0.25	>2	77.3	22.7	85.7	62.5
Levofloxacin	1	2	90.9	9.1	92.9	87.5
Tetracycline	1	>8	63.6	31.8	71.4	50.0

[a] Criteria as published by CLSI (2021).
[b] Percentage inhibited at ≤0.12 mg/L.
[c] CLSI and US FDA breakpoints were applied for all *Enterococcus* spp. isolates, but were only approved for vancomycin-susceptible *E. faecalis*.
[d] Percentage inhibited at ≤2 mg/L (CLSI breakpoint for *Enterococcus* spp. other than *E. faecium*).
[e] TMP-SMX, trimethoprim-sulfamethoxazole.

Figure 1. Frequency of Gram-positive organisms isolated from patients with bone and joint infections in US medical centers

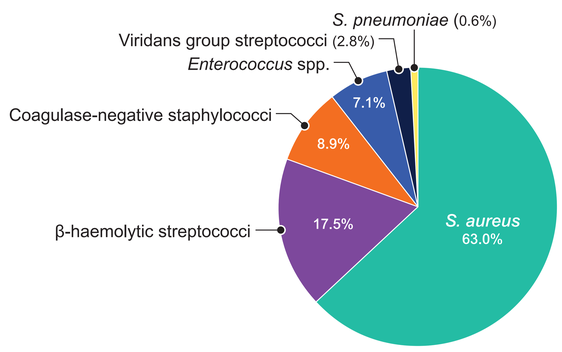
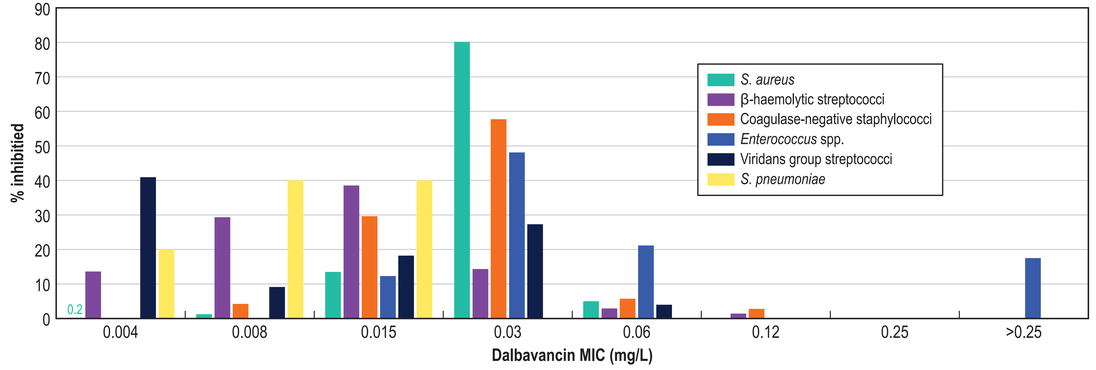


Figure 2. Summary of dalbavancin activity against Gram-positive organisms isolated from patients with bone and joint infections from US and European medical centers



INTRODUCTION

- Bone and joint infection (BJI) include a series of disorders, including septic arthritis, osteomyelitis, and prosthetic joint infections.
- Dalbavancin belongs to the lipoglycopeptide class of antimicrobial agents that interrupt bacterial cell wall synthesis, resulting in bacterial death.
- Dalbavancin was approved in the United States (2014) and Europe (2015) to treat adults with acute bacterial skin and skin structure infections.
- Dalbavancin allows for convenient parenteral administration, which can be a single dose of 1500 mg or a dose of 1000 mg followed by a dose of 500 mg a week later to treat ABSSSI.
- We evaluated the *in vitro* activity and potency of dalbavancin against a contemporary (2016–2020) collection of Gram-positive bacteria responsible for BJI, including osteomyelitis, recovered from adult and pediatric patients in United States (US) and European (EU) medical centers.

METHODS

Bacterial isolates

- A total of 798 organisms were evaluated, including 475 US isolates and 323 EU isolates.
- Isolates were collected from 62 US and 28 EU medical centers in 2016–2020.
- Isolates were determined to be clinically significant based on local guidelines and submitted to a central monitoring laboratory (JMI Laboratories, North Liberty, Iowa, USA) as part of the International Dalbavancin Evaluation of Activity (IDEA) surveillance program.
- Isolates were identified by the participating laboratory and confirmed by the reference monitoring laboratory by standard algorithms and MALDI–TOF–MS (Bruker Daltonics, Bremen, Germany).

METHODS

Antimicrobial susceptibility testing

- Isolates were tested for susceptibility by broth microdilution following guidelines in the CLSI M07–A10 (2018) document, with testing performed using reference 96-well panels manufactured by JMI Laboratories.
- The dalbavancin breakpoints approved by CLSI and the US FDA for the indicated species were applied (i.e., ≤0.25 mg/mL). CLSI breakpoint criteria were used for comparators.

DISCLOSURES

Contact Information

Helio S. Sader, MD, PhD
JMI Laboratories
345 Beaver Kreek Centre, Suite A
North Liberty, IA 52317
Phone: (319) 665-3370
Fax: (319) 665-3371
Email: helio-sader@jmilabs.com

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