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

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CONCLUSIONS

Dalbavancin exhibited potent *in vitro* activity against a large collection of gram-positive isolates recovered from patients with BSI, including IE, in US and European medical centers.

Dalbavancin MIC values were 8- to 16-fold lower than those of daptomycin and 32-fold lower than those of vancomycin when tested against *S. aureus*.

These results support further investigations to determine the role of dalbavancin in the treatment of infective endocarditis.

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References

1. Boucher HW, Wilcox M, Talbot GH, et al. (2014). Once-weekly dalbavancin versus daily conventional therapy for skin infection. *N Engl J Med* 370: 2169-2179.
2. Clinical and Laboratory Standards Institute (2018). *M07-A11: Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard—tenth edition*. Wayne, PA: CLSI.
3. Dalvance® (2021). Available at https://www.allergan.com/assets/pdf/dalvance_pi.
4. Garnock-Jones KP (2017). Single-dose dalbavancin: A review in acute bacterial skin and skin structure infections. *Drugs* 77: 75-83.
5. Gatti M, Andreoni M, Pea F, Viale P. (2021). Real-world use of dalbavancin in the era of empowerment of outpatient antimicrobial treatment: a careful appraisal beyond approved indications focusing on unmet clinical needs. *Drug Des Devel Ther* 15:3349-3378.

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INTRODUCTION

- Managing infective endocarditis (IE) requires aggressive, prolonged use of antimicrobials or a combination of antibiotics and surgery to control the infection source.
- Dalbavancin belongs to the lipoglycopeptide class of antimicrobial agents that act by interrupting bacterial cell wall synthesis, resulting in bacterial death.
- Dalbavancin was approved in the United States (US; 2014) and Europe (EU; 2015) to treat adults with acute bacterial skin and skin structure infection (ABSSSI).
- Dalbavancin allows for convenient parenteral administration for treating ABSSSI either in a single dose of 1500 mg or a dose of 1000 mg followed by 500 mg a week later.
- Dalbavancin is not licensed to treat IE, but it is potentially valuable for treating infections due to highly resistant gram-positive cocci (GPC).
- We evaluated dalbavancin *in vitro* activity and potency when tested against a large collection of GPC isolates responsible for IE.

MATERIALS AND METHODS

Bacterial Isolates

- A total of 16,164 GPC were consecutively collected from patients with bloodstream infections (BSIs) in the US (8,807 isolates from 79 hospitals) and EU (7,357 isolates from 42 hospitals in 20 countries) from 2016 to 2020 via the International Dalbavancin Evaluation of Activity (IDEA) Program.
- The collection includes 323 organisms recovered from patients with IE, 106 from the US and 217 from the EU.
- Isolates were determined to be clinically significant based on local guidelines and were submitted to a central monitoring laboratory (JMI Laboratories, North Liberty, Iowa, USA).
- Participating laboratories initially identified isolates and JMI confirmed these bacterial identifications by standard algorithms supported by matrix-assisted laser desorption ionization-time of flight mass spectrometry (Bruker Daltonics, Bremen, Germany).

Antimicrobial Susceptibility Testing

- Isolates were tested for susceptibility by broth microdilution following guidelines in the CLSI M07 (2018).
- The dalbavancin breakpoints approved by the US FDA and CLSI for indicated species were applied (i.e., ≤0.25 mg/L) and breakpoint criteria for comparator agents were from CLSI M100 (2021).
- Quality assurance was performed by concurrently testing CLSI-recommended quality control reference strains (*S. aureus* ATCC 29213, *E. faecalis* ATCC 29212, and *Streptococcus pneumoniae* ATCC 49619).

Table 1. Antimicrobial activity of dalbavancin and comparator agents tested against gram-positive bacteria isolated from patients with infective endocarditis (SENTRY Program, 2007–2017)

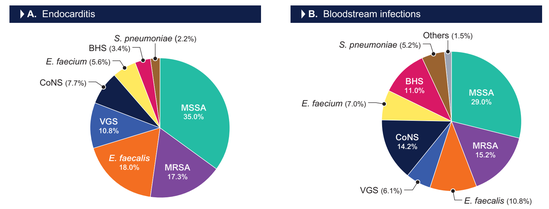
Organism / antimicrobial agent	MIC_{50} (mg/L)	MIC_{90} (mg/L)	% Susceptible[a] (no. tested) US	EU	US + EU
S. aureus			(60)	(109)	(169)
Dalbavancin	0.03	0.03	100.0	100.0	100.0
Daptomycin	0.25	0.5	100.0	100.0	100.0
Teicoplanin	≤0.5	≤0.5	100.0	100.0	100.0
Vancomycin	1	1	100.0	100.0	100.0
Oxacillin	0.5	>2	56.7	72.5	66.9
Ceftaroline	0.25	1	97.6	100.0	99.0
Levofloxacin	0.25	>4	66.7	71.6	69.8
Linezolid	1	2	100.0	100.0	100.0
Methicillin-resistant *S. aureus*			(26)	(30)	(56)
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	≤0.5	100.0	100.0	100.0
Vancomycin	1	1	100.0	100.0	100.0
Ceftaroline	0.5	1	94.1	100.0	96.6
Levofloxacin	>4	>4	30.8	23.3	26.8
Linezolid	1	2	100.0	100.0	100.0
E. faecalis			(18)	(40)	(58)
Dalbavancin	0.03	0.06	100.0[b]	97.5[b]	98.3[b]
Daptomycin	0.5	1	100.0	97.5	98.3
Teicoplanin	≤0.5	≤0.5	100.0	97.5	98.3
Vancomycin	1	2	100.0	97.5	98.3
Levofloxacin	2	>4	94.4	55.0	67.2
Linezolid	1	2	100.0	100.0	100.0
Ampicillin	1	2	100.0	100.0	100.0
Viridans group streptococci[c]			(10)	(25)	(35)
Dalbavancin	0.03	0.06	100.0[d]	100.0[d]	100.0[d]
Daptomycin	0.25	1	100.0	96.0	96.6
Vancomycin	0.5	1	100.0	100.0	100.0
Levofloxacin	1	2	100.0	96.0	97.1
Linezolid	1	1	100.0	100.0	100.0
Ceftriaxone	0.12	2	70.0	96.0	88.6
Penicillin	0.06	4	60.0	92.0	82.9
Coagulase-negative staphylococci (46)[e]			(7)	(18)	(25)
Dalbavancin	0.03	0.12	[100.0][f]	[100.0][f]	[100.0][f]
Daptomycin	0.25	0.5	100.0	100.0	100.0
Teicoplanin	2	8	100.0	94.4	96.0
Vancomycin	2	2	100.0	100.0	100.0
Oxacillin	>2	>2	14.3	27.8	24.0
Ceftaroline	0.25	0.5	[100.0][g]	[100.0][g]	[100.0][g]
Levofloxacin	4	>4	42.9	38.9	40.0
Linezolid	1	1	100.0	100.0	100.0
E. faecium (35)			(6)	(12)	(18)
Dalbavancin	0.06	>2	16.7[h]	100.0[h]	72.2[h]
Daptomycin	1	2	[100.0][h]	[100.0][h]	[100.0][h]
Teicoplanin	1	>16	16.7	100.0	72.2
Vancomycin	1	>16	16.7	91.7	66.7
Levofloxacin	>4	>4	16.7	8.3	5.6
Linezolid	1	2	100.0	100.0	100.0
Ampicillin	>16	>16	16.7	16.7	16.7

[a] Criteria as published by CLSI 2021.
[b] A breakpoint of ≤0.25 was applied to all *E. faecalis* and *E. faecium*, but this breakpoint only was approved for vancomycin-susceptible *E. faecalis*.
[c] Organisms included *Streptococcus anginosus* (2), *S. bovis* group (1), *S. constellatus* (1), *S. cristatus* (1), *S. gallolyticus* (10), *S. gordonii* (2), *S. mitis* group (4), *S. mutans* (2), *S. oralis* (5), *S. parasanguinis* (1), and *S. sanguinis* (6).
[d] A breakpoint of ≤0.25 mg/L was applied to all viridans group streptococci, but this breakpoint only was approved for *S. pyogenes*, *S. agalactiae*, *S. dysgalactiae*, and *S. anginosus* group.
[e] Organisms included *Staphylococcus cohnii* (1), *S. epidermidis* (13), *S. haemolyticus* (4), *S. hominis* (4), *S. lugdunensis* (1), *S. pettenkoferi* (1), and *S. warneri* (1).
[f] Values in brackets indicate the percentage inhibited at the susceptible breakpoint for *S. aureus* (≤0.25 mg/L).
[g] Values in brackets indicate the percentage inhibited at the susceptible breakpoint for *S. aureus* (≤1 mg/L).
[h] Values in brackets indicate the percentage inhibited at the susceptible breakpoint for *Enterococcus* spp. other than *E. faecium* (≤2 mg/L).

RESULTS

- *S. aureus* (52.3%) was the most common pathogen associated with IE, followed by *E. faecalis* (18.0%), viridans group streptococci (VGS; 10.8%), coagulase-negative staphylococci (CoNS; 7.7%), and *E. faecium* (5.6%; Figure 1).
- Among BSI isolates, the most common organisms were *S. aureus* (45.0%), β-hemolytic streptococci (BHS; 11.0%), and *E. faecalis* (10.8%; Figure 1).
- Dalbavancin was highly active against GPC isolates from patients with IE; all organisms, except vancomycin-resistant enterococci, were inhibited at ≤0.12 mg/L of dalbavancin (Figure 2).
- Dalbavancin exhibited similar activity against methicillin-resistant (MRSA) and methicillin-susceptible *S. aureus* (MSSA) causing IE (Figure 3), against MRSA causing IE in the US and EU (Figure 4), and against MRSA from IE and BSI (Figure 5).
- Dalbavancin (MIC_{50} and MIC_{90}, 0.03 mg/L) and daptomycin ($MIC_{50/90}$, 0.25/0.5 mg/L) showed complete activity (100.0%S) against *S. aureus*, but dalbavancin MIC values were 8- to 16-fold lower than those of daptomycin (Table 1).
- Against *S. aureus* from IE, teicoplanin, vancomycin, and linezolid were also active against 100.0% of isolates and ceftaroline was active against 99.0% of isolates (Table 1). Vancomycin inhibited 98.8% of isolates at ≤1 mg/L (data not shown).
- MRSA rates were 43.3% (US) and 27.5% (EU) among *S. aureus* from IE (n=169; Table 1), and 41.1% (US) and 24.0% (EU) among *S. aureus* from BSI (n=7,279; data not shown).
- All *E. faecalis* isolates from IE were susceptible to ampicillin and linezolid, whereas 98.3% were susceptible to dalbavancin ($MIC_{50/90}$, 0.03/0.06 mg/L), daptomycin ($MIC_{50/90}$, 0.5/1 mg/L), vancomycin ($MIC_{50/90}$, 1/2 mg/L), and teicoplanin ($MIC_{50/90}$, ≤0.5/≤0.5 mg/L; Table 1).
- Against *E. faecalis*, dalbavancin MIC values were 16-fold lower than daptomycin and vancomycin (Table 1).
- Among *E. faecalis* from BSI (n=1,748), susceptibility rates for dalbavancin, daptomycin, and vancomycin were 98.0%, 99.5%, and 97.7%, respectively (data not shown).
- All VGS isolates from IE (n=35) were susceptible to dalbavancin (all inhibited at ≤0.12 mg/L), vancomycin, and linezolid; 96.6% of VGS were susceptible to daptomycin (Table 1).
- All CoNS from IE were susceptible to dalbavancin ($MIC_{50/90}$, 0.03/0.12 mg/L; highest MIC, 0.12 mg/L), daptomycin ($MIC_{50/90}$, 0.25/0.5 mg/L), vancomycin ($MIC_{50/90}$, 2/2 mg/L), and linezolid ($MIC_{50/90}$, 1/1 mg/L; Table 1).
- Among *E. faecium* isolates from IE, 66.7% of isolates were susceptible to vancomycin (16.7% in the US and 91.7% in EU; Table 1) and 72.2% were inhibited at ≤0.12 mg/L of dalbavancin (Figure 2).
- BHS was susceptible (highest MIC, 0.03 mg/L) to most antimicrobial agents tested (Table 1 and Figure 2).

Figure 1. Frequency of gram-positive bacteria isolated from patients with infective endocarditis in US and European medical centers (2016–2020)



Abbreviations: MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; VGS, viridans group streptococci; CoNS, coagulase-negative staphylococci; BHS, β-hemolytic streptococci

Figure 2. Dalbavancin activity against organisms isolated from patients with infective endocarditis stratified by species

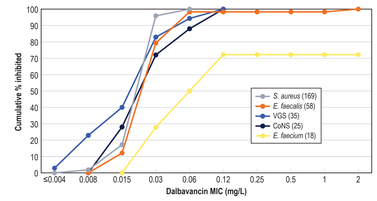


Figure 3. Dalbavancin activity against methicillin-susceptible (MSSA) and methicillin-resistant (MRSA) *S. aureus* from patients with IE

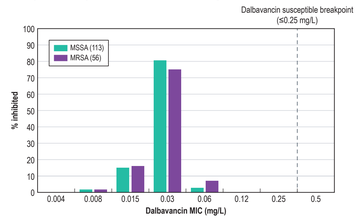


Figure 4. Dalbavancin activity against methicillin-resistant (MRSA) *S. aureus* from patients with IE stratified by geographic region

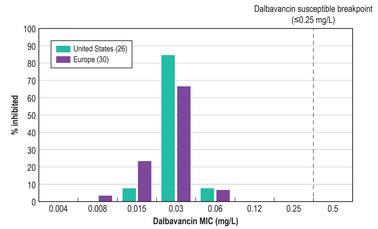


Figure 5. Comparative dalbavancin activity against methicillin-resistant (MRSA) *S. aureus* from patients with IE and BSI