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Update on the *In Vitro* Activity of Dalbavancin against Indicated Species (*Staphylococcus aureus, Enterococcus faecalis*, β-Hemolytic Streptococci, and *Streptococcus anginosus* Group) Collected from United States Hospitals in 2017–2018

Helio S. Sader, Jennifer M. Streit, S.J. Ryan Arends, Rodrigo E. Mendes, Robert K. Flamm

JMI Laboratories, North Liberty, Iowa, USA

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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INTRODUCTION

- Dalbavancin belongs to the lipoglycopeptide class of antimicrobial agents that act by interrupting bacterial cell wall synthesis, resulting in bacterial death
- Dalbavancin allows for very convenient parenteral administration, which can be a single dose of 1500 mg or a dose of 1000 mg followed by 500 mg a week later for treating acute bacterial skin and skin structure infections (ABSSSIs)
- Dalbavancin was approved in the United States (2014) and Europe (2015) to treat adults with ABSSSI caused by
  - Methicillin-resistant (MRSA) and -susceptible *Staphylococcus aureus* (MSSA)
  - *Streptococcus pyogenes*
  - *Streptococcus agalactiae*
  - *Streptococcus dysgalactiae*
  - *Streptococcus anginosus* group
  - Vancomycin-susceptible *Enterococcus faecalis*
- This study updates dalbavancin activity against contemporary isolates of these species/groups

MATERIALS AND METHODS

Bacterial isolates

- A total of 12,138 unique isolates of the indicated species were consecutively collected from 70 United States (US) medical centers in 2017–2018
- 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 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 (S) by broth microdilution following guidelines in the CLSI M07 document (2018)
- The dalbavancin breakpoints approved by the US Food and Drug Administration (FDA) and CLSI for indicated species were applied (i.e., ≤0.25 mg/L), and breakpoint criteria for comparator agents were those from CLSI (2019)
- 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)

RESULTS

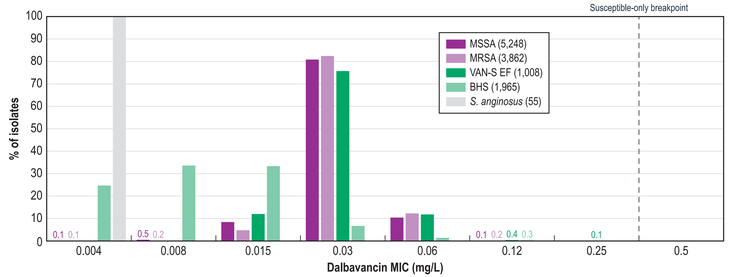
- Dalbavancin $MIC_{50/90}$ values were 0.03/0.06 mg/L against *S. aureus* (100.0%S), including MRSA isolates (Table 1 and Figure 1)
- Dalbavancin was 16- to 32-fold more active than vancomycin ($MIC_{50/90}$, 1/1 mg/L) and 4- to 8-fold more active than daptomycin ($MIC_{50/90}$, 0.25/0.25 mg/L) against MRSA (Table 1)
- Susceptibility rates for ceftaroline and trimethoprim-sulfamethoxazole (TMP-SMX) were 94.0% and 96.9%, respectively, among MRSA (Table 1)
- All (100.0%) vancomycin-susceptible *E. faecalis* isolates were dalbavancin-susceptible, with the highest dalbavancin MIC value of 0.25 mg/L (1,007/1,008 [99.9%] inhibited at ≤0.12 mg/L; Table 1 and Figure 1)
- Dalbavancin MIC values for vancomycin-susceptible *E. faecalis* isolates were 32-fold and 16-fold lower than those of vancomycin ($MIC_{50/90}$, 1/2 mg/L) and daptomycin ($MIC_{50/90}$, 0.5/1 mg/L), respectively (Table 1)
- Dalbavancin was highly active against β-hemolytic streptococci ($MIC_{50/90}$, 0.008/0.015 mg/L), with MIC_{90} values 16- to 32-fold lower than daptomycin (MIC_{90}, 0.25 mg/L) and vancomycin (MIC_{90}, 0.5 mg/L), respectively (Table 1)
- β-hemolytic streptococci susceptibility rates for tetracycline, clindamycin, and levofloxacin were 55.6%, 82.4%, and 99.2%, respectively (Table 1)
- All *S. anginosus* group isolates were inhibited at ≤0.004 mg/L of dalbavancin (Table 1 and Figure 1)
- *S. anginosus* group susceptibility rates for penicillin, clindamycin, and tetracycline were 100.0%, 83.6%, and 60.0%, respectively (Table 1)

Table 1 Activity of dalbavancin and comparator antimicrobial agents against clinical isolates of indicated species collected from US medical centers (2017–2018)

Antimicrobial agent / organism (no. tested)	MIC_{50}	MIC_{90}	CLSI[a] %S	CLSI[a] %R
Methicillin-susceptible *S. aureus* (5,248)				
Dalbavancin	0.03	0.06	100.0	
Telavancin	0.06	0.06	100.0	
Teicoplanin	0.5	0.5	100.0	0.0
Vancomycin	1	1	100.0	0.0
Daptomycin	0.25	0.25	100.0	
Linezolid	1	2	100.0	0.0
Ceftaroline	0.25	0.25	100.0	0.0
Oxacillin	0.5	1	100.0	0.0
Clindamycin	0.06	0.12	95.6	4.1
Erythromycin	0.25	>8	65.7	28.1
Levofloxacin	0.25	4	89.6	10.3
Tetracycline	≤0.5	≤0.5	95.4	3.4
TMP-SMX	≤0.5	≤0.5	99.4	0.6
Methicillin-resistant *S. aureus* (3,862)				
Dalbavancin	0.03	0.06	100.0	
Telavancin	0.06	0.06	100.0	
Teicoplanin	0.5	0.5	100.0	0.0
Vancomycin	1	1	100.0	0.0
Daptomycin	0.25	0.25	>99.9	
Linezolid	1	2	>99.9	<0.1
Ceftaroline	1	1	94.0	<0.1
Oxacillin	>2	>2	0.0	100.0
Clindamycin	0.06	>2	73.8	25.8
Erythromycin	>8	>8	13.8	83.3
Levofloxacin	4	>4	33.7	65.9
Tetracycline	≤0.5	1	92.5	6.5
TMP-SMX	≤0.5	≤0.5	96.9	3.1
Vancomycin-susceptible *E. faecalis* (1,008)				
Dalbavancin	0.03	0.06	100.0	
Telavancin	0.12	0.25	99.9	
Teicoplanin	0.5	0.5	100.0	0.0
Vancomycin	1	2	100.0	0.0
Daptomycin	0.5	1	97.1	0.0
Linezolid	1	2	99.9	0.0
Ampicillin	1	1	100.0	0.0
Levofloxacin	1	>4	80.4	19.3
β-hemolytic streptococci (1,965)				
Dalbavancin	0.008	0.015	100.0	
Vancomycin	0.5	0.5	100.0	
Daptomycin	≤0.06	0.25	100.0	
Linezolid	1	2	100.0	
Ceftaroline	≤0.008	0.015	100.0	
Ceftriaxone	0.03	0.06	100.0	
Penicillin	0.015	0.06	100.0	
Clindamycin	≤0.25	>2	82.4	16.6
Erythromycin	0.06	>16	65.9	33.1
Levofloxacin	0.5	1	99.2	0.7
Tetracycline	0.5	>4	55.6	43.8
TMP-SMX	≤0.12	0.25		
S. anginosus group (55)				
Dalbavancin	≤0.004	≤0.004	100.0	
Vancomycin	0.5	1	100.0	
Daptomycin	0.25	0.25	100.0	
Linezolid	1	2	100.0	
Ceftaroline	0.03	0.03		
Ceftriaxone	0.25	0.25	100.0	0.0
Penicillin	0.03	0.06	100.0	0.0
Clindamycin	≤0.25	>2	83.6	16.4
Erythromycin	≤0.015	>16	74.5	25.5
Levofloxacin	0.5	1	100.0	0.0
Tetracycline	1	>4	60.0	38.2
TMP-SMX	≤0.12	≤0.12		

TMP-SMX, trimethoprim-sulfamethoxazole
[a] Criteria as published by CLSI (2019).

Figure 1. Dalbavancin MIC distributions when tested against clinical isolates of indicated species collected from US medical centers (2017–2018)



MSSA, methicillin-susceptible *Staphylococcus aureus*; MRSA, methicillin-resistant *S. aureus*; VAN-S EF, vancomycin-susceptible *Enterococcus faecalis*; BHS, β-hemolytic streptococci.

CONCLUSIONS

- Dalbavancin retained activity against 100.0% of isolates from indicated species collected in US hospitals in 2017–2018 (n=12,138)
- Dalbavancin MIC_{50} values ranged from ≤0.004 mg/L to 0.03 mg/L and MIC_{90} values ranged from ≤0.004 mg/L to 0.06 mg/L for these isolates, with 99.99% of isolates inhibited at ≤0.12 mg/L of dalbavancin
- In summary, dalbavancin remains highly active against clinical isolates of indicated species causing infections in US medical centers

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