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# Antimicrobial Activity of Dalbavancin against Gram-Positive Bacteria Isolated from Patients Hospitalized with Bacteremia in United States and European Medical Centers: Results from the International Dalbavancin Evaluation of Activity (IDEA) Program (2018–2020)

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## CONCLUSIONS

Dalbavancin was very active against *S. aureus*, CoNS, vancomycin-susceptible enterococci, β-hemolytic steptococci, and viridans group streptococci isolated from patients with BSI in the US and Europe.

Based on $MIC_{50}$ values, dalbavancin was generally 8- to 32-fold more active than daptomycin and vancomycin against these organisms.

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

## RESULTS

- The most common gram-positive organisms were *S. aureus, E. faecalis, S. epidermidis,* β-hemolytic streptococci, and *E. faecium*, but rank order varied markedly by geographic region (Figure 1).
- Dalbavancin was highly active against methicillin-susceptible and -resistant (MRSA) *S. aureus*, with an $MIC_{90}$ of 0.03 mg/L in all 3 regions (Tables 1 and 2).
- Based on $MIC_{50/90}$ values, dalbavancin ($MIC_{50/90}$, 0.03/0.03 mg/L) was 8- to 16-fold more active than daptomycin ($MIC_{50/90}$, 0.25/0.5 mg/L) and 32-fold more active than vancomycin ($MIC_{50/90}$, 1/1 mg/L) against *S. aureus* (Table 2).
- Among *S. aureus*, MRSA rates were higher in the US (41.3%) than W-EU (21.5%) or E-EU (27.3%), and ceftaroline susceptibility ranged from 95.4% (W-EU) to 96.6% (US; Table 2).
- Vancomycin susceptibility varied from 97.3% (E-EU) to 98.3% (W-EU) among *E. faecalis* (97.5% in US; Table 2), and dalbavancin was active against all vancomycin-susceptible *E. faecalis* ($MIC_{50/90}$, 0.03/0.06 mg/L; 100.0%S; Table 1).
- Among *S. epidermidis*, all isolates were inhibited at ≤0.25 mg/L of dalbavancin ($MIC_{50/90}$, 0.03/0.06 mg/L) and oxacillin resistance ranged from 66.9% in W-EU to 86.5% in E-EU (73.2% in US; Tables 1 and 2).
- β-hemolytic streptococci exhibited low dalbavancin MIC values ($MIC_{50/90}$, 0.015/0.03 mg/L) and high susceptibility rates for most comparator agents tested (Tables 1 and 2).
- Among *E. faecium*, vancomycin susceptibility rates varied from 36.6% in the US to 61.6% in E-EU and 76.1% in W-EU, and dalbavancin inhibited all vancomycin-susceptible *E. faecium* at ≤0.25 mg/L ($MIC_{50/90}$, 0.03/0.12 mg/L; Tables 1 and 2).

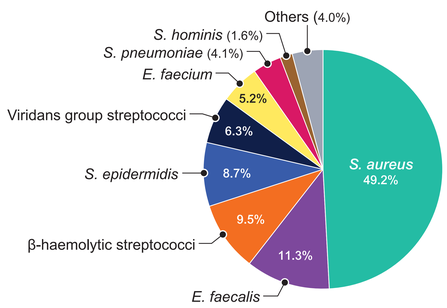
**Table 1. Antimicrobial activity of dalbavancin tested against the most common organisms and organism groups**

| Organism (no. of isolates) | No. and cumulative % of isolates inhibited at dalbavancin MIC (mg/L) of: | | | | | | | | | | | $MIC_{50}$ | $MIC_{90}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ≤0.004 | 0.008 | 0.015 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | >2 | | |
| *S. aureus* (3,908) | 4<br>0.1 | 31<br>0.9 | 970<br>25.7 | 2,840<br>98.4 | 62<br>>99.9 | 1<br>100.0 | | | | | | 0.03 | 0.03 |
| MSSA (2,607) | 3<br>0.1 | 25<br>1.1 | 661<br>26.4 | 1882<br>98.6 | 35<br>>99.9 | 1<br>100.0 | | | | | | 0.03 | 0.03 |
| MRSA (1,301) | 1<br>0.1 | 6<br>0.5 | 309<br>24.3 | 958<br>97.9 | 27<br>100.0 | | | | | | | 0.03 | 0.03 |
| *E. faecalis* (1,053) | | | 159<br>15.1 | 752<br>86.5 | 117<br>97.6 | 6<br>98.2 | 1<br>98.3 | 0<br>98.3 | 0<br>98.3 | 1<br>98.4 | 17<br>100.0 | 0.03 | 0.06 |
| VAN-S (≤4 mg/L) (1,030) | | | 159<br>15.4 | 752<br>88.4 | 112<br>99.3 | 6<br>99.9 | 1<br>100.0 | | | | | 0.03 | 0.06 |
| *S. epidermidis* (765) | 3<br>0.4 | 17<br>2.6 | 201<br>28.9 | 436<br>85.9 | 90<br>97.6 | 17<br>99.9 | 1<br>100.0 | | | | | 0.03 | 0.06 |
| β-hemolytic streptococci (735) | 130<br>17.7 | 213<br>46.7 | 307<br>88.4 | 66<br>97.4 | 17<br>99.7 | 2<br>100.0 | | | | | | 0.015 | 0.03 |
| *E. faecium* (659) | | | 71<br>10.8 | 155<br>34.3 | 138<br>55.2 | 52<br>63.1 | 15<br>65.4 | 6<br>66.3 | 3<br>66.8 | 11<br>68.4 | 208<br>100.0 | 0.06 | >2 |
| VAN-S (≤4 mg/L) (397) | | | 68<br>17.1 | 143<br>53.1 | 133<br>86.6 | 47<br>98.5 | 6<br>100.0 | | | | | 0.03 | 0.12 |
| Viridans group streptococci (508) | 116<br>22.8 | 126<br>47.6 | 140<br>75.2 | 100<br>94.9 | 20<br>98.8 | 6<br>100.0 | | | | | | 0.015 | 0.03 |
| *S. pneumoniae* (461) | 12<br>2.6 | 245<br>55.7 | 187<br>96.3 | 16<br>99.8 | 1<br>100.0 | | | | | | | 0.008 | 0.015 |
| *S. hominis* (175) | 1<br>0.6 | 4<br>2.9 | 52<br>32.6 | 95<br>86.9 | 19<br>97.7 | 4<br>100.0 | | | | | | 0.03 | 0.06 |
| *S. haemolyticus* (104) | | | 3<br>2.9 | 16<br>18.3 | 51<br>67.3 | 29<br>95.2 | 4<br>99.0 | 1<br>100.0 | | | | 0.06 | 0.12 |

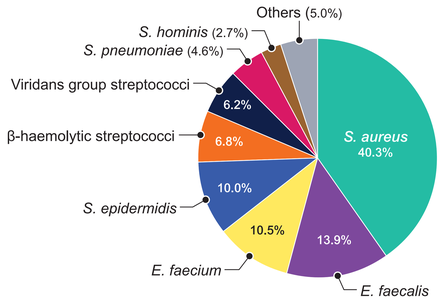
Abbreviations: VAN-S, vancomycin-susceptible.

**Figure 1. Frequency of gram-positive bacteria isolated from patients hospitalized with bacteremia in the United States, western Europe, and eastern Europe in 2018–2020**

**A.** United States




**B.** Western Europe




**C.** Eastern Europe

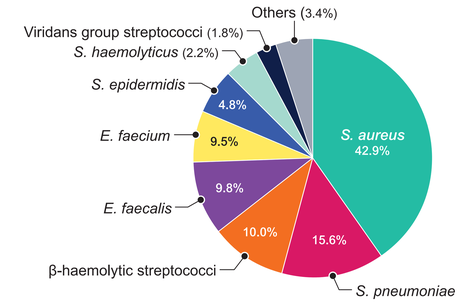



**Table 2. Antimicrobial activity of dalbavancin and comparator agents against the most common gram-positive cocci isolated from patients with BSI in the United States (US), western Europe (W-EU), and eastern Europe (E-EU)**

| Organism/ antimicrobial (no. tested) | $MIC_{50}$ [a] | $MIC_{90}$ [a] | % Susceptible per CLSI (no. of isolates) | | |
|---|---|---|---|---|---|
| | | | US | W-EU | E-EU |
| *S. aureus* (3,908) | | | (2,235) | (1,343) | (330) |
| Dalbavancin | 0.03 | 0.03 | 100.0 | 100.0 | 100.0 |
| Daptomycin | 0.25 | 0.5 | >99.9 | 100.0 | 100.0 |
| Vancomycin | 1 | 1 | 100.0 | 100.0 | 100.0 |
| Teicoplanin | 0.5 | 0.5 | 100.0 | 100.0 | 100.0 |
| Linezolid | 1 | 2 | 100.0 | 100.0 | 100.0 |
| Oxacillin | 0.5 | >2 | 58.7 | 78.5 | 72.7 |
| Ceftaroline | 0.25 | 1 | 96.6 | 95.4 | 96.4 |
| Clindamycin | 0.06 | >2 | 85.5 | 96.2 | 89.1 |
| Levofloxacin | 0.25 | >4 | 67.6 | 79.4 | 85.8 |
| Tetracycline | ≤0.5 | ≤0.5 | 95.1 | 96.0 | 83.6 |
| TMP-SMX[b] | ≤0.5 | ≤0.5 | 97.7 | 99.8 | 99.7 |
| *E. faecalis* (1,053) | | | (515) | (463) | (75) |
| Dalbavancin | 0.03 | 0.06 | 97.9 [c] | 98.7 [c] | 98.7 [c] |
| Daptomycin | 1 | 1 | 99.2 | 99.6 | 100.0 |
| Vancomycin | 1 | 2 | 97.5 | 98.3 | 97.3 |
| Teicoplanin | 0.5 | 0.5 | 97.9 | 98.7 | 98.7 |
| Linezolid | 1 | 2 | 99.8 | 99.8 | 97.3 |
| Ampicillin | 1 | 1 | 100.0 | 100.0 | 100.0 |
| Levofloxacin | 1 | >4 | 78.8 | 73.4 | 70.7 |
| *S. epidermidis* (765) | | | (396) | (332) | (37) |
| Dalbavancin | 0.03 | 0.06 | [100.0][d] | [100.0][d] | [100.0][d] |
| Daptomycin | 0.25 | 0.5 | 100.0 | 100.0 | 100.0 |
| Vancomycin | 2 | 2 | 100.0 | 100.0 | 100.0 |
| Teicoplanin | 2 | 8 | 99.2 | 99.4 | 97.3 |
| Linezolid | 1 | 1 | 93.9 | 96.4 | 94.6 |
| Oxacillin | >2 | >2 | 26.8 | 33.1 | 13.5 |
| Clindamycin | 0.06 | >2 | 52.5 | 66.6 | 70.3 |
| Levofloxacin | 4 | >4 | 40.9 | 44.6 | 24.3 |
| Tetracycline | 1 | >8 | 80.8 | 85.2 | 73.0 |
| TMP-SMX[b] | 1 | 8 | 54.3 | 58.4 | 73.0 |
| β-hemolytic streptococci (735) | | | (430) | (228) | (77) |
| Dalbavancin | 0.015 | 0.03 | 100.0[e] | 100.0[e] | 100.0[e] |
| Daptomycin | ≤0.06 | 0.25 | 100.0 | 100.0 | 100.0 |
| Vancomycin | 0.5 | 0.5 | 100.0 | 100.0 | 100.0 |
| Linezolid | 1 | 2 | 100.0 | 100.0 | 100.0 |
| Ceftriaxone | 0.03 | 0.06 | 100.0 | 100.0 | 100.0 |
| Ceftaroline | ≤0.008 | 0.015 | 100.0 | 100.0 | 100.0 |
| Penicillin | 0.015 | 0.06 | 100.0 | 100.0 | 100.0 |
| Clindamycin | ≤0.25 | >2 | 79.8 | 87.7 | 85.7 |
| Levofloxacin | 0.5 | 1 | 98.1 | 97.4 | 98.7 |
| Tetracycline | >4 | >4 | 41.7 | 52.2 | 55.8 |
| *E. faecium* (659) | | | (238) | (348) | (73) |
| Dalbavancin | 0.06 | >2 | [38.7][c] | [81.9][c] | [74.0][c] |
| Daptomycin | 1 | 2 | [96.2][f] | [100.0][f] | [100.0][f] |
| Vancomycin | 0.5 | >16 | 36.6 | 76.1 | 61.6 |
| Teicoplanin | 1 | >16 | 39.9 | 82.2 | 67.1 |
| Linezolid | 1 | 2 | 99.2 | 99.7 | 100.0 |
| Ampicillin | >16 | >16 | 18.5 | 12.6 | 2.7 |
| Levofloxacin | >4 | >4 | 14.7 | 10.1 | 2.7 |

[a] $MIC_{50}$ and $MIC_{90}$ values for the US, W-EU, and E-EU collections combined.
[b] Trimethoprim-sulfamethoxazole.
[c] These breakpoints have been applied to all *E. faecalis* and *E. faecium* but are only approved for vancomycin-susceptible *E. faecalis*.
[d] The percentage inhibited at ≤0.25 mg/L, the susceptible breakpoint for *S. aureus*.
[e] These breakpoints have been applied to all *Streptococcus spp.* other than *S. pneumoniae*, but are only approved for *S. pyogenes, S. agalactiae*, and *S. dysgalactiae* group.
[f] The value in the brackets indicates percentage susceptible dose-dependent (SDD).

## INTRODUCTION

- The IDEA Program monitors the *in vitro* activity of dalbavancin and comparators against gram-positive bacteria causing bloodstream infection (BSI) and other infections in the United States (US) and Europe (EU).
- The etiology of BSI may vary significantly according to the type of patient and source of infection.
- Dalbavancin allows for 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 ABSSSI.
- Dalbavancin is not licensed to treat BSI but is potentially important in treating infections due to highly resistant gram-positive cocci.
- We evaluated dalbavancin *in vitro* activity and potency when tested against a large collection of gram-positive bacteria collected from patients with BSIs.

## METHODS

- A total of 8,643 organisms were consecutively collected (1/patient) from 74 medical centers located in the US (n=4,544; 33 centers), western EU (W-EU; n=3,330; 28 centers from 10 countries: Belgium, France, Germany, Ireland, Italy, Portugal, Spain, Sweden, Switzerland, and the United Kingdom), and eastern EU (E-EU; n=769; 13 centers from 10 countries: Belarus, Czech Republic, Greece, Hungary, Israel, Poland, Romania, Russia, Slovenia, and Turkey).
- 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).

## METHODS

- Participating laboratories initially identified isolates and JMI confirmed bacterial identifications by standard algorithms and/or MALDI-TOF.
- Isolates were tested for susceptibility by broth microdilution following guidelines in the Clinical and Laboratory Standards Institute (CLSI) M07 (2018).
- The dalbavancin breakpoints approved by the US FDA and/or CLSI for indicated species were applied (i.e., an MIC ≤0.25 mg/L), and breakpoint criteria for comparator agents were from the CLSI M100 (2021).

## DISCLOSURES

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