Dalbavancin for difficult to treat Gram-positive infections

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Mentimeter 1

Do you get requests for dalbavancin testing in your clinical lab?

- Never happened
- Increasingly, but still seldom
- Every week or more frequently

Mentimeter 2

Do you perform dalbavancin testing?
(only 1 answer possible)

- No, not available
- No, we refer to reference lab
- Yes, with BMD (in-house)
- Yes, with BMD (commercial)
- Yes, with gradient test

Mentimeter 3

For which species?
(more than one answer possible)

- *Staphylococcus* spp.
- *Enterococcus* spp.
- *Corynebacterium* spp.
- Other

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Agenda

- What is dalbavancin?
- What is the clinical use of dalbavancin?
- How is testing for dalbavancin performed?
- For which species has EUCAST set clinical breakpoints?
- Some special points for staphylococci, enterococci
- Can *Corynebacterium* spp. infections be treated with dalbavancin?
- An ongoing NordicAST study on testing of dalbavancin
  (no results yet!)

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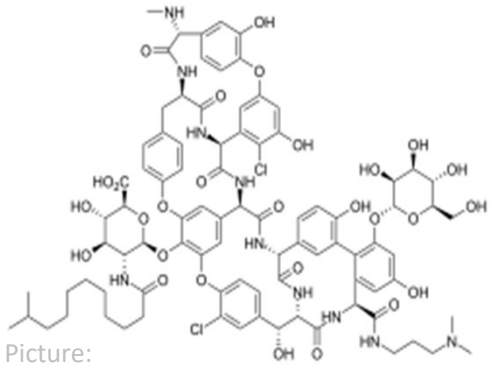
What is dalbavancin?



Picture:
https://en.wikipedia.org/wiki/Dalbavancin

- Longacting Lipoglycopeptide (half-life 1-2 weeks)

  Molina KC et al. *Clin Pharmacokinet*. 2022;61(3):363-374.
  Senneville E et al. *Int J Antimicrob Agents*. 2023;62(5):106960.

- Approved by the European Medicines Agency in 2015 for the treatment of skin and soft tissue infections.
  Dosing 1.500 mg

  1.500 mg on day 1 OR 1.000 mg on day 1 + 500 mg on day 8

  https://www.ema.europa.eu/en/medicines/human/EPAR/xydalba

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What is the clinical use of dalbavancin?

Increasingly used for infections requiring prolonged antibiotic treatment, including bone and joint infections and endocarditis

Bone and Joint Infections

Meta-analysis: 6 comparative studies (1 RCT)

Predominantly *S. aureus*

Dalbavancin as effective as comparator (vancomycin, daptomycin, linezolid)

Almangour TA et al. *J Infect Chemother*. 2025;31(1):102473

Infective endocarditis

Spanish-French retrospective observational study of patients with enterococcal IE

98 patients, Dalbavancin in consolidation phase; *E. faecalis* 86.7 %

Good outcome: relapse rate 8.2 %, 1-year IE-related mortality 3.1 %

Hidalgo-Tenorio C et al. J Microbiol Immunol Infect. 2025;58(4):429-436.

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What is the clinical use of dalbavancin?

In the Nordic setting for these indications mostly relevant for

- Gram-positive multidrug-resistant isolates
  (Methicillin-resistant *S. aureus*, Coagulase-negative staphylococci, *Enterococcus faecium*?, *Corynebacterium* spp?)
- Allergic patients
- Compliance problems

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How is antimicrobial susceptibility testing of dalbavancin performed?

- Only MIC-testing
- ISO 20776-1 standard: MICs must be determined in the presence of polysorbate-80 (0.002%)
- Incubation time?

Koeth LM et al. J Vis Exp. 2015 Sep 9;(103):53028.

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For which species has EUCAST set clinical breakpoints?

- **Staphylococcus spp: S≤0.25; R>0.25 mg/L**
- Enterococcus spp.: insufficient evidence (IE)
- **Streptococcus groups A, B, C and G: S≤0.125; R>0.125 mg/L**
- *Streptococcus pneumoniae*: IE
- ***S. anginosus* group: S≤0.125; R>0.125 mg/L**
- *Corynebacterium* spp.: no breakpoints

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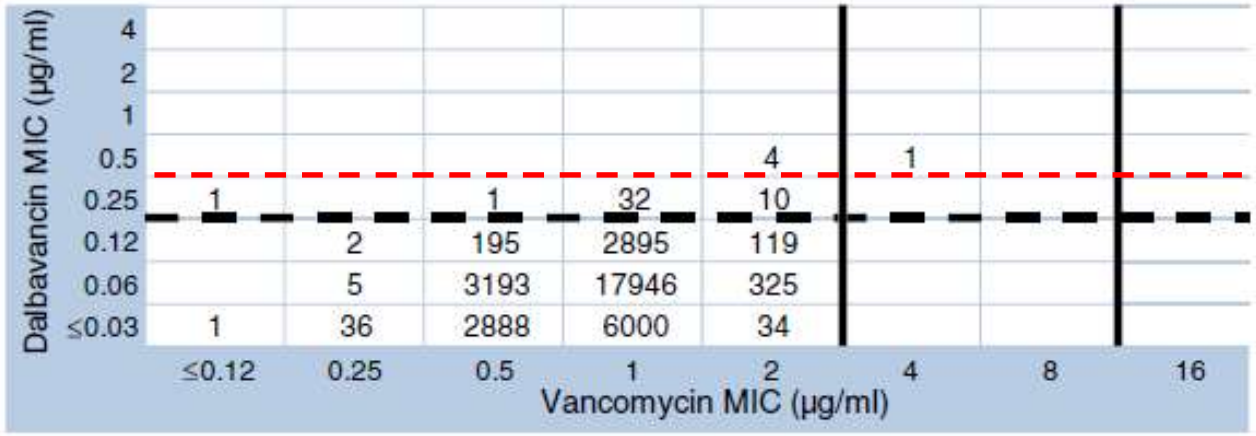
Can dalbavancin susceptibility be inferred from vancomycin and/or teicoplanin in staphylococci?

No, previous EUCAST recommendation for *Staphylococcus* spp. has been removed!

SENTRY 2011-2013: 33.688 *S. aureus* isolates



Jones RN et al. Diagn Microbiol Infect Dis. 2015 May;82(1):73-7.

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Expected susceptible phenotype

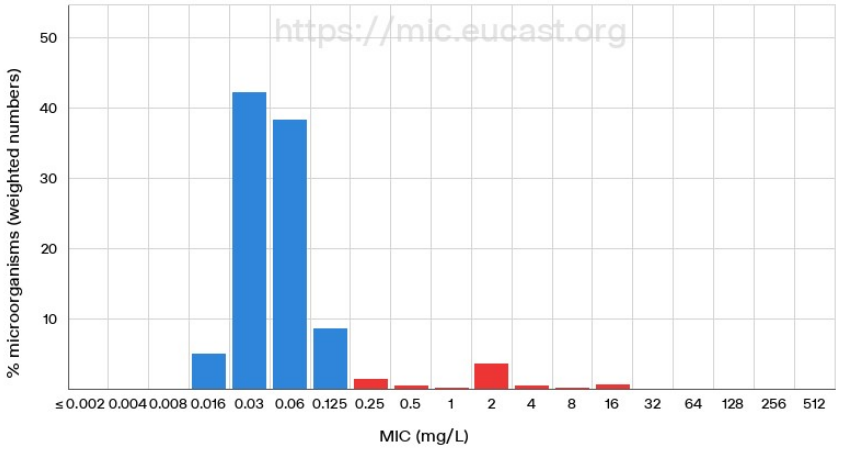
Table 2 Expected susceptible phenotype (resistance not expected) in gram-positive bacteria

Rule	Organisms	Unusual phenotypes
2.1	*Staphylococcus aureus*	Resistant to vancomycin, teicoplanin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin, tigecycline, eravacycline or omadacycline
2.2	Coagulase-negative staphylococci	Resistant to vancomycin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid[1], tedizolid[1], quinupristin-dalfopristin[1], tigecycline, eravacycline or omadacycline
2.3	*Corynebacterium* spp.	Resistant to vancomycin, teicoplanin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin or tigecycline
2.4	*Streptococcus pneumoniae*	Resistant to carbapenems, vancomycin, teicoplanin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin, tigecycline, eravacycline, omadacycline or rifampicin.
2.5	Group A, B, C and G β-haemolytic streptococci	Resistant to penicillin, cephalosporins, vancomycin, teicoplanin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin, tigecycline, eravacycline or omadacycline
2.6	*Enterococcus* spp.	Resistant to daptomycin, linezolid, tigecycline, eravacycline or omadacycline Resistant to teicoplanin but not vancomycin
2.7	*Enterococcus faecalis*	Resistant to ampicillin
2.8	*Enterococcus faecalis, Enterococcus gallinarum, Enterococcus casseliflavus, Enterococcus avium*	Susceptible to quinupristin-dalfopristin, consider misidentification. If also resistant to ampicillin it is almost certainly *E. faecium*

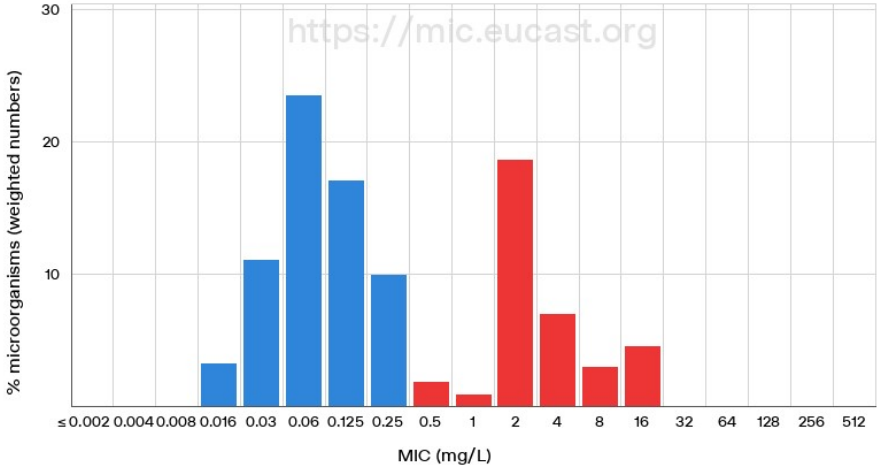
Dalbavancin susceptibility in enterococci

MIC distributions

E. faecalis



E. faecium



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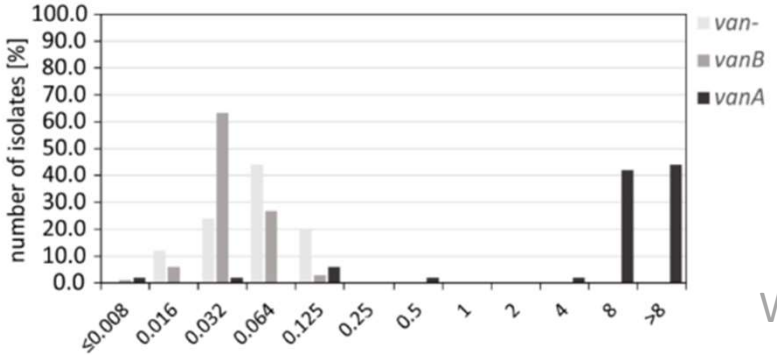
Can dalbavancin susceptibility be inferred from *van*-genotype for *Enterococci*?

German study:

25 vancomycin-susceptible, 50 *vanA*, and 101 *vanB E. faecium* isolates



Weber RE et al. Antibiotics (Basel). 2021 Jul 27;10(8):915.

EDL-study:

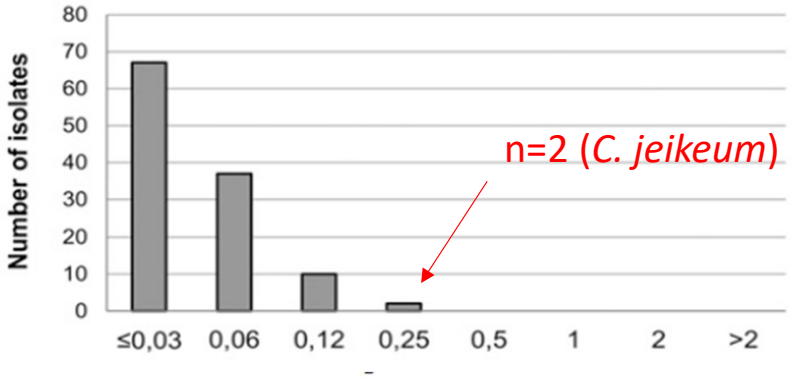
- Vancomycin R/ Teicoplanin R phenotype are dalbavancin non-wild type
- **Vancomycin R/ Teicoplanin S phenotype (most *vanB*-positive) can be dalbavancin wild type or non-wild type**

Agnes Duhan, short oral presentation at NordicAST workshop 2024

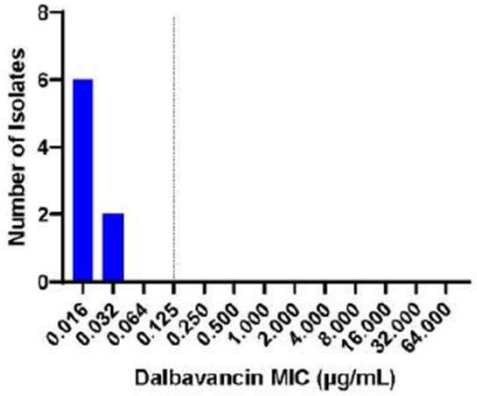
Dalbavancin and *Corynebacterium* spp.

Scarce MIC data:

French study
116 invasive isolates, BMD



US study
7 (?) PJI cases, BMD



Bichali AR et al. Microb Drug Resist. 2025 Jul;31(7):211-218.
Doub JB. Germs. 2023 Jun 30;13(2):151-157.

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Dalbavancin and *Corynebacterium* spp.

Scarce clinical data:

- Case reports and series
- Literature review 2024:

Table 1 *C. striatum* infections treated with dalbavancin

Author [reference], year	Number of cases	Type of infection	Corynebacterium species	Previous therapies	Dalbavancin indication	Dalbavancin dose regimen	Adverse effects	Outcome
Molina-Collada [6], 2017	n=1	Septic native knee arthritis	*C. striatum*	Linezolid Teicoplanin	Failure (n=1)	1500 mg (one dose)	None (n=1)	Cure (n=1)
Navarro-Jiménez [7], 2022	n=7	Diabetic foot osteomyelitis	*C. striatum*	Cotrimoxazole, tedizolid, ciprofloxacin, linezolid, amoxicillin-clavulanate, clindamycin	Failure (n=3) Side effects (n=3) Failure and Side effects (n=1)	1500 mg (one dose) to 1500 mg weekly for 5 weeks	None (n=5) Nausea (n=1)	Cure (n=6) Failure (n=1)
Mansoor [8], 2023	n=6	LVAD	*C. striatum*	Vancomycin, tedizolid, daptomycin, levofloxacin, omadacycline	Convenience (n=5) Side effects (n=1)	1500 mg every two weeks	None (n=6)	Cure (n=3) Heart transplantation (n=1) Failure (n=1) LVAD thrombosis (n=1)
Soderqüist [9],2023	n=1	PJI	*C. striatum*	Vancomycin, linezolid, daptomycin	Side effects (n=1)	1500 mg every week for 12 weeks	None (n=1)	Cure (n=1)
Camara [present case], 2023	n=1	PJI	*C. striatum*	vancomycin	Convenience (n=1)	1000 mg (load dose) and 500 mg weekly for 6 weeks.	None (n=1)	Cure (n=1)

LVAD: Left Ventricular Assist Device; PJI: Periprosthetic joint infection.

Camara-Rodriguez Met al. Rev Esp Quimioter. 2024 Jun;37(3):276-278.

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An ongoing NordicAST study: Comparison of different Dalbavancin MIC testing methods for *Staphylococcus* spp. and *Enterococcus* spp.

- Collaboration between EUCAST Development Laboratory, Växjö and Statens Serum Institut, Copenhagen
- 20 *S. aureus*, 20 *S. epidermidis*, 20 *E. faecalis*, 20 *E. faecium*
- Comparison of reference plates (produced manually according to ISO-standard) with
  - Commercially available BMD: Sensititre, ComASP
  - Gradient tests: MTS

Take home messages

- There is an increasing demand for AST for dalbavancin due to off-label use in invasive infections
- There are EUCAST breakpoints for *Staphylococcus* spp., Group A,B,C,G *Streptococcus* and *S. anginosus* group
- For AST, MIC has to be determined (BMD: addition of polysorbate-80)
- There is no surrogate marker for dalbavancin susceptibility in *Staphylococcus* spp., but the expected phenotype is susceptible
- There is conflicting data on the dalbavancin phenotype in *vanB*-positive enterococcal isolates.
- For *Corynebacterium* spp. there is sparse MIC and clinical data
- NordicAST is conducting a study on dalbavancin AST evaluating commercially available MIC tests

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