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Oritavancin Activity Against Gram-Positive Pathogens Causing Bloodstream Infections in Hematology/Oncology and Transplant Units in US Medical Centers (2010–2019)

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Introduction

- Bacterial bloodstream infections (BSI) complicate the course of immunocompromised patients, significantly contributing to morbidity and mortality.
- Rising antimicrobial resistance rates may impact the efficacy of empirical and target antibiotic treatment in high-risk patients undergoing hematologic, oncologic, and/or transplant treatment.
- Appropriate antimicrobial management is crucial for patients with suspected or confirmed BSI.
- We evaluated the *in vitro* activity of oritavancin and comparators against Gram-positive isolates causing BSI in patients from hematology/oncology and transplant units (HTU) in US medical centers.

Methods

- A total of 1,217 Gram-positive isolates causing bloodstream infections in HTU patients were consecutively collected during 2010–2019 as part of the SENTRY Antimicrobial Surveillance Program.
- A single isolate per patient was collected in 33 US medical centers located in all 9 US Census Divisions.
- Only isolates determined to be significant by local criteria as the reported probable cause of infection were included in the program.
- Bacterial identification was performed by MALDI-TOF (Bruker Daltonics, Billerica, MA, USA) and/or standard microbiological testing methods.
- Antimicrobial susceptibility testing was performed using CLSI broth microdilution methodology in a central laboratory (JMI Laboratories).
- CLSI M100 (2022) breakpoints were applied for comparator agents.
- For *in vitro* comparisons, the oritavancin CLSI susceptible breakpoints for *S. aureus* (≤0.12 mg/L) and vancomycin-susceptible *E. faecalis* (≤0.12 mg/L) were applied to all *Staphylococcus* spp. and *Enterococcus* spp. isolates, respectively.
- The oritavancin CLSI susceptible breakpoints were applied for β-hemolitic streptococci (BHS; ≤0.25 mg/L) and Viridans group streptococci (VGS; ≤0.25mg/L).
- Oritavanin and comparators were also evaluated against MRSA, MRCoNS, and VRE resistant subsets, as well as, a subset of susceptible dose-dependent *E. faecium* isolates displaying high daptomycin MIC values (2–4 mg/L).

Table 1. Activity of oritavancin and comparators against Gram-positive pathogens causing BSI in HTU patients in US medical centers

Organism group (no. of isolates)	Oritavancin			Vancomycin			Linezolid			Daptomycin		
	MIC_{50}	MIC_{90}	%S	MIC_{50}	MIC_{90}	%S	MIC_{50}	MIC_{90}	%S	MIC_{50}	MIC_{90}	%S
E. faecalis (174)	0.015	0.03	98.9[a]	1	2	97.1	1	2	100.0	1	1	98.3
E. faecium (246)	0.03	0.12	96.7[a]	>16	>16	27.2	1	2	100.0	2	2	99.2[b]
VRE (179)	0.03	0.12	95.5[a]	>16	>16	0.0	1	2	100.0	2	2	98.9[b]
Dapto MIC 2-4 mg/L (136)	0.03	0.12	95.6[a]	>16	>16	31.6	1	2	100.0	2	4	100.0[b]
S. aureus (434)	0.03	0.06	99.3	1	1	100.0	1	2	100.0	0.25	0.5	100.0
MRSA (158)	0.03	0.06	99.4	1	1	100.0	1	1	100.0	0.25	0.5	100.0
CoNS (144)	0.03	0.12	96.5[c]	1	2	100.0	0.5	1	100.0	0.25	0.5	100.0
MR-CoNS (110)	0.06	0.12	95.5[c]	2	2	100.0	0.5	1	100.0	0.5	0.5	100.0
BHS (42)	0.03	0.25	95.2	0.5	0.5	100.0	1	1	100.0	0.12	0.25	100.0
VHS (117)	0.015	0.25	96.6	0.5	0.5	100.0	1	1	99.1	0.25	0.5	100.0

[a] Oritavancin breakpoint published for vancomycin-susceptible *E. faecalis* (≤0.12 mg/L) was applied to all *Enterococcus* isolates (CLSI, 2022).
[b] Susceptible dose-dependent.
[c] Oritavancin breakpoint published for *S. aureus* (≤0.12 mg/L) was applied to all CoNS isolates (CLSI, 2022).

Results

- *Enterococcus* spp. (overall, 36.1%; *E. faecium*, 20.2%; *E. faecalis*, 14.3%) and *S. aureus* (35.7%; 36.4% methicillin-resistant [MRSA]) were the most common organism groups, followed by coagulase-negative *Staphylococcus* (CoNS; 11.8%; 76.4% MR), VGS (9.6%), and BHS (3.5%; Figures 1 and 2).

Activity against enterococci

- Oritavancin inhibited 96.7% and 98.9% of *E. faecium* and *E. faecalis* at ≤0.12 mg/L, respectively (susceptible breakpoint for vancomycin-susceptible *E. faecalis*; Figure 3).
- Ampicillin (100.0% susceptible [S]), linezolid (100.0%S), daptomycin (98.3%S), and vancomycin (97.1%S) were also active against *E. faecalis* (Figure 3).
- Oritavancin (96.7% inhibited at ≤0.12 mg/L) and linezolid (100.0%S) remained active against *E. faecium* isolates, while only 27.2% were susceptible to vancomycin and 99.2% were daptomycin susceptible dose-dependent (Figure 3).
- Vancomycin-resistant *Enterococcus* (VRE) phenotype was noted in 72.8% of *E. faecium*, and oritavancin inhibited 95.5% of these isolates at ≤0.12 mg/L (Figures 2 and 3).
- Oritavancin inhibited 95.6% of *E. faecium* isolates displaying elevated daptomycin MIC (2–4 mg/L) values, which were noted in 55.3% of all *E. faecium* isolates (Figures 2 and 3).

Activity against staphylococci

- Oritavancin displayed equivalent $MIC_{50/90}$ (0.03/0.06 mg/L) values against MSSA (99.3%S) and MRSA (99.4%S; Table 1 and Figure 4).
- Oritavancin inhibited 95.5% of MRCoNS at ≤0.12 mg/L (*S. aureus* susceptible breakpoint).
- Vancomycin, daptomycin, and linezolid remained active against MRSA and MRCoNS (Figure 4).

Activity against streptococci

- Oritavancin was also active against BHS ($MIC_{50/90}$, 0.03/0.25 mg/L; 95.2%S) and VGS ($MIC_{50/90}$, 0.015/0.25 mg/L; 96.6%S), as was vancomycin (100.0%S), daptomycin (100.0%S), and linezolid (100.0%/99.1%S, respectively; Table 1 and Figure 4).

Figure 1. Distribution of Gram-positive pathogens causing BSI in HTU patients in US medical centers (2010–2019)

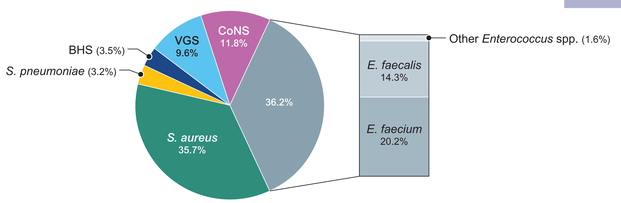
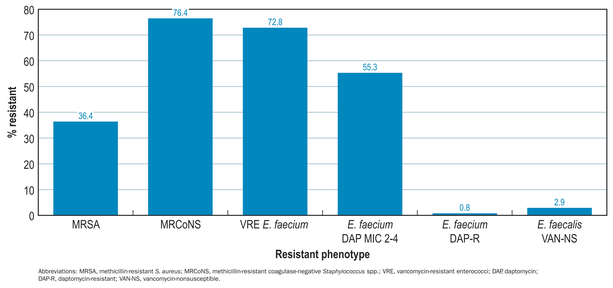
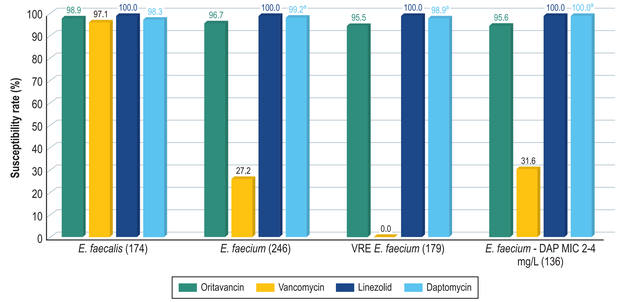


Figure 2. Resistant phenotype rates observed in Gram-positive pathogens causing BSI in HTU patients in US medical centers (2017–2019)



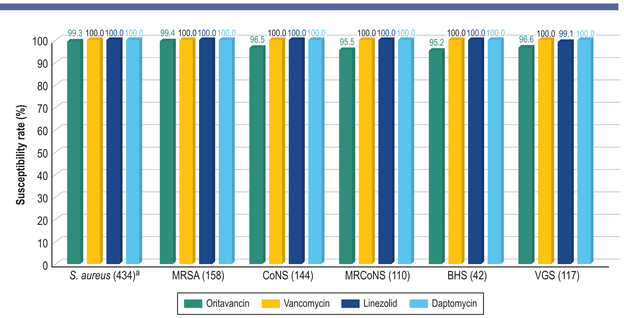
Abbreviations: MRSA, methicillin-resistant *S. aureus*; MRCoNS, methicillin-resistant coagulase-negative *Staphylococcus* spp.; VRE, vancomycin-resistant enterococci; DAP, daptomycin; DAP-R, daptomycin-resistant; VAN-NS, vancomycin-nonsusceptible.

Figure 3. Oritavancin and comparators' susceptibility rates against *Enterococcus* spp. and resistant phenotypes



Abbreviation: VRE, vancomycin-resistant enterococci.
* Susceptible dose-dependent.
The oritavancin breakpoint published for vancomycin-susceptible *E. faecalis* (≤0.12 mg/L) was applied to all *Enterococcus* isolates per CLSI M100 (2022) criteria.

Figure 4. Susceptibility rates of oritavancin and comparators against staphylococci and streptococci causing BSI in HTU patients in US medical centers



Abbreviations: MRSA, methicillin-resistant *S. aureus*; CoNS, coagulase-negative *Staphylococcus* spp.; MRCoNS, methicillin-resistant coagulase-negative *Staphylococcus* spp.; BHS, β-hemolytic streptococci; VGS, Viridans group streptococci.
[a] The oritavancin susceptible breakpoint published for *S. aureus* (≤0.12 mg/L) was applied to all CoNS isolates per CLSI M100 (2022) criteria.

Conclusions

- Overall, 36.1% of the isolates were *Enterococcus* spp., 20.2% were *E. faecium*, 72.8% of *E. faecium* were resistant to vancomycin, and 55.3% displayed daptomycin MIC values of 2–4 mg/L.
- High resistance rates were noted among Gram-positive pathogens recovered from BSI in HTU patients in US, including MRSA (36.4%), MRCoNS (76.4%), and VRE in *E. faecium* (72.8%).
- Oritavancin was active against *S. aureus* and CoNS (>95.5% inhibited at ≤0.12 mg/L), including MRSA and MRCoNS.
- Oritavancin inhibited >96% of *E. faecalis* and *E. faecium* isolates at ≤0.12 mg/L, including >95% of isolates within resistant subsets, such as VRE *E. faecium* and *E. faecium* displaying elevated daptomycin MIC values (2–4 mg/L).

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