Oritavancin In Vitro Activity Against a Collection of Molecularly-characterized Staphylococci and Displaying Elevated Linezolid MIC Values

Abstract

Staphylococci, particularly methicillin-resistant St. aureus (MRSA), coagulase-negative staphylococci (CoNS), and Staphylococcus intermedius are important nosocomial pathogens for a variety of clinical infections. MRSA and CoNS are among the most studied enterococci (E. faecalis, E. faecium, vancomycin-intermediate, 16S rRNA mosaicisms, which cause the majority of USA nosocomial infections and are refractory to most clinically available agents. Linezolid was the first oxazolidinone available and also acts on the 23S rRNA (L51) and one of the few drugs approved for the treatment of vancomycin-resistant Enterococcus (VRE) resistance. Its formulation remains limited in comparison with its importance in clinical isolates. Oritavancin (S-25), a new glycylcycline, has been shown to be potentially active against linezolid-resistant enterococci (E. faecalis, E. faecium) and other Gram-positive pathogens. The purpose of this study was to describe the susceptibility of a collection of molecularly characterized linezolid-resistant Gram-positive isolates to oritavancin, and to determine the impact of selected genetic mechanisms on oritavancin and linezolid MICs. The study included 45 enterococci (linezolid MIC values ≥4 μg/mL) and 45 staphylococci (MIC ≥4 μg/mL) with or without the presence of linezolid-resistant mechanisms.

Methods

Bacterial strain collection. A total of 195 staphylococci (70 S. epidermidis, 45 S. capitis, 45 S. hominis, 45 S. haemolyticus, 10 S. conii, 10 S. aureus) and 45 enterococci (15 E. faecalis, 15 E. faecium, 15 S. bovis) were included from a network of medical centers as part of the SENTRY Antimicrobial Surveillance Program and authorized by a central monitoring laboratory (JMI Laboratories, North Liberty, IA, USA), with additional clinical isolates from the Hospital of the University of Pennsylvania, PA, USA, and the University of Colorado Medical Center, Denver, CO, USA. S. epidermidis, S. capitis, and S. hominis were included to study potential interlaboratory variability. A total of 25 S. aureus isolates was included for the study. All isolates were used for the study, except where noted. Genotypic analysis was performed, and relevant characteristics were recorded. The study was conducted to measure the in vitro activity of oritavancin against a molecularity-characterized set of isolates displaying elevated linezolid MIC values.

Results

- Table 1 describes the challenge set of organisms utilized in the study. A total of 169 isolates had MIC of ≤2 μg/mL, 28 had MIC of ≥4 μg/mL, and 5 had MIC of >8 μg/mL (Table 1).
- Oritavancin had potent in vitro activity against Cfr and oritavancin had a MIC of ≤2 μg/mL against most isolates. Oritavancin was active against 100% of Cfr E. faecium.
- For oritavancin, the activity was reduced by 2-fold lower than that of daptomycin (MIC >2 μg/mL). Oditavancin was active against 100% of Cfr E. faecium.
- For oritavancin, the activity was reduced by 2-fold lower than that of daptomycin (MIC >2 μg/mL).

Conclusions

Oritavancin had potent in vitro activity against this collection of Gram-positive isolates exhibiting elevated linezolid MIC results with characterized resistance mechanisms utilized in this study. Oritavancin was approved by the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) in 2015 for the treatment of complicated skin and skin structure infections caused by Gram-positive organisms. Oritavancin is the first glycylcycline approved for the treatment of Gram-positive infections and has been shown to be active against many linezolid-resistant isolates. Oritavancin has a novel mechanism of action and does not have a cross-resistance pattern with other classes of antibiotics.

References