Assessment of Oritavancin Activity in Combination with Beta-lactams against Vancomycin-resistant Enterococci

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Abstract

Objective: Optimal treatments for infections caused by vancomycin-resistant enterococci (VRE) remain to be elucidated. Combinations of beta-lactams and lipopeptides exhibit synergy against VRE, as do combinations of daptomycin and BLs or glycopeptides.

Methods: Clinical isolates of E. faecium (Melotti et al., 10 isolates), E. faecalis (B7231527, VanA) and E. faecalis (Efa VanB) strains were used in checkerboard experiments of daptomycin (MER), oritavancin (ORI) and/or beta-lactams (BLs) with the constraint that the MIC of the BL in the combination had to be ≤32 µg/mL. Time-kill kinetics: Time-kill assays followed CLSI guideline M26-A3. MICs of ORI against E. faecium (Melotti et al., 10 isolates) were determined by serial dilution, including the use of 25 µL clonal suspension to limit (0.1%) loss of ORI activity in combination in BL MIC≤32 µg/mL. Elucidation of synergy was defined as a ≤2-log decrease in CFU/mL from the most active single drug.

Results: ORI MIC range against the VREs was 0.004–128 µg/mL, with MICs ≤32 µg/mL in each combination that demonstrated potentiation. ORI activity in combination with BLs in 76% of the 21 VRE isolates tested demonstrated in 4, 3 and 2 of these isolates using CPT, MER and PEN combinations, respectively. Time-kill kinetics studies confirmed the increased activity of ORI/BL combinations against VRE compared to the activity of each respective agent tested alone.

Conclusions: CPT, MER and PEN potentiated ORI in vitro activity against VRE, with the exception of Efm VanA.

Among the 21 VRE isolates tested in this study, CPT, MER and PEN potentiated ORI MICs in 11, 11 and 8 isolates, respectively, with the BLs ≤32 µg/mL in each combination that demonstrated potentiation.

The 5 tested isolates of Efm VanA had high BL MICs (256 to 2048 µg/mL). Potentiation of ORI activity in combination in BL MIC≤32 µg/mL were demonstrated in 4, 3 and 2 of these isolates using CPT, MER and PEN combinations, respectively.

Time-kill kinetics studies confirmed the increased activity of ORI/BL combinations against VRE compared to the activity of each respective agent tested alone.

Disclosures

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References

1. Antimicrobial Agents and Chemotherapy. Instructions to Authors, 2015.