**Objectives:** To evaluate oritavancin activity against a recent collection of enterococcal isolates responsible for documented infections in European countries and adjacent regions. Oritavancin has documented in vitro activity and spectrum against numerous species of Gram-positive pathogens, which results from three distinct mechanisms of action.

**Methods:** A total of 3321 enterococci, mostly *E. faecalis* (1950) and *E. faecium* (1272) were collected from 16 European countries (32 sites) and Israel (one site). Isolates were submitted to a monitoring laboratory as part of the SENTRY Antimicrobial Surveillance Program for 2009 through 2013. Identification was confirmed by standard algorithms and MALDI-TOF. Susceptibility testing was performed by CLSI methods (M07-A9) while interpretation of MIC results used the CLSI (2013) and EUCAST (2013) breakpoint criteria. Isolates displaying vancomycin and teicoplanin MIC results of >4 and >8 mg/L, respectively, were classified as VanA-phenotype whereas those with vancomycin and teicoplanin MIC results of >4 and <=8 mg/L, respectively, were classified as VanB-phenotype. *E. gallinarum* (24 isolates) and *E. casseliflavus* (14 isolates) were also included (intrinsic VanC producers).

**Results:** Against all *E. faecalis*, oritavancin (MIC50/90, 0.015/0.03 mg/L) demonstrated a MIC50 value at least 64-fold lower than ampicillin (MIC50/90, <=1/2 mg/L), vancomycin (MIC50/90, 1/2 mg/L), daptomycin (MIC50/90, 1/2 mg/L) and linezolid (MIC50/90, 1/2 mg/L), which all had susceptibility rates of >98.0%. Oritavancin was equally active when tested against vancomycin-susceptible and -resistant (VRE; VanB-phenotype) *E. faecalis*, MIC50, 0.015 mg/L, for both) and *E. faecium* (MIC50, <=0.008 mg/L, for both; Table). Vancomycin-resistant *E. faecalis* (VanA) had oritavancin MIC results 16-fold higher than the susceptible counterpart isolates. Only daptomycin (MIC50/90, 2/4 mg/L) and linezolid (MIC50/90, 1/2 mg/L) had in vitro activity (>=99.5% susceptible) against *E. faecium*. Enterococcal isolates other than *E. faecalis* and *E. faecium* (including VanC producers) showed oritavancin MIC50 and MIC90 results of <=0.008 and 0.015 mg/L, respectively. *E. gallinarum* and *E. casseliflavus* isolates showed variable vancomycin MIC results (MIC50/90, 4/8 mg/L; 65.8% susceptible). These VanC-producing isolates were inhibited by oritavancin at 0.03 mg/L, except for one VanA vancomycin-resistant isolate of *E. gallinarum* (MIC, 0.5 mg/L).

**Conclusions:** Oritavancin demonstrated in vitro activity greater than comparators when tested against this collection of enterococcal isolates, regardless of vancomycin phenotype. Of note, when tested against VanA-phenotype isolates, oritavancin was less active (four- to 16-fold) than against the vancomycin-susceptible and Van-B-phenotype counterparts; however, all isolates were inhibited at <=0.5 mg/mL. These results may warrant further investigations to assess the potential of oritavancin for the treatment of infections caused by multidrug-resistant enterococci, including VRE.