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P1883 Activity of tedizolid and comparators against *Enterococcus* spp. that include multidrug-resistant clinical isolates from European and US medical centres (2016-2018)

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Background: *Enterococcus* spp. pathogens are the second most common cause of gram-positive hospital-associated infections with significant mortality rates. Vancomycin-resistant enterococci (VRE), mainly *E. faecium*, commonly exhibit a multidrug-resistance phenotype, causing infections with limited treatment options. This study assessed the *in vitro* activity of tedizolid and comparators against a contemporary collection of enterococci, including VRE and isolates exhibiting high-level aminoglycoside (gentamicin and streptomycin) resistance (HLAR).

Materials/methods: A total of 2,854 enterococci (1,835 *E. faecalis*, 947 *E. faecium*, and 72 other *Enterococcus* spp.) were collected from US and European (and adjacent) regions during 2016–2018. MALDI-TOF MS confirmed bacterial identification, and isolates were susceptibility (S) tested and screened for HLAR by EUCAST method.

Results: Overall, tedizolid inhibited all but 5 enterococci at ≤0.5 mg/L. Isolates with VRE and/or HLAR phenotypes showed similar tedizolid MIC_{50} (0.12-0.25 mg/L) and MIC_{90} results (0.25-0.5 mg/L), regardless of enterococcal species (Table). Although VRE isolates were more frequently observed in the US than in European hospitals (63.2% vs.17.1% of *E. faecium* and 3.7% vs. 0.4% of *E. faecalis,* respectively), tedizolid MIC_{50} and MIC_{90} results remained at 0.12-0.25 mg/L and 0.25-0.5 mg/L ranges, respectively, against enterococci from both regions. *E. faecalis* showed high S rates (≥98.0%S) to linezolid, vancomycin, and ampicillin, and these agents, except vancomycin, remained active against the combined VRE and HLAR subset (1.3% of all *E. faecalis*). Overall, linezolid was very active ($MIC_{50/90}$, 1/2 mg/L; 99.6%S) against *E. faecium*, but tedizolid ($MIC_{50/90}$, 0.25/0.25 mg/L) had MIC results 4- to 8-fold lower than linezolid. A total of 4.1% of *E. faecium* were highly resistant (VRE and HLAR), and similar tedizolid MIC results were obtained against the VRE, HLAR, or both VRE/HLAR subsets ($MIC_{50/90}$, 0.25/0.25 mg/L). In this collection 4 linezolid non-S isolates (MIC, >4 mg/L) were observed, and all were inhibited by tedizolid at ≤1 mg/L. Two VRE isolates that showed elevated daptomycin MIC results (MIC >4 mg/L) were inhibited by tedizolid at ≤0.5 mg/L.

Conclusions: Overall, tedizolid remained potent against this challenge set of enterococcal clinical isolates, regardless of resistance phenotype. Tedizolid may be considered for treating serious enterococcal infections, granted clinical approval.

Organism (no. tested) Phenotype	$MIC_{50/90}$ (%S EUCAST)			
	Tedizolid	Linezolid	Daptomycin	Ampicillin
All (2,854)	0.25/0.25 (-)	1/2 (99.9)	1/2 (-)	1/>16 (71.2)
E. faecalis (1,835)	0.25/0.25 (-)	1/2 (100)	0.5/1 (-)	1/1 (100)
HLAR (200)	0.25/0.25 (-)	1/2 (100)	0.5/1 (-)	1/2 (100)
VRE (36)	0.25/0.25 (-)	1/2 (-)	0.5/1 (-)	1/2 (100)
HLAR and VRE (23)	0.25/0.25 (-)	1/1 (100)	0.5/1 (-)	1/2 (100)
E. faecium (947)	0.25/0.25 (-)	1/2 (99.6)	1/2 (-)	>16/>16 (13.3)
HLAR (117)	0.25/0.25 (-)	1/2 (98.3)	2/2 (-)	>16/>16 (3.4)
VRE (356)	0.25/0.25 (-)	1/2 (99.7)	1/2 (-)	>16/>16 (1.0)
HLAR and VRE (39)	0.25/0.25 (-)	1/2 (100)	2/2 (-)	>16/>16 (0.0)
Other *Enterococcus* spp. (72)	0.25/0.5 (-)	1/2 (100)	0.5/1 (-)	≤0.5/1 (98.6)
Vancomycin non S (13)	0.25/0.5 (-)	1/2 (100)	1/2 (-)	1/2 (100)