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P1806 Current in vitro analysis of tedizolid activity against Gram-positive clinical isolates causing bloodstream infections in Europe and surrounding areas (2014-2017)

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Background: Tedizolid is approved to treat acute bacterial skin and skin structure infections in Europe, the US, and other parts of the world. This study evaluated tedizolid and comparator activities against gram-positive isolates causing bloodstream infections (BSI) in hospitalised patients.

Materials/methods: A total of 5,319 gram-positive non-duplicate single-patient isolates were collected from patients hospitalised with documented BSI. Isolates originated from 20 European countries/regions (40 sites) and were submitted to a monitoring laboratory as part of the Surveillance of Tedizolid Activity and Resistance (STAR) program. Identification was confirmed and susceptibility testing was performed by CLSI methods. MIC interpretation used CLSI and/or EUCAST criteria.

Results: Tedizolid ($MIC_{50/90}$, 0.12/0.25 mg/L) showed MIC_{90} values 2-, 4-, and 4-fold lower than daptomycin ($MIC_{50/90}$, 0.25/0.5 mg/L), linezolid ($MIC_{50/90}$, 1/1 mg/L), and vancomycin ($MIC_{50/90}$, 0.5/1 mg/L), respectively, against MRSA. Tedizolid ($MIC_{50/90}$, 0.12/0.12 mg/L) and tigecycline ($MIC_{50/90}$, 0.06/0.12 mg/L) had similar MIC_{90} values against CoNS, which were 4- to 8-fold lower than daptomycin ($MIC_{50/90}$, 0.5/0.5 mg/L), linezolid ($MIC_{50/90}$, 0.5/1 mg/L), and ceftaroline ($MIC_{50/90}$, 0.25/1 mg/L) and 16-fold lower than vancomycin ($MIC_{50/90}$, 1/2 mg/L). All *Enterococcus faecalis* were susceptible to ampicillin and high susceptibility rates were obtained for tedizolid, linezolid, daptomycin, tigecycline, and vancomycin. A total of 18.8% of *Enterococcus faecium* were VRE, and only tedizolid ($MIC_{50/90}$, 0.12/0.25 mg/L), linezolid ($MIC_{50/90}$, 1/1-2 mg/L), and daptomycin ($MIC_{50/90}$, 2/2 mg/L) were active against all *E. faecium* or the VRE population. A total of 22.7% and 11.2% of *S. pneumoniae* were penicillin- and/or ceftriaxone-nonsusceptible, respectively, and tedizolid inhibited all isolates at ≤0.5 mg/L. Ceftaroline (MIC_{90}, ≤0.015 mg/L), ceftriaxone (MIC_{90}, ≤0.06 mg/L), and penicillin (MIC_{90}, ≤0.06 mg/L) showed the lowest MICs against BHS, followed by tedizolid (MIC_{90}, 0.25 mg/L) and daptomycin (MIC_{90}, 0.25 mg/L). A total of 19.5% and 13.0% of viridans group streptococci (VGS) were nonsusceptible to penicillin and/or ceftriaxone, respectively. Tedizolid (MIC_{90}, 0.25 mg/L), ceftaroline (MIC_{90}, 0.06 mg/L), and vancomycin (MIC_{90}, 0.5 mg/L) had the lowest MIC_{90} values against VGS.

Organism[a] (no. tested)	MIC$_{90}$ (mg/L)/% susceptible[b]					
	TZD	LZD	VAN	DAP	CRO	PEN
MRSA (604)	0.25/99.8	1/100.0	1/100.0	0.5/99.8	NA	NA
MSSA (1,754)	0.25/99.9	1/100.0	1/100.0	0.5/100.0	NA	NA
CoNS (895)	0.12/99.6	1/99.6	2/100.0	0.5/99.8	NA	NA
E. faecalis (598)	0.25/100.0[b]	2/100.0	2/99.0	1/100.0[b]	NA	2/100.0[b]
E. faecium (409)	0.25/-	2/99.3	>16/81.2	2/100.0[b]	NA	>8/6.1[b]
VRE (77)	0.25/-	1/98.7	>16/0.0	2/100.0[b]	NA	>8/0.0[b]
S. pneumoniae (313)	0.25/-	2/100.0	0.25/100.0	NA	1/88.8	1/77.3
BHS (384)	0.25/100.0	1/100.0	0.5/100.0	0.25/100.0	≤0.06/100.0	≤0.06/100.0
VGS (333)	0.25/99.7	1/100.0	0.5/100.0	1/99.3[b]	1/87.0	2/80.5

[a] MRSA = methicillin-resistant *S. aureus*; MSSA = methicillin-susceptible *S. aureus*; CoNS = coagulase-negative staphylococci; BHS = β-haemolytic streptococci; VGS = viridans group streptococci.

[b] TZD, tedizolid; LZD, linezolid; VAN, vancomycin; DAP, daptomycin; CRO, ceftriaxone; PEN, penicillin. Susceptibility based on EUCAST criteria, unless specified. Penicillin results against enterococci are from ampicillin.

Conclusions: Tedizolid showed potent activity against isolates causing BSI in hospitalised patients in Europe, including against VRE. These data warrant the clinical development of tedizolid for treating BSI.