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P1807 Evaluation of tedizolid activity against Gram-positive clinical isolates causing pneumonia in Europe and surrounding areas (2014-2017)

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Background: Tedizolid is currently approved to treat acute bacterial skin and skin structure infections (ABSSSI) and is in an ongoing Phase 3 clinical trial for nosocomial pneumonia. This study evaluated the tedizolid and comparator activities in vitro against gram-positive isolates causing pneumonia in hospitalized patients.

Materials/methods: A total of 1,824 gram-positive non-duplicate single-patient isolates were collected from the respiratory tract of patients hospitalized with pneumonia. Isolates originated from 19 European countries/regions (37 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 EUCAST criteria and community- (CA) and hospital-associated (HA) MRSA infections were defined based on CDC criteria.

Results: Overall, tedizolid showed MIC_{50} and MIC_{90} values of 0.12 and 0.25 mg/L against all *S. aureus*, or the methicillin-susceptible, -resistant, CA- or HA-MRSA subsets. Tigecycline ($MIC_{50/90}$, 0.06/0.12 mg/L), tedizolid ($MIC_{50/90}$, 0.12/0.25 mg/L), and vancomycin ($MIC_{50/90}$, 0.5/1 mg/L) were the most active agents against MRSA. Tedizolid inhibited all coagulase-negative staphylococci (CoNS; 84.8% methicillin-resistant) at ≤0.25 mg/L, and tedizolid and tigecycline ($MIC_{50/90}$, 0.06/0.25 mg/L; 100.0% susceptible) showed the lowest MIC values against CoNS. All *Enterococcus faecalis* remained susceptible to ampicillin, vancomycin, and the oxazolidinones. A total of 15.4% of *Enterococcus faecium* isolates were vancomycin-resistant and only tedizolid ($MIC_{50/90}$, 0.12/0.25 mg/L) and linezolid ($MIC_{50/90}$, 1/1 mg/L) were active *in vitro*. Tedizolid (MIC_{90}, 0.25 mg/L), ceftaroline (MIC_{90}, 0.12 mg/L), and vancomycin (MIC_{90}, 0.25 mg/L) were the most active against *Streptococcus pneumoniae,* and similar MIC_{90} results were observed against penicillin-resistant (≥2 mg/L) *S. pneumoniae.* Tedizolid (MIC_{90}, 0.25 mg/L), ceftaroline (MIC_{90}, 0.12 mg/L), and vancomycin (MIC_{90}, 0.5 mg/L) had the lowest MIC_{90} values against viridans group streptococci (32.0% penicillin-nonsusceptible), whereas ceftaroline (MIC_{90}, ≤0.015 mg/L), penicillin (MIC_{90}, ≤0.06 mg/L), ceftriaxone (MIC_{90}, 0.12 mg/L), and tedizolid (MIC_{90}, 0.25 mg/L) were most potent against β-haemolytic streptococci.

Conclusions: In general, tedizolid showed potent and greater activity than comparator agents against isolates causing pneumonia in hospitalized patients in Europe. These in vitro data warrant the clinical development of tedizolid for treating pneumonia.

Organism[a] (no. tested)	MIC_{50}/MIC_{90} (mg/L)[b]					
	TZD	LZD	VAN	CPT	CRO	PEN
MRSA (400)	0.12/0.25	1/1	0.5/1	1/2	NA	NA
MSSA (1,134)	0.12/0.25	1/2	1/1	0.25/0.25	NA	NA
CoNS (46)	0.12/0.12	0.5/1	1/2	0.5/2	NA	NA
E. faecalis (46)	0.25/0.25	1/2	1/2	NA	NA	NA
E. faecium (26)	0.12/0.25	1/1	≤0.5/>16	NA	NA	NA
S. pneumoniae (101)	0.12/0.25	1/1	0.25/0.25	≤0.015/0.12	≤0.06/1	≤0.06/2
BHS (46)	0.12/0.25	1/2	0.25/0.5	≤0.015/≤0.015	≤0.06/0.12	≤0.06/≤0.06
VGS (25)	0.12/0.25	0.5/1	0.5/0.5	0.03/0.12	0.25/2	≤0.06/2

[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; CPT, ceftaroline; CRO, ceftriaxone; PEN, penicillin.