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The Activity of Tedizolid against Gram-positive Pathogens Isolated from Patients in Medical Centres in Europe, Turkey and Israel: 2014 Surveillance

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Introduction and Purpose

- Tedizolid phosphate, the prodrug of the oxazolidinone tedizolid, has been approved for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in Europe, the United States and some other countries throughout the world[1,2]
- Two Phase 3 trials, ESTABLISH-1 (NCT01170221) and ESTABLISH-2 (NCT01421511), demonstrated the non-inferior efficacy of tedizolid phosphate (200 mg once daily for 6 days) to linezolid (600 mg twice daily for 10 days) in patients with ABSSSI[3-5]
- Tedizolid is generally at least 4-fold more potent *in vitro*, based on minimum inhibitory concentration (MIC) required to inhibit growth of 90% of the isolates (MIC$_{90}$), than linezolid against susceptible and non-susceptible strains of staphylococci (including methicillin-resistant *Staphylococcus aureus* [MRSA]); β-haemolytic streptococci (BHS) of groups A, B, C and G; viridans group streptococci (VGS) (*Streptococcus anginosus* group only); and *Enterococcus faecalis* (including vancomycin-resistant enterococci)[6-8]
- Surveillance of Tedizolid Activity and Resistance[9] (STAR) is an ongoing programme to monitor the activity of tedizolid against clinically relevant Gram-positive pathogens; STAR also monitors the emergence of resistance
- We report the *in vitro* activity of tedizolid when tested against Gram-positive pathogens isolated from patients in Europe, Turkey and Israel as part of the STAR programme in 2014

Methods

Sampling sites and organisms

- Non-duplicate, single-patient, clinically significant isolates of *S. aureus* (1,933), coagulase-negative staphylococci (CoNS; 452), BHS (239), VGS (110) and enterococci (766) causing a variety of clinical infections (skin and skin structure infections, 34.6%; pneumonia, 28.0%; bacteraemia, 27.6%; and other infections, 9.8%) were consecutively collected in 2014
  - Isolates were recovered from hospitalised patients in 34 medical centres across 13 European countries, Turkey and Israel
  - The following countries (number of medical centres) participated: Belgium (1), France (4), Germany (5), Greece (1), Ireland (2), Israel (1), Italy (4), Poland (1), Portugal (1), Russia (3), Spain (3), Sweden (2), Turkey (2), Ukraine (1) and United Kingdom (3)

Antimicrobial susceptibility testing

- MIC values were determined in accordance with the Clinical and Laboratory Standards Institute (CLSI) broth microdilution method (M07-A10)[10]
- Quality control ranges and interpretive criteria for comparator compounds were determined in accordance with CLSI M100-S26[11] and European Committee on Antimicrobial Susceptibility Testing (EUCAST), version 6.0 (2016)[12] guidelines
- Isolates were tested for antibacterial susceptibility (S) using broth microdilution per CLSI guidelines
  - Tedizolid and linezolid MIC values were read by two methods:
    - Reading the MIC at the first well at which trailing begins without regard for pinpoint trailing in the wells, per CLSI M07-A10[10] and M100-S26[11] document instructions for reading linezolid (i.e. '80% inhibition'; these reads have been designated tedizolid80 and linezolid80)
    - At 100% inhibition of growth (designated tedizolid100 and linezolid100)

Results

- Tedizolid MIC distributions for all organisms and resistant subsets are summarised in **Table 1**
- The activities of tedizolid and comparator agents tested against bacterial clinical isolates from the STAR programme are presented in **Table 2**

S. aureus

- 1,933 *S. aureus* isolates were evaluated
  - 100% of isolates were inhibited at tedizolid 80/100 MIC values of 0.25/0.5 mg/L; the minimum inhibitory concentration required to inhibit growth of 50% and 90% of isolates (MIC$_{50/90}$) values for tedizolid80 (0.12/0.12 mg/L) was 1 doubling dilution lower than that of tedizolid100 (0.25/0.25 mg/L)
  - Based on CLSI and EUCAST approved breakpoints, 100.0% of isolates were susceptible to tedizolid (**Table 2**)
  - 1,447 isolates (74.9%) were methicillin-resistant *S. aureus* (MSSA) and 486 (25.1%) were MRSA; tedizolid80 MIC$_{50/90}$ values (0.12/0.12 mg/L) were identical for MSSA, MRSA and overall (**Table 1**)
- Against all 1,933 isolates, susceptibility (EUCAST interpretations) rates for erythromycin and levofloxacin were 73.7% and 75.2%, respectively (**Table 2**)
  - Susceptibility rates were much higher for clindamycin (92.2%), tetracycline (93.7%), trimethoprim/sulfamethoxazole (99.3%), ceftaroline (96.0%), linezolid (100.0%), daptomycin (99.9%), tigecycline (100.0%) and vancomycin (100.0%) (**Table 2**)
  - Tedizolid was up to 4-fold more potent than linezolid (**Table 2**)

CoNS

- 452 CoNS isolates were tested
  - 100.0% of isolates were inhibited at tedizolid80/100 MIC values of 0.25/0.5 mg/L
  - The MIC$_{50/90}$ values for tedizolid80 (0.06/0.12 mg/L) were 1 doubling dilution lower than that of tedizolid100 (0.12/0.25 mg/L; **Table 1**)
  - Using breakpoints approved by EUCAST, 100.0% of isolates were susceptible to tedizolid (**Table 2**)
- Overall, 31.4% of isolates were methicillin-susceptible (MS)-CoNS and 68.6% were methicillin-resistant (MR)-CoNS (**Table 1**)
  - Tedizolid80 MIC$_{50/90}$ values (0.06/0.12 mg/L) were identical for MS-CoNS, MR-CoNS and overall (**Table 1**)
  - Tedizolid was 4-fold more potent than linezolid (**Table 2**)
  - Susceptibility of CoNS to linezolid, daptomycin and vancomycin was 100.0% (**Table 2**)

Streptococcus spp.

- 94 *S. pyogenes* isolates were tested
  - All isolates were inhibited at tedizolid80/100 MIC values of 0.25/0.5 mg/L
  - The MIC$_{50/90}$ values for tedizolid80 (0.12/0.12 mg/L) were up to 1 doubling dilution lower than for tedizolid100 (0.12/0.25 mg/L (**Table 1**)
  - Based on breakpoints approved by CLSI and EUCAST, 100.0% of isolates were susceptible to tedizolid (**Table 2**)
- 100 *S. agalactiae* isolates were tested and inhibited at tedizolid80/100 MIC values of 0.25/0.25 mg/L
  - The MIC$_{50/90}$ values for tedizolid80 (0.12/0.12 mg/L) were 1 doubling dilution lower than for tedizolid100 (0.25/0.25 mg/L; **Table 1**)
  - Using breakpoints approved by EUCAST, 100.0% of isolates were susceptible to tedizolid (**Table 2**)
- 45 *S. dysgalactiae* isolates were tested, and 100.0% were inhibited at tedizolid80/100 MIC values of 0.25/0.25 mg/L
  - The MIC$_{90}$ value for tedizolid80 (0.12 mg/L) was 1 doubling dilution lower than for tedizolid100 (0.25 mg/L; **Table 1**)
  - Using breakpoints approved by EUCAST, 100.0% of isolates were susceptible to tedizolid (**Table 2**)
- Tedizolid was very active against 110 VGS isolates, inhibiting all isolates at MIC values of ≤0.25 mg/L, with tedizolid100 being up to 4-fold more potent (MIC$_{50/90}$, 0.12/0.25 mg/L; **Table 1**) than linezolid100 (MIC$_{50/90}$, 1/1 mg/L; data not shown**)**
  - Using breakpoints approved by CLSI and EUCAST, 100.0% of 34 *S. anginosus* group isolates tested were susceptible to tedizolid
  - 100.0% of strains were inhibited at tedizolid80/100 MIC$_{90}$ values of 0.12/0.25 mg/L (**Table 2**)
  - The MIC$_{50/90}$ values for tedizolid80 (0.06/0.12 mg/L) were 1 doubling dilution lower than for tedizolid100 (0.12/0.25 mg/L; **Table 1**)
- Tedizolid100 was also very active (MIC$_{50/90}$, 0.25/0.25 mg/L) against 739 pneumococcal isolates, and all isolates were susceptible to linezolid (**Tables 1 and 2**)
  - The MIC$_{50/90}$ values for tedizolid80 (0.12/0.25 mg/L) were up to 1 doubling dilution lower than for tedizolid100 (0.25/0.25 mg/L; **Table 1**)
  - Tedizolid was 4- to 8-fold more potent than linezolid against pneumococci (**Table 2**)

Enterococcus spp.

- Among 472 *E. faecalis* isolates tested, 100.0% of strains were inhibited at an MIC value of ≤1 mg/L, and tedizolid80/100 MIC$_{90}$ values were 0.25/0.5 mg/L
  - The MIC$_{50/90}$ values for tedizolid80 (0.12/0.25 mg/L) were 1 doubling dilution lower than for tedizolid100 (0.25/0.5 mg/L; **Table 1**)
  - Using breakpoints approved by CLSI, 99.6% of isolates were susceptible to linezolid and 99.8% of isolates were susceptible to tedizolid (**Table 2**)
  - Tedizolid was 4-fold more potent than linezolid (**Table 2**)
- Among 281 *E. faecium* isolates tested, tedizolid80/100 MIC$_{90}$ values were 0.25/0.5 mg/L
  - The MIC$_{50/90}$ values for tedizolid80 (0.12/0.25 mg/L) were 1 doubling dilution lower than for tedizolid100 (0.25/0.5 mg/L; **Table 1**)

Table 1. Summary of tedizolid activity tested against bacterial isolates from patients with SSSI (2014)

Organism (n)	Agent/Read†	Number of Isolates (cumulative %) Inhibited at MIC, mg/L								
		≤0.015	0.03	0.06	0.12	0.25	0.5	1	MIC$_{50}$	MIC$_{90}$
Staphylococcus aureus (1,933)	Tedizolid80	0 (0.0)	20 (1.0)	404 (21.9)	1457 (97.3)	52 (100.0)			0.12	0.12
	Tedizolid100	0 (0.0)	2 (0.1)	39 (2.1)	741 (40.5)	1089 (96.8)	62 (100.0)		0.25	0.25
MSSA (1,447)	Tedizolid80	0 (0.0)	12 (0.8)	285 (20.5)	1111 (97.3)	39 (100.0)			0.12	0.12
	Tedizolid100	0 (0.0)	0 (0.0)	28 (1.9)	545 (39.6)	835 (97.3)	39 (100.0)		0.25	0.25
MRSA (486)	Tedizolid80	0 (0.0)	8 (1.6)	119 (26.1)	346 (97.3)	13 (100.0)			0.12	0.12
	Tedizolid100	0 (0.0)	2 (0.4)	11 (2.7)	196 (43.0)	254 (95.3)	23 (100.0)		0.25	0.25
CoNS‡ (452)	Tedizolid80	1 (0.2)	19 (4.4)	261 (62.2)	169 (99.6)	2 (100.0)			0.06	0.12
	Tedizolid100	1 (0.2)	0 (0.2)	62 (13.9)	319 (84.5)	65 (98.9)	5 (100.0)		0.12	0.25
MS-CoNS (142)	Tedizolid80	0 (0.0)	5 (3.5)	91 (67.6)	46 (100.0)				0.06	0.12
	Tedizolid100	0 (0.0)	0 (0.0)	17 (12.0)	109 (88.7)	15 (99.3)	1 (100.0)		0.12	0.25
MR-CoNS (310)	Tedizolid80	1 (0.3)	14 (4.8)	170 (59.7)	123 (99.4)	2 (100.0)			0.06	0.12
	Tedizolid100	1 (0.3)	0 (0.3)	45 (14.8)	210 (82.6)	50 (98.7)	4 (100.0)		0.12	0.25
Streptococcus pyogenes (94)	Tedizolid80	0 (0.0)	0 (0.0)	19 (20.2)	74 (98.9)	1 (100.0)			0.12	0.12
	Tedizolid100	0 (0.0)	0 (0.0)	4 (4.3)	64 (72.3)	25 (98.9)	1 (100.0)		0.12	0.25
Streptococcus agalactiae (100)	Tedizolid80	0 (0.0)	0 (0.0)	7 (7.0)	89 (96.0)	4 (100.0)			0.12	0.12
	Tedizolid100	0 (0.0)	0 (0.0)	1 (1.0)	42 (43.0)	57 (100.0)			0.25	0.25
Streptococcus dysgalactiae (45)	Tedizolid80	0 (0.0)	0 (0.0)	4 (8.9)	40 (97.8)	1 (100.0)			0.12	0.12
	Tedizolid100	0 (0.0)	0 (0.0)	0 (0.0)	27 (60.0)	18 (100.0)			0.12	0.25
VGS (110)§	Tedizolid80	0 (0.0)	7 (6.4)	43 (45.5)	55 (95.5)	5 (100.0)			0.12	0.12
	Tedizolid100	0 (0.0)	4 (3.6)	15 (17.3)	70 (80.9)	21 (100.0)			0.12	0.25
Streptococcus anginosus group‖ (34)	Tedizolid80	0 (0.0)	4 (11.8)	17 (61.8)	12 (97.1)	1 (100.0)			0.06	0.12
	Tedizolid100	0 (0.0)	2 (5.9)	9 (32.4)	17 (82.4)	6 (100.0)			0.12	0.25
Streptococcus pneumoniae (739)	Tedizolid80	4 (0.5)	6 (1.4)	67 (10.4)	571 (87.7)	91 (100.0)			0.12	0.25
	Tedizolid100	2 (0.3)	3 (0.7)	25 (4.1)	268 (40.3)	436 (99.3)	5 (100.0)		0.25	0.25
Enterococcus faecalis (472)	Tedizolid80	0 (0.0)	0 (0.0)	9 (1.9)	238 (52.3)	223 (99.6)	1 (99.8)	1 (100.0)	0.12	0.25
	Tedizolid100	0 (0.0)	0 (0.0)	0 (0.0)	40 (8.5)	353 (83.3)	75 (99.2)	4 (100.0)	0.25	0.5
Enterococcus faecium (281)	Tedizolid80	0 (0.0)	1 (0.4)	19 (7.1)	210 (81.9)	51 (100.0)			0.12	0.25
	Tedizolid100	0 (0.0)	0 (0.0)	1 (0.4)	63 (22.8)	171 (83.6)	37 (96.8)	8 (99.6)	0.25	0.5

CoNS = coagulase-negative staphylococci; MIC = minimum inhibitory concentration; MIC$_{50}$ = minimum inhibitory concentration required to inhibit growth of 50% of isolates; MIC$_{90}$ = minimum inhibitory concentration required to inhibit growth of 90% of isolates; MR-CoNS = methicillin-resistant coagulase-negative staphylococci; MRSA = methicillin-resistant *S. aureus*; MS-CoNS = methicillin-susceptible coagulase-negative staphylococci; MSSA = methicillin-susceptible *S. aureus*; SSSI = skin and skin structure infection; VGS = viridans group streptococci.

†Antimicrobial agent (tedizolid). 100 = MIC read at first well that shows no growth. 80 = MIC read at the first microtitre well in which trailing begins, with tiny buttons being ignored (as per CLSI document M07-10, 2015 and M100-S26, 2016).[10,11]

‡Includes *Staphylococcus capitis* (29), *Staphylococcus caprae* (2), *Staphylococcus cohnii* (1), *Staphylococcus epidermidis* (247), *Staphylococcus haemolyticus* (57), *Staphylococcus hominis* (42), *Staphylococcus intermedius* (1), *Staphylococcus lugdunensis* (26), *Staphylococcus pettenkoferi* (2), *Staphylococcus pseudintermedius* (1), *Staphylococcus saprophyticus* (17), *Staphylococcus schleiferi* (1), *Staphylococcus sciuri* (1), *Staphylococcus simulans* (4), *Staphylococcus warneri* (19), *Staphylococcus xylosus* (2).

§Includes *Streptococcus anginosus* (20), *S. anginosus* group (1), *Streptococcus australis* (1), *Streptococcus canis* (1), *Streptococcus constellatus* (13), *Streptococcus gallolyticus* (3), *Streptococcus gordonii* (3), *Streptococcus infantis* (1), *Streptococcus lutetiensis* (1), *Streptococcus mitis* (3), *S. mitis* group (6), *S. mitis/Streptococcus oralis* (19), *S. oralis* (19), *Streptococcus parasanguinis* (3), *Streptococcus salivarius* (7), *S. salivarius* group (2), *Streptococcus sanguinis* (6), *Streptococcus suis* (1).

‖*S. anginosus* subgroup of VGS, includes *S. anginosus* (20), *S. anginosus* group (1), *Streptococcus constellatus* (13).

Table 2. Activity of tedizolid and comparator antimicrobial agents when tested against bacterial isolates from patients in Europe, Turkey and Israel, 2014

Organism (n) / antimicrobial agent	MIC, mg/L		%S / %I / %R†	
	MIC$_{50}$	MIC$_{90}$	CLSI	EUCAST
***Staphylococcus aureus* (1,933)**				
Tedizolid80	0.12	0.12	100.0 / 0.0 / 0.0	100.0 / – / 0.0
Tedizolid100	0.25	0.25	– / – / –	– / – / –
Linezolid80	1	1	100.0 / – / 0.0	100.0 / – / 0.0
Linezolid100	1	2	– / – / –	– / – / –
Ceftaroline	0.25	1	96.0 / 3.9 / 0.2	96.0 / – / 4.0
Clindamycin	≤0.25	≤0.25	92.6 / 0.1 / 7.4	92.2 / 0.4 / 7.4
Daptomycin	0.25	0.5	99.9 / – / –	99.9 / – / 0.1
Erythromycin	0.25	>16	73.2 / 3.2 / 23.6	73.7 / 0.9 / 25.5
Levofloxacin	0.25	>4	75.2 / 0.3 / 24.6	75.2 / 0.3 / 24.6
Oxacillin	0.5	>2	74.9 / – / 25.1	74.9 / – / 25.1
Tetracycline	≤0.5	≤0.5	93.9 / 0.6 / 5.5	93.7 / 0.1 / 6.2
Tigecycline‡	0.06	0.06	100.0 / – / –	100.0 / – / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	99.3 / – / 0.7	99.3 / 0.3 / 0.4
Vancomycin	1	1	100.0 / 0.0 / 0.0	100.0 / – / 0.0
CoNS (452)§				
Tedizolid80	0.06	0.12	– / – / –	100.0 / – / 0.0
Tedizolid100	0.12	0.25	– / – / –	– / – / –
Linezolid80	0.5	0.5	100.0 / – / 0.0	100.0 / – / 0.0
Linezolid100	1	1	– / – / –	– / – / –
Ceftaroline	0.25	1	– / – / –	– / – / –
Clindamycin	≤0.25	>2	76.3 / 0.2 / 23.5	74.6 / 1.8 / 23.7
Daptomycin	0.25	0.5	100.0 / – / –	100.0 / – / 0.0
Erythromycin	16	>16	40.6 / 1.8 / 57.6	41.0 / 0.2 / 58.8
Levofloxacin	1	>4	50.0 / 4.4 / 45.6	50.0 / 4.4 / 45.6
Oxacillin	>2	>2	31.4 / 0.0 / 68.6	31.4 / 0.0 / 68.6
Tetracycline	≤0.5	>8	86.0 / 2.0 / 12.0	81.8 / 2.7 / 15.5
Tigecycline‡	0.06	0.12	– / – / –	100.0 / – / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	>4	70.8 / – / 29.2	70.8 / 14.6 / 14.6
Vancomycin	1	2	100.0 / 0.0 / 0.0	100.0 / – / 0.0
***Streptococcus pyogenes* (94)**				
Tedizolid80	0.12	0.12	100.0 / – / –	100.0 / – / 0.0
Tedizolid100	0.12	0.25	– / – / –	– / – / –
Linezolid80	0.5	1	100.0 / – / –	100.0 / 0.0 / 0.0
Linezolid100	1	2	– / – / –	– / – / –
Ceftaroline	≤0.015	≤0.015	100.0 / – / –	100.0 / – / 0.0
Clindamycin	≤0.25	≤0.25	94.7 / 0.0 / 5.3	94.7 / – / 5.3
Daptomycin	≤0.06	0.12	100.0 / – / –	100.0 / – / 0.0
Erythromycin	≤0.12	≤0.12	94.6 / 0.0 / 5.4	94.6 / 0.0 / 5.4
Levofloxacin	0.5	1	100.0 / 0.0 / 0.0	95.7 / 4.3 / 0.0
Tetracycline	≤0.5	>8	73.1 / 0.0 / 26.9	72.0 / 1.1 / 26.9
Vancomycin	0.25	0.25	100.0 / – / –	100.0 / – / 0.0
***Streptococcus agalactiae* (100)**				
Tedizolid80	0.12	0.12	100.0 / – / –	100.0 / – / 0.0
Tedizolid100	0.25	0.25	– / – / –	– / – / –
Linezolid80	1	1	100.0 / – / 0.0	100.0 / 0.0 / 0.0
Linezolid100	1	1	– / – / –	– / – / –
Ceftaroline	≤0.015	≤0.015	100.0 / – / –	100.0 / – / 0.0
Clindamycin	≤0.25	>2	78.0 / 1.0 / 21.0	79.0 / – / 21.0
Daptomycin	0.25	0.25	100.0 / – / –	100.0 / – / 0.0
Erythromycin	≤0.12	>16	68.0 / 1.0 / 31.0	68.0 / 1.0 / 31.0
Levofloxacin	0.5	1	99.0 / 0.0 / 1.0	98.0 / 1.0 / 1.0
Tetracycline	>8	>8	27.0 / 0.0 / 73.0	26.0 / 1.0 / 73.0
Vancomycin	0.5	0.5	100.0 / – / –	100.0 / – / 0.0
***Streptococcus dysgalactiae* (45)**				
Tedizolid80	0.12	0.12	– / – / –	100.0 / – / 0.0
Tedizolid100	0.12	0.25	– / – / –	– / – / –
Linezolid80	0.5	1	100.0 / – / –	100.0 / 0.0 / 0.0
Linezolid100	1	1	– / – / –	– / – / –
Ceftaroline	≤0.015	≤0.015	100.0 / – / –	100.0 / – / 0.0
Clindamycin	≤0.25	>2	89.3 / 0.0 / 10.7	89.3 / – / 10.7
Daptomycin	≤0.06	≤0.06	100.0 / – / –	100.0 / – / 0.0
Erythromycin	≤0.12	2	78.6 / 0.0 / 21.4	78.6 / 0.0 / 21.4
Levofloxacin	0.5	0.5	100.0 / 0.0 / 0.0	100.0 / 0.0 / 0.0
Tetracycline	2	>8	51.9 / 18.5 / 29.6	48.1 / 3.8 / 48.1
Vancomycin	0.25	0.25	100.0 / – / –	100.0 / – / 0.0
***Streptococcus anginosus* group‖ (34)**				
Tedizolid80	0.06	0.12	100.0 / – / –	100.0 / – / 0.0
Tedizolid100	0.12	0.25	– / – / –	– / – / –
Linezolid80	0.5	1	100.0 / – / 0.0	100.0 / 0.0 / 0.0
Linezolid100	1	1	– / – / –	– / – / –
Penicillin	≤0.06	0.12	100.0 / 0.0 / 0.0	100.0 / 0.0 / 0.0
Ceftaroline	0.03	0.06	– / – / –	– / – / –
Clindamycin	≤0.25	≤0.25	91.2 / 0.0 / 8.8	91.2 / – / 8.8
Daptomycin	0.25	0.5	100.0 / – / –	– / – / –
Erythromycin	≤0.12	1	88.2 / 0.0 / 11.8	– / – / –
Levofloxacin	0.5	0.5	100.0 / 0.0 / 0.0	– / – / –
Tetracycline	≤0.5	>8	82.4 / 0.0 / 17.6	– / – / –
Vancomycin	0.5	1	100.0 / – / –	100.0 / – / 0.0
***Streptococcus pneumoniae* (739)**				
Tedizolid 80	0.12	0.25	– / – / –	– / – / –
Tedizolid100	0.25	0.25	– / – / –	– / – / –
Linezolid 80	1	1	100.0 / – / 0.0	100.0 / 0.0 / 0.0
Linezolid100	1	2	– / – / –	– / – / –
Amoxicillin/clavulanate	≤1	2	92.0 / 2.4 / 5.5¶	– / – / –
Penicillin	≤0.06	2	66.8 / 19.5 / 13.7††	66.8 / 28.1 / 5.0¶
Ceftriaxone	≤0.06	1	92.7 / 6.4 / 10.9¶	82.0 / 17.1 / 0.9
Clindamycin	≤0.25	>2	79.0 / 1.1 / 19.9	80.1 / – / 19.9
Erythromycin	≤0.12	>16	71.1 / 0.4 / 28.5	71.1 / 0.4 / 28.5
Levofloxacin	1	1	98.9 / 0.3 / 0.8	98.9 / – / 0.1
Tetracycline	≤0.5	>8	73.0 / 0.7 / 26.3	73.0 / 0.7 / 26.3
Vancomycin	0.25	0.25	100.0 / – / –	100.0 / – / 0.0
***Enterococcus faecalis* (472)**				
Tedizolid80	0.12	0.25	99.8 / – / –	– / – / –
Tedizolid100	0.25	0.5	– / – / –	– / – / –
Linezolid80	1	1	99.6 / 0.2 / 0.2	99.8 / – / 0.2
Linezolid100	2	2	– / – / –	– / – / –
Daptomycin	1	2	100.0 / – / –	– / – / –
Levofloxacin	1	>4	67.8 / 0.4 / 31.8	68.2 / – / 31.8‡‡
Vancomycin	1	2	98.9 / 0.2 / 0.8	98.9 / – / 1.1
***Enterococcus faecium* (281)**				
Tedizolid80	0.12	0.25	– / – / –	– / – / –
Tedizolid100	0.25	0.5	– / – / –	– / – / –
Linezolid80	1	1	100.0 / 0.0 / 0.0	100.0 / – / 0.0
Linezolid100	2	2	– / – / –	– / – / –
Daptomycin	2	4	100.0 / – / –	– / – / –
Levofloxacin	>4	>4	6.4 / 2.5 / 91.1	8.9 / – / 91.1‡‡
Vancomycin	1	>16	72.6 / 0.7 / 26.7	72.6 / – / 27.4

CLSI = Clinical and Laboratory Standards Institute; CoNS = coagulase-negative staphylococci; EUCAST = European Committee on Antimicrobial Susceptibility Testing; MIC, minimum inhibitory concentration; MIC$_{50}$ = minimum inhibitory concentration required to inhibit growth of 50% of isolates; MIC$_{90}$ = minimum inhibitory concentration required to inhibit growth of 90% of isolates; R = resistant; I = intermediate; S = susceptible.

†Criteria as published by the CLSI (2016)[11] and EUCAST (2016).[12]
‡In the absence of a CLSI breakpoint, US Food and Drug Administration breakpoints were applied.[13]

§Includes *Staphylococcus capitis* (29), *Staphylococcus caprae* (2), *Staphylococcus cohnii* (1), *Staphylococcus epidermidis* (247), *Staphylococcus haemolyticus* (57), *Staphylococcus hominis* (42), *Staphylococcus intermedius* (1), *Staphylococcus lugdunensis* (26), *Staphylococcus pettenkoferi* (2), *Staphylococcus pseudintermedius* (1), *Staphylococcus saprophyticus* (17), *Staphylococcus schleiferi* (1), *Staphylococcus sciuri* (1), *Staphylococcus simulans* (4), *Staphylococcus warneri* (19), *Staphylococcus xylosus* (2).
‖Includes *Streptococcus anginosus* (20), *S. anginosus* group (1), *Streptococcus constellatus* (13).
¶Using non-meningitis breakpoints.
††Using oral breakpoints.
‡‡Uncomplicated urinary tract infection only.

Conclusions

- Tedizolid demonstrated higher *in vitro* activity (2- to 4-fold depending on the 80% or 100% read-matched comparisons) than linezolid when tested against Gram-positive pathogens isolated from patients in medical centres across Europe, Turkey and Israel in 2014
- Generally, MIC values (including MIC distributions and MIC$_{50/90}$) for tedizolid and linezolid read without regard for pinpoint trailing colonies (80% read) were 1 doubling dilution lower than those read at 100% inhibition
- Tedizolid resistance was not observed in this study, and, using CLSI and EUCAST approved breakpoints, 100.0% of 1,933 *S. aureus* isolates (25.1% MRSA) were susceptible to tedizolid
  - Using EUCAST breakpoints, 100.0% of CoNS and *S. dysgalactiae* isolates were susceptible to tedizolid
  - Using CLSI breakpoints, 100.0% of *S. pyogenes* and *S. agalactiae* isolates and 99.8% of *E. faecalis* isolates were susceptible to tedizolid
  - Tedizolid was also very active against *E. faecium*, VGS and *S. pneumoniae*
- Continued surveillance of tedizolid activity is important for monitoring *in vitro* activity and potential emergence of resistance

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