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In Vitro Activity of Tedizolid Against Gram-Positive Pathogens Isolated From Patients With Skin and Skin Structure Infections in the United States and Europe During 2014

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Introduction

- Tedizolid is approved for treatment of acute bacterial skin and skin structure infections (ABSSSI) in the United States (USA), European Union (EU), and Canada[1-3]
- Two Phase 3 trials, ESTABLISH-1 (NCT01170221) and ESTABLISH-2 (NCT01421511), demonstrated the noninferior efficacy of tedizolid (200 mg once daily for 6 days) to linezolid (600 mg twice daily for 10 days) in patients with ABSSSI[4-6]
- The Surveillance of Tedizolid Activity and Resistance (STAR) Program is an ongoing effort to monitor the activity of tedizolid against clinically relevant Gram-positive pathogens[7]
- We report the *in vitro* activity of tedizolid when tested against Gram-positive pathogens isolated from patients with SSSI collected in the USA and EU (including Turkey and Israel) as part of the STAR Program in 2014

Methods

Sampling Sites and Organisms

- Nonduplicate, single patient SSSI clinical isolates (USA/EU) of *Staphylococcus aureus* (SA; 1,671/962), coagulase-negative staphylococci (CoNS; 88/159), β-hemolytic streptococci (BHS; 302/126), and enterococci (ENT; 121/203) were consecutively collected in 2014 from 28 medical centers located across all 9 USA census regions and from 33 medical centers in the EU (including Turkey and Israel)
- For the USA, the following states (number of medical centers) participated: Arkansas (1), California (1), Colorado (1), Florida (2), Georgia (1), Iowa (1), Indiana (1), Kentucky (2), Massachusetts (2), Michigan (1), Missouri (1), Nebraska (1), New Jersey (1), New York (3), Ohio (1), Texas (2), Utah (1), Virginia (1), Vermont (1), Washington (2), and Wisconsin (1)
- For the EU, the following countries (number of medical centers) participated: Belgium (1), France (4), Germany (5), Greece (1), Ireland (2), Israel (1), Italy (3), Poland (1), Portugal (1), Russia (3), Spain (3), Sweden (2), Turkey (2), United Kingdom (3), and Ukraine (1)

Antimicrobial Susceptibility Testing

- Minimum inhibitory concentration (MIC) values were determined using the reference Clinical and Laboratory Standards Institute (CLSI) broth microdilution method (M07-A10)[8]
- Quality control ranges and interpretive criteria for comparator compounds used the CLSI M100-S25 and EUCAST v5.0 (2015) guidelines[9-10]
- Tedizolid and linezolid MIC values were read by two methods: without regard for pinpoint trailing in the wells ("80%" read, as per CLSI M07-A10 instructions for reading linezolid; these reads have been designated tedizolid 80 and linezolid 80) and at 100% inhibition of growth (designated tedizolid 100 and linezolid 100)

Results

- Summaries of tedizolid MIC distributions for all organisms and resistant subsets for all isolates tested (USA and EU combined) are summarized in **Table 1**
- The activities of tedizolid and comparator agents tested against bacterial clinical isolates from the STAR Program are presented in **Table 2** for USA isolates and **Table 3** for EU isolates

Staphylococcus aureus

- A total of 2,633 *S. aureus* strains were evaluated; 100.0% of strains were inhibited at tedizolid 80/100 MIC values of 0.25/0.5 µg/mL
  - The $MIC_{50/90}$ values for tedizolid 80 (0.12/0.12 µg/mL) were one doubling dilution lower than tedizolid 100 (0.25/0.25 µg/mL)
  - Using USA-FDA breakpoints and breakpoints approved by EUCAST, 100.0% of isolates were susceptible to tedizolid (**Table 1**)
- Overall, 1,586 (60.2%) isolates were MSSA and 1,047 (39.8%) were MRSA. Tedizolid 80 $MIC_{50/90}$ values (0.12/0.12 µg/mL) were identical for MSSA, MRSA, and overall (**Table 1**)
- For 1,671 *S. aureus* from the USA, 50.2% of isolates were MRSA
  - Susceptibility (CLSI interpretations) rates to clindamycin, erythromycin, and levofloxacin were 87.8%, 38.9%, and 64.6%, respectively
  - Susceptibility rates were much higher for tetracycline (95.1%), trimethoprim/sulfamethoxazole (98.7%), ceftaroline (99.0%), daptomycin (99.9%), linezolid (100.0%), tigecycline (100.0%), and vancomycin (100.0%)
  - Tedizolid was four-fold more potent than linezolid (**Table 2**)
- For 962 *S. aureus* isolated in the EU, 22.3% of isolates were MRSA
  - Susceptibility (EUCAST interpretations) rates to erythromycin and levofloxacin were 77.1% and 77.7%, respectively
  - Susceptibility rates were much higher for clindamycin (93.3%), tetracycline (94.2%), trimethoprim/sulfamethoxazole (99.2%), ceftaroline (98.3%), linezolid (100.0%), daptomycin (100.0%), tigecycline (100.0%), and vancomycin (100.0%)
  - Tedizolid was four-fold more potent than linezolid (**Table 3**)

Coagulase-negative staphylococci (CoNS)

- A total of 247 CoNS were tested; 100.0% of strains were inhibited at tedizolid 80/100 MIC values of 0.12/0.5 µg/mL
  - The $MIC_{50/90}$ values for tedizolid 80 (0.06/0.12 µg/mL) were one doubling dilution lower than tedizolid 100 (0.12/0.25 µg/mL; **Table 1**)
  - Using breakpoints approved by EUCAST, 100.0% of isolates were susceptible to tedizolid in the USA and EU (**Tables 2** and **3**)
- Overall/USA/EU, 48.6/29.5/38.2% of isolates were methicillin-susceptible (MS)-CoNS and 51.4/70.5/69.8% were methicillin-resistant (MR)-CoNS (**Tables 1** to **3**)
  - Tedizolid 80 $MIC_{50/90}$ values (0.06/0.12 µg/mL) were identical for MS-CoNS, MR-CoNS, and overall (**Table 1**)
  - Susceptibility of CoNS to linezolid, daptomycin, and vancomycin was 100.0% in the USA (**Table 2**) and in the EU (**Table 3**)

***Enterococcus* spp.**

- Of 212 *E. faecalis* isolates tested, 100.0% of strains were inhibited at tedizolid 80/100 MIC values of 0.5/1 µg/mL
  - The $MIC_{50/90}$ values for tedizolid 80 (0.12/0.25 µg/mL) were one doubling dilution lower than tedizolid 100 (0.25/0.5 µg/mL; **Table 1**)
  - In the USA and EU, using USA-FDA breakpoints, 100.0% of isolates were susceptible to tedizolid, and tedizolid was four-fold more potent than linezolid (**Tables 2** and **3**)
- Of 108 *E. faecium* isolates tested, 100.0% of strains were inhibited at tedizolid 80/100 MIC values of 0.5/1 µg/mL
  - The $MIC_{50/90}$ values for tedizolid 80 (0.12/0.25 µg/mL) were one doubling dilution lower than tedizolid 100 (0.25/0.5 µg/mL; **Table 1**)

β-haemolytic streptococci

- A total of 216 *S. pyogenes* were tested; all strains were inhibited at tedizolid 80/100 MIC values of 0.25/0.5 µg/mL
  - The $MIC_{50/90}$ values for tedizolid 80 (0.12/0.12 µg/mL) were up to one doubling dilution lower than tedizolid 100 (0.12/0.25 µg/mL; **Table 1**)
  - Using breakpoints approved by the USA-FDA and EUCAST, 100.0% of isolates were susceptible to tedizolid in the USA and EU (**Tables 2** and **3**)
- Of 141 *S. agalactiae* tested, again all strains were inhibited at tedizolid 80/100 MIC values of 0.25/0.25 µg/mL
  - The $MIC_{50/90}$ values for tedizolid 80 (0.12/0.12 µg/mL) were one doubling dilution lower than tedizolid 100 (0.25/0.25 µg/mL; **Table 1**)
  - Using breakpoints approved by the USA-FDA and EUCAST, 100.0% of isolates were susceptible to tedizolid in the USA and EU (**Tables 2** and **3**)
- Of 70 *S. dysgalactiae* tested, 100.0% of strains were inhibited at tedizolid 80/100 MIC values of 0.12/0.25 µg/mL
  - The $MIC_{50/90}$ values for tedizolid 80 (0.12/0.12 µg/mL) were one doubling dilution lower than tedizolid 100 (0.25/0.25 µg/mL; **Table 1**)
  - Using breakpoints approved by EUCAST, 100.0% of isolates were susceptible to tedizolid in the USA and EU (**Tables 2** and **3**)

Table 1. Summary of Tedizolid Activity Tested Against Bacterial Isolates From Patients with SSSI (USA and EU combined, 2014)

Organism (n)	Agent/read[a]	Number (cumulative %) of isolates inhibited at MIC (µg/mL)									
		0.015	0.03	0.06	0.12	0.25	0.5	1	>1	MIC_{50}	MIC_{90}
S. aureus (2,633)	Tedizolid 80	1 (0.0)	13 (0.5)	447 (17.5)	2079 (96.5)	93 (100.0)				0.12	0.12
	Tedizolid 100	–[b]	1 (0.0)	36 (1.4)	1092 (42.9)	1438 (97.5)	66 (100.0)			0.25	0.25
MSSA[c] (1,586)	Tedizolid 80	1 (0.1)	8 (0.6)	243 (15.9)	1279 (96.5)	55 (100.0)				0.12	0.12
	Tedizolid 100	–	–	20 (1.3)	564 (36.8)	955 (97.0)	47 (100.0)			0.25	0.25
MRSA[c] (1,047)	Tedizolid 80	–	5 (0.5)	204 (20.0)	800 (96.4)	38 (100.0)				0.12	0.12
	Tedizolid 100	–	1 (0.1)	16 (1.6)	528 (52.1)	483 (98.2)	19 (100.0)			0.12	0.25
CoNS[d] (247)	Tedizolid 80	–	17 (6.9)	159 (71.3)	71 (100.0)					0.06	0.12
	Tedizolid 100	–	1 (0.3)	41 (16.6)	178 (88.7)	27 (99.6)	1 (100.0)			0.12	0.25
MS-CoNS[c] (120)	Tedizolid 80	–	8 (6.7)	80 (73.3)	32 (100.0)					0.06	0.12
	Tedizolid 100	–	–	21 (17.5)	88 (90.8)	11 (100.0)				0.12	0.12
MR-CoNS[c] (127)	Tedizolid 80	–	9 (7.1)	79 (69.3)	39 (100.0)					0.06	0.12
	Tedizolid 100	–	–	20 (15.8)	90 (86.6)	16 (99.2)	1 (100.0)			0.12	0.25
E. faecalis (212)	Tedizolid 80	–	–	7 (6.5)	79 (79.6)	21 (99.1)	1 (100.0)			0.12	0.25
	Tedizolid 100	–	–	–	22 (10.4)	147 (79.7)	41 (99.1)	2 (100.0)		0.25	0.5
E. faecium (108)	Tedizolid 80	–	1 (0.6)	11 (7.3)	121 (80.6)	30 (98.8)	2 (100.0)			0.12	0.25
	Tedizolid 100	–	–	–	22 (20.4)	60 (75.9)	18 (92.6)	7 (99.1)	1 (100.0)	0.25	0.5
S. pyogenes (216)	Tedizolid 80	–	–	59 (27.3)	154 (98.6)	3 (100.0)				0.12	0.12
	Tedizolid 100	–	–	9 (4.2)	128 (63.4)	77 (99.1)	2 (100.0)			0.12	0.25
S. agalactiae (141)	Tedizolid 80	–	–	19 (13.5)	118 (97.2)	4 (100.0)				0.12	0.12
	Tedizolid 100	–	–	–	56 (39.7)	85 (100.0)				0.25	0.25
S. dysgalactiae (70)	Tedizolid 80	–	–	17 (24.3)	53 (100.0)					0.12	0.12
	Tedizolid 100	–	–	–	44 (62.9)	26 (100.0)				0.25	0.25

[a] Antimicrobial agent (tedizolid). 100 = MIC read at first well that shows no growth. 80 = MIC read at the first microtiter well where trailing begins with tiny buttons being ignored (as per CLSI document M07-10, 2015).
[b] No isolates found at this MIC value = "–".
[c] MSSA = methicillin-susceptible *S. aureus*; MRSA = methicillin-resistant *S. aureus*; CoNS = coagulase-negative staphylococci; MS-CoNS = methicillin-susceptible coagulase-negative staphylococci; MR-CoNS = methicillin-resistant coagulase-negative staphylococci.
[d] Includes: *Staphylococcus capitis* (10 strains), *S. schleiferi* (1 strain), *S. cohnii* (1 strain), *S. caprae* (2 strains), *S. epidermidis* (121 strains), *S. haemolyticus* (24 strains), *S. hominis* (11 strains), *S. intermedius* (3 strains), *S. lugdunensis* (48 strains), *S. pseudintermedius* (1 strain), *S. pseudintermedius / intermedius* (1 strain), *S. saprophyticus* (2 strains), *S. sciuri* (1 strain), *S. simulans* (7 strains), *S. warneri* (12 strains), *S. xylosus* (2 strains).

Table 2. Activity of Tedizolid and Comparator Antimicrobial Agents When Tested Against Bacterial Isolates From Patients With SSSI (USA, 2014)

Organisms (no. tested)/antimicrobial agent	MIC (µg/mL)		%S / %I / %R	
	MIC_{50}	MIC_{90}	CLSI[a]	EUCAST[a]
***S. aureus* (1,671)**				
Tedizolid 80	0.12	0.12	– / – / –[b]	– / – / –
Tedizolid 100	0.25	0.25	100.0 / 0.0 / 0.0[c]	100.0 / – / 0.0
Linezolid 80	1	1	100.0 / – / 0.0	100.0 / – / 0.0
Linezolid 100	1	2	– / – / –	– / – / –
Ceftaroline	0.5	1	99.0 / 1.0 / 0.0	99.0 / – / 1.0
Clindamycin	≤0.25	>2	87.8 / 0.1 / 12.1	87.6 / 0.2 / 12.2
Daptomycin	0.25	0.5	99.9 / – / –	99.9 / – / 0.1
Erythromycin	16	>16	38.9 / 4.0 / 57.1	39.3 / 1.2 / 59.5
Levofloxacin	0.25	>4	64.6 / 0.6 / 34.8	64.6 / 0.6 / 34.8
Oxacillin	2	>2	50.2 / – / 49.8	50.2 / – / 49.8
Tetracycline	≤0.5	≤0.5	95.1 / 0.5 / 4.4	92.7 / 1.0 / 6.3
Tigecycline	0.06	0.06	100.0 / – / –[d]	100.0 / – / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	98.7 / – / 1.3	98.7 / 0.2 / 1.1
Vancomycin	1	1	100.0 / 0.0 / 0.0	100.0 / – / 0.0
Coagulase-negative staphylococci (88)[e]				
Tedizolid 80	0.06	0.12	– / – / –	– / – / –
Tedizolid 100	0.12	0.25	– / – / –	100.0 / – / 0.0
Linezolid 80	0.5	0.5	100.0 / – / 0.0	100.0 / – / 0.0
Linezolid 100	1	1	– / – / –	– / – / –
Ceftaroline	0.25	0.5	– / – / –	– / – / –
Clindamycin	≤0.25	>2	77.3 / 1.1 / 21.6	72.7 / 4.6 / 22.7
Daptomycin	0.25	0.5	100.0 / – / –	100.0 / – / 0.0
Erythromycin	0.25	>16	56.8 / 1.2 / 42.0	56.8 / 0.0 / 43.2
Levofloxacin	0.25	>4	75.0 / 1.1 / 23.9	75.0 / 1.1 / 23.9
Oxacillin	1	>2	29.5 / – / 70.5	29.5 / – / 70.5
Tetracycline	≤0.5	>8	87.4 / 1.1 / 11.5	80.5 / 2.3 / 17.2
Tigecycline	0.06	0.12	– / – / –	100.0 / – / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	4	89.8 / – / 10.2	89.8 / 7.9 / 2.3
Vancomycin	1	2	100.0 / 0.0 / 0.0	100.0 / – / 0.0
***S. pyogenes* (155)**				
Tedizolid 80	0.12	0.12	– / – / –	– / – / –
Tedizolid 100	0.12	0.25	100.0 / – / –[c]	100.0 / – / 0.0
Linezolid 80	0.5	1	100.0 / – / 0.0	100.0 / 0.0 / 0.0
Linezolid 100	1	1	– / – / –	– / – / –
Ceftaroline	≤0.015	≤0.015	100.0 / – / –	100.0 / – / 0.0
Clindamycin	≤0.25	≤0.25	92.9 / 0.0 / 7.1	92.9 / – / 7.1
Daptomycin	≤0.06	0.12	100.0 / – / –	100.0 / – / 0.0
Erythromycin	≤0.12	4	85.8 / 0.7 / 13.5	85.8 / 0.7 / 13.5
Levofloxacin	0.5	1	99.4 / 0.0 / 0.6	97.4 / 2.0 / 0.6
Tetracycline	≤0.5	>8	83.2 / 2.0 / 14.8	81.9 / 1.3 / 16.8
Vancomycin	0.25	0.5	100.0 / – / –	100.0 / – / 0.0
***S. agalactiae* (104)**				
Tedizolid 80	0.12	0.12	– / – / –	– / – / –
Tedizolid 100	0.25	0.25	100.0 / – / –[c]	100.0 / – / 0.0
Linezolid 80	0.5	1	100.0 / – / 0.0	100.0 / 0.0 / 0.0
Linezolid 100	1	1	– / – / –	– / – / –
Ceftaroline	≤0.015	0.03	100.0 / – / –	100.0 / – / 0.0
Clindamycin	≤0.25	>2	68.0 / 0.9 / 31.1	68.9 / – / 31.1
Daptomycin	0.25	0.25	100.0 / – / –	100.0 / – / 0.0
Erythromycin	1	>16	47.6 / 0.9 / 51.5	47.6 / 0.9 / 51.5
Levofloxacin	0.5	1	99.0 / 0.0 / 1.0	99.0 / 0.0 / 1.0
Tetracycline	>8	>8	20.2 / 1.0 / 78.8	20.2 / 0.0 / 79.8
Vancomycin	0.5	0.5	100.0 / – / –	100.0 / – / 0.0
***S. dysgalactiae* (42)**				
Tedizolid 80	0.12	0.12	– / – / –	– / – / –
Tedizolid 100	0.12	0.25	– / – / –	100.0 / – / –
Linezolid 80	0.5	1	100.0 / – / –	100.0 / 0.0 / 0.0
Linezolid 100	1	1	– / – / –	– / – / –
Ceftaroline	≤0.015	≤0.015	100.0 / – / –	100.0 / – / 0.0
Clindamycin	≤0.25	≤0.25	92.9 / 2.3 / 4.8	95.2 / – / 4.8
Daptomycin	≤0.06	0.12	100.0 / – / –	100.0 / – / 0.0
Erythromycin	≤0.12	16	71.4 / 4.8 / 23.8	71.4 / 4.8 / 23.8
Levofloxacin	0.5	1	100.0 / 0.0 / 0.0	100.0 / 0.0 / 0.0
Tetracycline	4	>8	47.6 / 7.2 / 45.2	47.6 / 0.0 / 52.4
Vancomycin	0.25	0.25	100.0 / – / –	100.0 / – / 0.0
***E. faecalis* (87)**				
Tedizolid 80	0.25	0.25	– / – / –	– / – / –
Tedizolid 100	0.25	0.5	100.0 / –/ –[c]	– / – / –
Linezolid 80	1	1	100.0 / 0.0 / 0.0	100.0 / – / 0.0
Linezolid 100	1	1	– / – / –	– / – / –
Daptomycin	1	2	100.0 / – / –	– / – / –
Levofloxacin	1	>4	70.1 / 0.0 / 29.9	70.1 / – / 29.9[f]
Vancomycin	1	2	98.9 / 0.0 / 1.1	98.9 / – / 1.1
***E. faecium* (32)**				
Tedizolid 80	0.12	0.12	– / – / –	– / – / –
Tedizolid 100	0.25	0.25	– / – / –	– / – / –
Linezolid 80	1	1	96.9 / 3.1 / 0.0	100.0 / – / 0.0
Linezolid 100	1	2	– / – / –	– / – / –
Daptomycin	2	2	100.0 / – / –	– / – / –
Levofloxacin	>4	>4	3.1 / 0.0 / 96.9	3.1 / – / 96.9
Vancomycin	>16	>16	9.4 / 0.0 / 90.6	9.4 / – / 90.6

[a] Criteria as published by the CLSI [2015] and EUCAST [2015].
[b] No breakpoint available for interpretation = "–".
[c] In the absence of CLSI breakpoint, USA-FDA breakpoints were applied [Sivextro Product Insert, 2014].
[d] In the absence of CLSI breakpoint, USA-FDA breakpoints were applied [Tygacil Product Insert, 2012].
[e] Includes: *Staphylococcus capitis* (4 strains), *S. caprae* (1 strain), *S. epidermidis* (40 strains), *S. haemolyticus* (5 strains), *S. hominis* (6 strains), *S. intermedius* (2 strains), *S. lugdunensis* (25 strains), *S. pseudintermedius* (1 strain), *S. pseudintermedius / intermedius* (1 strain), *S. simulans* (3 strains).
[f] Uncomplicated UTI only.

Table 3. Activity of Tedizolid and Comparator Antimicrobial Agents When Tested Against Bacterial Isolates From Patients With SSSI (Europe, 2014)

Organisms (no. tested)/antimicrobial agent	MIC (µg/mL)		%S / %I / %R	
	MIC_{50}	MIC_{90}	CLSI[a]	EUCAST[a]
***S. aureus* (962)**				
Tedizolid 80	0.12	0.12	– / – / –[b]	– / – / –
Tedizolid 100	0.25	0.25	100.0 / 0.0 / 0.0[c]	100.0 / – / 0.0
Linezolid 80	1	1	100.0 / – / 0.0	100.0 / – / 0.0
Linezolid 100	1	2	– / – / –	– / – / –
Ceftaroline	0.25	1	98.3 / 1.7 / 0.0	98.3 / – / 1.7
Clindamycin	≤0.25	≤0.25	93.5 / 0.0 / 6.5	93.3 / 0.2 / 6.5
Daptomycin	0.25	0.5	100.0 / – / –	100.0 / – / 0.0
Erythromycin	0.25	>16	76.4 / 3.3 / 20.3	77.1 / 0.9 / 22.0
Levofloxacin	0.25	>4	78.6 / 0.1 / 21.3	78.6 / 0.1 / 21.3
Oxacillin	0.5	>2	77.7 / – / 22.3	77.7 / – / 22.3
Tetracycline	≤0.5	≤0.5	94.4 / 0.9 / 4.7	94.2 / 0.2 / 5.6
Tigecycline	0.06	0.06	100.0 / – / –[d]	100.0 / – / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	99.2 / – / 0.8	99.2 / 0.4 / 0.4
Vancomycin	1	1	100.0 / 0.0 / 0.0	100.0 / – / 0.0
Coagulase-negative staphylococci (159)[e]				
Tedizolid 80	0.06	0.12	– / – / –	– / – / –
Tedizolid 100	0.12	0.12	– / – / –	100.0 / – / 0.0
Linezolid 80	0.5	0.5	100.0 / – / 0.0	100.0 / – / 0.0
Linezolid 100	1	1	– / – / –	– / – / –
Ceftaroline	0.25	1	– / – / –	– / – / –
Clindamycin	≤0.25	>2	82.4 / 0.6 / 17.0	80.5 / 1.9 / 17.6
Daptomycin	0.25	0.5	100.0 / – / –	100.0 / – / 0.0
Erythromycin	1	>16	49.7 / 1.9 / 48.4	50.9 / 0.0 / 49.1
Levofloxacin	0.25	>4	61.6 / 3.2 / 35.2	61.6 / 3.2 / 35.2
Oxacillin	1	>2	30.2 / 0.0 / 69.8	30.2 / 0.0 / 69.8
Tetracycline	≤0.5	>8	84.8 / 1.9 / 13.3	80.4 / 1.9 / 17.7
Tigecycline	0.06	0.12	– / – / –	100.0 / – / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	>4	76.7 / - / 23.3	76.7 / 9.5 / 13.8
Vancomycin	1	2	100.0 / 0.0 / 0.0	100.0 / – / 0.0
***S. pyogenes* (61)**				
Tedizolid 80	0.12	0.12	– / – / –	– / – / –
Tedizolid 100	0.12	0.25	100.0 / – / –[c]	100.0 / - / 0.0
Linezolid 80	0.5	1	100.0 / – / –	100.0 / 0.0 / 0.0
Linezolid 100	1	2	– / – / –	– / – / –
Ceftaroline	≤0.015	≤0.015	100.0 / – / –	100.0 / – / 0.0
Clindamycin	≤0.25	≤0.25	96.7 / 0.0 / 3.3	96.7 / – / 3.3
Daptomycin	≤0.06	0.12	100.0 / – / –	100.0 / – / 0.0
Erythromycin	≤0.12	≤0.12	96.7 / 0.0 / 3.3	96.7 / 0.0 / 3.3
Levofloxacin	0.5	1	100.0 / 0.0 / 0.0	95.1 / 4.9 / 0.0
Tetracycline	≤0.5	>8	71.7 / 0.0 / 28.3	70.0 / 1.7 / 28.3
Vancomycin	0.25	0.25	100.0 / – / –	100.0 / – / 0.0
***S. agalactiae* (37)**				
Tedizolid 80	0.12	0.12	– / – / –	– / – / –
Tedizolid 100	0.25	0.25	100.0 / – / –[c]	100.0 / – / 0.0
Linezolid 80	0.5	1	100.0 / – / 0.0	100.0 / 0.0 / 0.0
Linezolid 100	1	1	– / – / –	– / – / –
Ceftaroline	≤0.015	≤0.015	100.0 / – / –	100.0 / – / 0.0
Clindamycin	≤0.25	>2	78.4 / 0.0 / 21.6	78.4 / – / 21.6
Daptomycin	0.25	0.25	100.0 / – / –	100.0 / – / 0.0
Erythromycin	1	>16	47.6 / 0.9 / 51.5	47.6 / 0.9 / 51.5
Levofloxacin	0.5	1	100.0 / 0.0 / 0.0	97.3 / 2.7 / 0.0
Tetracycline	>8	>8	29.7 / 0.0 / 70.3	29.7 / 0.0 / 70.3
Vancomycin	0.5	0.5	100.0 / – / –	100.0 / – / 0.0
***S. dysgalactiae* (28)**				
Tedizolid 80	0.12	0.12	– / – / –	– / – / –
Tedizolid 100	0.12	0.25	– / – / –	100.0 / – / 0.0
Linezolid 80	0.5	1	100.0 / – / –	100.0 / 0.0 / 0.0
Linezolid 100	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
***E. faecalis* (125)**				
Tedizolid 80	0.25	0.25	– / – / –	– / – / –
Tedizolid 100	0.25	0.5	98.4 / – / –[c]	– / – / –
Linezolid 80	1	2	100.0 / 0.0 / 0.0	100.0 / – / 0.0
Linezolid 100	2	2	– / – / –	– / – / –
Daptomycin	1	2	100.0 / – / –	– / – / –
Levofloxacin	2	>4	67.2 / 0.0 / 32.8	67.2 / – / 32.8[f]
Vancomycin	1	2	99.2 / 0.0 / 0.8	99.2 / – / 0.8
***E. faecium* (76)**				
Tedizolid 80	0.12	0.25	– / – / –	– / – / –
Tedizolid 100	0.25	0.5	– / – / –	– / – / –
Linezolid 80	1	1	100.0 / 0.0 / 0.0	100.0 / - / 0.0
Linezolid 100	2	4	– / – / –	– / – / –
Daptomycin	2	4	100.0 / – / –	– / – / –
Levofloxacin	>4	>4	9.2 / 1.3 / 89.5	10.5 / – / 89.5[f]
Vancomycin	1	>16	71.1 / 0.0 / 28.9	71.1 / – / 28.9

[a] Criteria as published by the CLSI [2015] and EUCAST [2015].
[b] No breakpoint available for interpretation = "–".
[c] In the absence of CLSI breakpoint, USA-FDA breakpoints were applied [Sivextro Product Insert, 2014].
[d] In the absence of CLSI breakpoint, USA-FDA breakpoints were applied [Tygacil Product Insert, 2012].
[e] Includes: *Staphylococcus capitis* (6 strains), *S. schleiferi* (1 strain), *S. cohnii* (1 strain), *S. caprae* (1 strain), *S. epidermidis* (81 strains), *S. haemolyticus* (19 strains), *S. hominis* (5 strains), *S. intermedius* (1 strain), *S. lugdunensis* (23 strains), S. saprophyticus (2 strains), *S. sciuri* (1 strain), *S. simulans* (4 strains), *S. warneri* (12 strains), *S. xylosus* (2 strains).
[f] Uncomplicated UTI only.

Conclusions

- Tedizolid demonstrated higher *in vitro* activity (two- to four-fold depending on the 80% or 100% read matched comparisons) than linezolid when tested against Gram-positive pathogens isolated from patients with SSSI in medical centers across the USA and EU (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 one doubling dilution lower than those read at 100% inhibition
- Using USA-FDA breakpoints and breakpoints approved by EUCAST, 100.0% of 2,633 *S. aureus* isolates (39.8% of which were MRSA) were susceptible to tedizolid
  - Using EUCAST breakpoints, 100.0% of CoNS and *S. dysgalactiae* isolates were susceptible (EUCAST criteria) to tedizolid
  - Using USA-FDA breakpoints, 100.0% of *E. faecalis, S. pyogenes,* and *S. agalactiae* isolates were susceptible to tedizolid

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