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In vitro Evaluation of Delafloxacin Activity When Tested against Contemporary ABSSSI Isolates from Europe and Surrounding Areas (2014-2016): Results from the SENTRY Antimicrobial Surveillance Program

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Revised Abstract

Background: Delafloxacin is a broad-spectrum fluoroquinolone (FQ) antibacterial in late-stage clinical development (oral and intravenous formulations) for the treatment of acute bacterial skin and skin structure infections (ABSSSI). Delafloxacin has potent activity against Gram-positive and -negative bacterial pathogens frequently associated with ABSSSI that include methicillin- and FQ-resistant staphylococci, β-haemolytic streptococci, viridans group streptococci, *Enterococcus faecalis*, *Enterobacteriaceae*, and *Pseudomonas aeruginosa*. The *in vitro* susceptibility results for delafloxacin and comparator agents tested against bacterial clinical isolates collected from patients with ABSSSI in European medical centres participating in the SENTRY surveillance program during 2014-2016 are presented (Table).

Methods: A total of 903 staphylococci, 254 β-haemolytic streptococci, 27 viridans group streptococci, 173 *E. faecalis*, 867 *Enterobacteriaceae*, and 275 *P. aeruginosa* isolates from patients with ABSSSI were collected during 2014-2016 and included only one isolate/patient/infection episode. A central monitoring laboratory confirmed isolate identifications using standard bacteriologic algorithms, matrix-assisted laser desorption/ionization (MALDI) mass spectrometry, and/or molecular characterization. Susceptibility testing was performed according to reference broth microdilution methodology, and results were interpreted per EUCAST breakpoints.

Results: Delafloxacin demonstrated potent *in vitro* activity against *Staphylococcus aureus* ($MIC_{50/90}$ ≤0.004/0.25 mg/L) and coagulase-negative staphylococci (CoNS; $MIC_{50/90}$ 0.015/0.5 mg/L) where FQ (levofloxacin) resistance was 16.8% and 35.2%, respectively. Delafloxacin was highly active against methicillin-resistant *S. aureus* (19.6% MRSA; $MIC_{50/90}$ 0.25/1 mg/L) and MR-CoNS (48.5% MR-CoNS; $MIC_{50/90}$ 0.25/1 mg/L) where FQ resistance was 71.2%. β-haemolytic streptococci were inhibited by low levels of delafloxacin ($MIC_{50/90}$ 0.015/0.03 mg/L; highest MIC 0.06 mg/L) whereas resistance to levofloxacin (99.2% susceptible), erythromycin (83.1% susceptible), clindamycin (90.9% susceptible), and tetracycline (58.3% susceptible) was observed. Delafloxacin was the most active agent tested against viridans group streptococci ($MIC_{50/90}$ 0.008/0.03 mg/L). Against enterococci, delafloxacin inhibited 95.4% of *E. faecalis* isolates at ≤1 mg/L. Similarly, delafloxacin inhibited 70.8% of *Enterobacteriaceae* and 68.0% of *P. aeruginosa* at ≤1 mg/L and was comparable in activity to levofloxacin (75.9% and 62.9% inhibited at ≤1 mg/L, respectively).

Conclusions: Delafloxacin demonstrated potent *in vitro* antibacterial activity against FQ-susceptible and -resistant bacterial pathogens frequently associated with ABSSSI, including MRSA, MR-CoNS, β-haemolytic streptococci, *E. faecalis*, and some *Enterobacteriaceae*. These data support the continued development of delafloxacin to treat ABSSSI.

Organism	No. tested	Delafloxacin MIC (mg/L)		Levofloxacin MIC (mg/L)		
		MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}	%S
S. aureus	903	≤0.004	0.25	0.25	>4	83.2
S. aureus (MRSA)	177	0.25	1	>4	>4	28.8
CoNS	165	0.015	0.5	0.25	>4	64.8
β-haemolytic streptococci	254	0.015	0.03	0.5	1	99.2
Viridans group streptococci	27	0.008	0.03	0.5	1	—
E. faecalis	173	0.12	1	1	>4	74.0
Enterobacteriaceae	867	0.12	>4	≤0.12	>4	71.2
E. coli	262	0.06	4	≤0.12	>4	63.0
P. aeruginosa	275	0.5	>4	0.5	>4	62.9

Introduction

- Delafloxacin is a broad-spectrum anionic fluoroquinolone (FQ) antibacterial in late-stage clinical development (oral and intravenous formulations) for the treatment of acute bacterial skin and skin structure infections (ABSSSI). The anionic properties of delafloxacin may enhance its effectiveness in acidic environments, which is characteristic at infection sites
- Unlike comparator fluoroquinolones that usually demonstrate a binding preference for DNA gyrase or topoisomerase IV, delafloxacin is unique in possessing equal activity against both. This dual enzyme targeting is believed to help reduce the selection of resistant mutants
- Delafloxacin is active against a broad range of Gram-positive and Gram-negative bacterial pathogens and has demonstrated potent antibacterial activity against bacterial isolates frequently associated with ABSSSI, including methicillin- and FQ-resistant staphylococci, β-haemolytic streptococci, viridans group streptococci, *Enterococcus faecalis*, *Enterobacteriaceae*, and *Pseudomonas aeruginosa*
- *In vitro* susceptibility results for delafloxacin and comparator agents tested against 2,664 bacterial clinical isolates collected from patients with ABSSSI in European medical centres participating in the SENTRY surveillance program during 2014-2016 are presented

Materials and Methods

- Bacterial isolates were identified by the submitting laboratories and confirmed by JMI Laboratories using matrix-assisted laser desorption/ionization-time of flight mass spectrometry (Bruker Daltonics, Bremen, Germany).
- Bacterial isolates (2,664 nonduplicate) were collected from patients with ABSSSI in European medical centres during 2014-2016 and included 903 *Staphylococcus aureus*, 165 CoNS, 254 β-haemolytic streptococci, 27 viridans group streptococci, 173 *E. faecalis*, 867 *Enterobacteriaceae* (262 *Escherichia coli*), and 275 *P. aeruginosa*
- Susceptibility testing was performed according to CLSI (M07-A10, 2015) reference broth microdilution methodology and results were interpreted using EUCAST (2017) breakpoint interpretive criteria
  - CLSI quality control (QC) reference strains (M100-S27, 2017) were tested concurrently and included *S. aureus* ATCC 29213, *E. faecalis* ATCC 29212, *E. coli* ATCC 25922 and ATCC 35218, *K. pneumoniae* ATCC 700603, and *P. aeruginosa* ATCC 27853

Results

- Delafloxacin demonstrated potent *in vitro* antibacterial activity against *S. aureus* ($MIC_{50/90}$ ≤0.004/0.25 mg/L) from ABSSSI with MIC_{90} values ≥8-fold lower than moxifloxacin and levofloxacin (MIC_{90}, 2 and >4 mg/L, respectively) (Table 1)
- Delafloxacin (MIC_{90} 0.25 mg/L; Table 2) inhibited 99.7% of *S. aureus* from ABSSSI at ≤1 mg/L (Table 1) and was 4-fold more active than ceftaroline, linezolid, and vancomycin (MIC_{90}, 1 mg/L; Table 2)
- Oxacillin- and levofloxacin-resistance (R) rates in *S. aureus* from ABSSSI were 19.6% and 16.8%, respectively (Table 2)
- The most potent antimicrobials against levofloxacin-R *S. aureus* were delafloxacin ($MIC_{50/90}$, 0.25/1 mg/L), tigecycline ($MIC_{50/90}$, 0.06/0.12 mg/L), trimethoprim-sulfamethoxazole ($MIC_{50/90}$, ≤0.5/≤0.5 mg/L), daptomycin ($MIC_{50/90}$, 0.5/0.5 mg/L), and vancomycin ($MIC_{50/90}$, 0.5/1 mg/L) (Table 2)
- MRSA comprised 19.6% of *S. aureus* ABSSSI isolates. Of these, 68.3% and 71.2% were resistant to moxifloxacin and levofloxacin, respectively, whereas delafloxacin ($MIC_{50/90}$, 0.25/1 mg/L; Table 2) remained highly active
- Delafloxacin was very active against CoNS including oxacillin-R (48.5% MR-CoNS) and levofloxacin-R (32.1% levofloxacin-R CoNS) isolates with $MIC_{50/90}$ values of 0.25/1 mg/L (Tables 1 and 2). Comparators including daptomycin, linezolid, tigecycline, and vancomycin were also active against CoNS from ABSSSI (100.0% susceptible; Table 2)
- β-haemolytic streptococci (*Streptococcus agalactiae*, *S. dysgalactiae*, and *S. pyogenes*) were inhibited by low concentrations of delafloxacin ($MIC_{50/90}$ 0.015/0.03 mg/L; highest MIC 0.06 mg/L). Resistance rates for levofloxacin, moxifloxacin, clindamycin, erythromycin, and tetracycline were 0.8%, 0.6%, 9.1%, 16.1%, and 39.8%, respectively (Table 2)
- Delafloxacin was the most active fluoroquinolone tested ($MIC_{50/90}$ 0.008/0.03 mg/L; highest MIC 0.03 mg/L) against viridans group streptococci (Tables 1 and 2) compared to levofloxacin ($MIC_{50/90}$ 0.5/1 mg/L; highest MIC >4 mg/L) and moxifloxacin ($MIC_{50/90}$ ≤0.12/0.25 mg/L; highest MIC 2 mg/L)
- Delafloxacin inhibited 95.4% of *E. faecalis* ($MIC_{50/90}$ 0.12/1 mg/L) and 82.2% of levofloxacin-R *E. faecalis* ($MIC_{50/90}$ 1/2 mg/L) isolates from ABSSSI at ≤1 mg/L
- Against Gram-negatives, delafloxacin was comparable in activity to other fluoroquinolones inhibiting 70.8%, 63.0%, and 68.0% of *Enterobacteriaceae*, *E. coli*, and *P. aeruginosa* isolates from ABSSSI at ≤1 mg/L

Table 1 Antimicrobial activity of delafloxacin and comparators against the main organisms and organism groups responsible for ABSSSI in Europe (2014-2016)

Organisms / Antimicrobial (no. tested)	No. of isolates at MIC (mg/L; cumulative %)[a] ≤0.002	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	>	MIC_{50}	MIC_{90}
Staphylococcus aureus															
Delafloxacin (903)		468 51.8	249 79.4	35 83.3	3 83.6	6 84.3	30 87.6	49 93.0	37 97.1	23 99.7	1 99.8		2 100.0	≤0.004	0.25
Levofloxacin (903)							335 37.1	389 80.2	22 82.6	5 83.2	1 83.3	24 85.9	127 100.0	0.25	>4
Moxifloxacin (747)						612 81.9	13 83.7	1 83.8	1 83.9	16 86.1	44 92.0	44 97.9	16 100.0	≤0.06	2
Levofloxacin-R *Staphylococcus aureus*															
Delafloxacin (151)	0 0.0	1 0.7	0 0.7	1 1.3	1 2.0	6 6.0	30 25.8	49 58.3	37 82.8	23 98.0	1 98.7		2 100.0	0.25	1
Levofloxacin (151)											0 0.0	24 15.9	127 100.0	>4	>4
Moxifloxacin (121)						1 0.8	0 0.8	0 0.8	0 0.8	16 14.0	44 50.4	44 86.8	16 100.0	2	>4
MSSA															
Delafloxacin (726)		444 61.2	223 91.9	32 96.3	3 96.7	2 97.0	3 97.4	11 98.9	4 99.4	3 99.9	0 99.9	1 100.0		≤0.004	0.008
Levofloxacin (726)							324 44.6	349 92.7	22 95.7	5 96.4	1 96.6	5 97.2	20 100.0	0.25	0.25
Moxifloxacin (602)						566 94.0	13 96.2	1 96.3	1 96.5	3 97.0	9 98.5	6 99.5	3 100.0	≤0.06	≤0.06
MRSA															
Delafloxacin (177)		24 13.6	26 28.2	3 29.9	0 29.9	4 32.2	27 47.5	38 68.9	33 87.6	20 98.9	1 99.4		1 100.0	0.25	1
Levofloxacin (177)						0 0.0	11 6.2	40 28.8	0 28.8	0 28.8	0 28.8	19 39.5	107 100.0	>4	>4
Moxifloxacin (145)						46 31.7	0 31.7	0 31.7	0 31.7	13 40.7	35 64.8	38 91.0	13 100.0	2	4
CoNS															
Delafloxacin (165)		38 23.0	40 47.3	21 60.0	8 64.8	2 66.1	12 73.3	20 85.5	13 93.3	7 97.6	3 99.4		1 100.0	0.015	0.5
Levofloxacin (165)							39 23.6	56 57.6	10 63.6	2 64.8	5 67.9	14 76.4	39 100.0	0.25	>4
Moxifloxacin (89)						32 36.0	19 57.3	3 60.7	6 67.4	7 75.3	12 88.8	4 93.3	6 100.0	0.12	4
Levofloxacin-R CoNS															
Delafloxacin (53)					0 0.0	1 1.9	8 17.0	20 54.7	13 79.2	7 92.5	3 98.1		1 100.0	0.25	1
Levofloxacin (53)											0 0.0	14 26.4	39 100.0	>4	>4
Moxifloxacin (31)								0 0.0	3 9.7	6 29.0	12 67.7	4 80.6	6 100.0	2	>4
MR-CoNS (80)															
Delafloxacin (80)		6 7.5	12 22.5	4 27.5	1 28.8	2 31.2	12 46.2	20 71.2	12 86.2	7 95.0	3 98.8		1 100.0	0.25	1
Levofloxacin (80)							8 10.0	12 25.0	3 28.8	0 28.8	5 35.0	14 52.5	38 100.0	4	>4
Moxifloxacin (46)						8 17.4	3 23.9	1 26.1	6 39.1	7 54.3	12 80.4	3 87.0	6 100.0	1	>4
β-haemolytic streptococci															
Delafloxacin (254)		16 6.3	93 42.9	100 82.3	43 99.2	2 100.0								0.015	0.03
Levofloxacin (254)							0 0.0	37 14.6	155 75.6	54 96.9	6 99.2	1 99.6	1 100.0	0.5	1
Moxifloxacin (165)							125 75.8	37 98.2	2 99.4	0 99.4	1 100.0			0.12	0.25
Viridans group streptococci															
Delafloxacin (27)		8 29.6	8 59.3	5 77.8	6 100.0									0.008	0.03
Levofloxacin (27)					1 3.7	0 3.7	2 11.1	4 25.9	12 70.4	7 96.3	0 96.3	0 96.3	1 100.0	0.5	1
Moxifloxacin (16)							14 87.5	1 93.8	0 93.8	0 93.8	1 100.0			0.12	0.25
Enterococcus faecalis															
Delafloxacin (173)		1 0.6	0 0.6	0 0.6	4 2.9	27 18.5	79 64.2	25 78.6	7 82.7	22 95.4	8 100.0			0.12	1
Levofloxacin (173)							0 0.0	1 0.6	9 5.8	90 57.8	27 73.4	1 74.0	45 100.0	1	>4
Moxifloxacin (109)						0 0.0	18 16.5	51 63.3	12 74.3	5 78.9	3 81.7	4 85.3	16 100.0	0.25	>4
Levofloxacin-R *Enterococcus faecalis*															
Delafloxacin (45)						0 0.0	3 6.7	6 20.0	7 35.6	21 82.2	8 100.0			1	2
Levofloxacin (45)												0 0.0	45 100.0	>4	>4
Moxifloxacin (25)									0 0.0	3 12.0	2 20.0	4 36.0	16 100.0	>4	>4
Enterobacteriaceae															
Delafloxacin (867)			0 0.0	22 2.5	112 15.5	203 38.9	144 55.5	56 61.9	29 65.3	48 70.8	84 80.5	76 89.3	93 100.0	0.12	>4
Levofloxacin (867)							540 62.3	42 67.1	35 71.2	41 75.9	25 78.8	20 81.1	164 100.0	≤0.12	>4
Moxifloxacin (619)								390 63.0	32 68.2	28 72.7	17 75.4	17 78.2	135 100.0	0.25	>4
Ciprofloxacin (866)					484 55.9	53 62.0	39 66.5	29 69.9	27 73.0	22 75.5	23 78.2	15 79.9	174 100.0	0.03	>4
Escherichia coli															
Delafloxacin (262)			0 0.0	18 6.9	65 31.7	50 50.8	10 54.6	13 59.5	2 60.3	7 63.0	29 74.0	42 90.1	26 100.0	0.06	4
Levofloxacin (262)							133 50.8	16 56.9	16 63.0	7 65.6	3 66.8	10 70.6	77 100.0	≤0.12	>4
Moxifloxacin (217)								126 58.1	8 61.8	11 66.8	4 68.7	3 70.0	65 100.0	0.25	>4
Ciprofloxacin (262)					130 49.6	2 50.4	16 56.5	10 60.3	14 65.5	0 65.6	3 66.8	5 68.7	82 100.0	0.06	>4
Pseudomonas aeruginosa															
Delafloxacin (275)				0 0.0	3 1.1	4 2.5	17 8.7	73 35.3	74 62.2	16 68.0	19 74.9	10 78.5	59 100.0	0.5	>4
Levofloxacin (275)							4 1.5	30 12.4	111 52.7	28 62.9	20 70.2	12 74.5	70 100.0	0.5	>4
Moxifloxacin (243)								3 1.2	26 11.9	94 50.6	27 61.7	21 70.4	72 100.0	1	>4
Ciprofloxacin (275)					3 1.1	31 12.4	109 52.0	25 61.1	19 68.0	15 73.5	8 76.4	3 77.5	62 100.0	0.12	>4

[a] MIC_{50} values are underlined; MIC_{90} values are bold

Table 2 Activity of delafloxacin and comparator agents against key organism groups responsible for ABSSSI in Europe (2014-2016)

Organism (no. tested) / Antimicrobial agent (no. tested)	MIC_{50}	MIC_{90}	Range	EUCAST[a] %S	%I	%R
Staphylococcus aureus (903)						
Delafloxacin	≤0.004	0.25	≤0.004 – >2	—	—	—
Levofloxacin	0.25	>4	≤0.12 – >4	83.2		16.8
Moxifloxacin (747)	≤0.06	2	≤0.06 – >4	83.8		16.2
Ceftaroline	0.25	1	≤0.06 – 2	99.1		0.9
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	93.7	0.1	6.2
Daptomycin	0.25	0.5	≤0.12 – 1	100.0		0.0
Erythromycin	0.25	>8	≤0.12 – >8	78.0	1.2	20.8
Linezolid	1	1	0.25 – 2	100.0		0.0
Oxacillin	0.5	>2	≤0.25 – >2	80.4		19.6
Tetracycline	≤0.5	≤0.5	≤0.5 – >8	93.4	0.0	6.6
Tigecycline	0.06	0.12	0.03 – 0.5	100.0		0.0
Trimethoprim-sulfamethoxazole	≤0.5	≤0.5	≤0.5 – >4	99.7	0.1	0.2
Vancomycin	0.5	1	≤0.12 – 1	100.0		0.0
Levofloxacin-R *S. aureus* (151)						
Delafloxacin	0.25	1	0.004 – >2	—	—	—
Levofloxacin	>4	>4	4 – >4	0.0		100.0
Moxifloxacin (121)	2	>4	≤0.06 – >4	0.8		99.2
Ceftaroline	1	1	0.12 – 2	94.7		5.3
Clindamycin	≤0.25	>2	≤0.25 – >2	70.2	0.0	29.8
Daptomycin	0.5	0.5	≤0.12 – 1	100.0		0.0
Erythromycin	>8	>8	≤0.12 – >8	41.7	0.0	58.3
Linezolid	1	1	0.25 – 2	100.0		0.0
Oxacillin	>2	>2	≤0.25 – >2	16.6		83.4
Tetracycline	≤0.5	>8	≤0.5 – >8	88.1	0.0	11.9
Tigecycline	0.06	0.12	0.03 – 0.5	100.0		0.0
Trimethoprim-sulfamethoxazole	≤0.5	≤0.5	≤0.5 – 4	99.3	0.7	0.0
Vancomycin	0.5	1	0.25 – 1	100.0		0.0
S. aureus MRSA (177)						
Delafloxacin	0.25	1	≤0.004 – >2	—	—	—
Levofloxacin	>4	>4	0.12 – >4	28.8		71.2
Moxifloxacin (145)	2	4	≤0.06 – >4	31.7		68.3
Ceftaroline	1	1	0.25 – 2	95.5		4.5
Clindamycin	≤0.25	>2	≤0.25 – >2	76.3	0.0	23.7
Daptomycin	0.5	0.5	≤0.12 – 1	100.0		0.0
Erythromycin	>8	>8	≤0.12 – >8	44.6	1.7	53.7
Linezolid	1	1	0.25 – 2	100.0		0.0
Oxacillin	>2	>2	>2 – >2	0.0		100.0
Tetracycline	≤0.5	>8	≤0.5 – >8	80.2	0.0	19.8
Tigecycline	0.12	0.12	0.03 – 0.5	100.0		0.0
Trimethoprim-sulfamethoxazole	≤0.5	≤0.5	≤0.5 – >4	99.4	0.0	0.6
Vancomycin	0.5	1	0.25 – 1	100.0		0.0
CoNS[b] (165)						
Delafloxacin	0.015	0.5	≤0.004 – >2	—	—	—
Levofloxacin	0.25	>4	≤0.12 – >4	64.8		35.2
Moxifloxacin (89)	0.12	4	≤0.06 – >4	60.7		39.3
Clindamycin	≤0.25	>2	≤0.25 – >2	84.8	1.2	13.9
Daptomycin	0.5	0.5	≤0.12 – 1	100.0		0.0
Erythromycin	0.25	>8	≤0.12 – >8	51.5	0.6	47.9
Linezolid	0.5	1	0.25 – 1	100.0		0.0
Oxacillin	1	>2	≤0.25 – >2	51.5		48.5
Tetracycline	≤0.5	>8	≤0.5 – >8	82.4	2.4	15.2
Tigecycline	0.06	0.12	≤0.015 – 0.5	100.0		0.0
Trimethoprim-sulfamethoxazole	≤0.5	>4	≤0.5 – >4	77.6	7.9	14.5
Vancomycin	1	2	≤0.12 – 4	100.0		0.0
Levofloxacin-R CoNS[c] (53)						
Delafloxacin	0.25	1	0.06 – >2	—	—	—
Levofloxacin	>4	>4	4 – >4	0.0		100.0
Moxifloxacin (31)	2	>4	0.5 – >4	0.0		100.0
Clindamycin	≤0.25	>2	≤0.25 – >2	64.2	3.8	32.1
Daptomycin	0.5	0.5	0.12 – 1	100.0		0.0
Erythromycin	>8	>8	≤0.12 – >8	20.8	1.9	77.4
Linezolid	0.5	1	0.25 – 1	100.0		0.0
Oxacillin	>2	>2	≤0.25 – >2	1.9		98.1
Tetracycline	≤0.5	8	≤0.5 – >8	79.2	5.7	15.1
Tigecycline	0.06	0.25	0.03 – 0.5	100.0		0.0
Trimethoprim-sulfamethoxazole	4	>4	≤0.5 – >4	41.5	17.0	41.5
Vancomycin	1	2	0.5 – 4	100.0		0.0
MR-CoNS[d] (80)						
Delafloxacin	0.25	1	≤0.004 – >2	—	—	—
Levofloxacin	4	>4	0.12 – >4	28.8		71.2
Moxifloxacin (46)	1	>4	≤0.06 – >4	26.1		73.9
Clindamycin	≤0.25	>2	≤0.25 – >2	71.2	2.5	26.2
Daptomycin	0.5	0.5	≤0.12 – 1	100.0		0.0
Erythromycin	>8	>8	≤0.12 – >8	20.0	1.2	78.8
Linezolid	0.5	1	0.25 – 1	100.0		0.0
Tetracycline	≤0.5	>8	≤0.5 – >8	73.8	5.0	21.2
Tigecycline	0.06	0.25	0.03 – 0.25	100.0		0.0
Trimethoprim-sulfamethoxazole	1	>4	≤0.5 – >4	56.2	15.0	28.8
Vancomycin	1	2	≤0.12 – 4	100.0		0.0
β-haemolytic streptococci[e] (254)						
Delafloxacin	0.015	0.03	≤0.004 – 0.06	—	—	—
Levofloxacin	0.5	1	0.25 – >4	99.2		0.8
Moxifloxacin (165)	≤0.12	0.25	≤0.12 – 2	99.4		0.6
Amoxicillin-clavulanic acid	≤1	≤1	≤1 – ≤1	100.0		0.0
Ceftaroline	≤0.015	≤0.015	≤0.015 – 0.03	100.0		0.0
Ceftriaxone	≤0.06	≤0.06	≤0.06 – 0.12	100.0		0.0
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	90.9		9.1
Erythromycin	≤0.12	2	≤0.12 – >4	83.1	0.8	16.1
Meropenem	≤0.015	0.03	≤0.015 – 0.06	100.0		0.0
Penicillin	≤0.06	≤0.06	≤0.06 – 0.12	100.0		0.0
Tetracycline	≤0.5	>8	≤0.5 – >8	58.3	2.0	39.8
Vancomycin	0.25	0.5	0.12 – 0.5	100.0		0.0
Viridans group streptococci[f] (27)						
Delafloxacin	0.008	0.03	≤0.004 – 0.03	—	—	—
Levofloxacin	0.5	1	≤0.03 – >4	—	—	—
Moxifloxacin (16)	≤0.12	0.25	≤0.12 – 2	—	—	—
Amoxicillin-clavulanic acid	≤1	≤1	≤1 – 4	96.3	3.7	0.0
Ceftriaxone	0.12	0.25	≤0.06 – 2	96.3		3.7
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	96.3		3.7
Meropenem	0.03	0.12	≤0.015 – >1	100.0		0.0
Penicillin	≤0.06	0.12	≤0.06 – 2	96.3	3.7	0.0
Vancomycin (12)	0.5	1	0.5 – 1	100.0		0.0
Enterococcus faecalis (173)						
Delafloxacin	0.12	1	≤0.004 – 2	—	—	—
Levofloxacin	1	>4	0.25 – >4	74.0		26.0[g]
Moxifloxacin (109)	0.25	>4	0.12 – >4	—	—	—
Ampicillin	1	2	≤0.5 – 8	99.4	0.6	0.0
Linezolid	1	2	0.25 – 2	100.0		0.0
Teicoplanin	≤2	≤2	≤2 – ≤2	100.0		0.0
Tigecycline	0.06	0.12	≤0.015 – 0.12	100.0	0.0	0.0
Vancomycin	1	2	≤0.5 – 4	100.0		0.0
Levofloxacin-R *E. faecalis* (45)						
Delafloxacin	1	2	0.12 – 2	—	—	—
Levofloxacin	>4	>4	>4 – >4	0.0		100.0[g]
Moxifloxacin (25)	>4	>4	1 – >4	—	—	—
Ampicillin	1	2	≤0.5 – 4	100.0	0.0	0.0
Linezolid	1	1	0.5 – 2	100.0		0.0
Teicoplanin	≤2	≤2	≤2 – ≤2	100.0		0.0
Tigecycline	0.06	0.12	0.06 – 0.12	100.0	0.0	0.0
Vancomycin	1	1	0.5 – 2	100.0		0.0
Enterobacteriaceae[h] (867)						
Delafloxacin	0.12	>4	0.015 – >4	—	—	—
Levofloxacin	≤0.12	>4	≤0.12 – >4	71.2	4.7	24.1
Moxifloxacin (619)	≤0.25	>4	≤0.25 – >4	63.0		37.0
Ciprofloxacin	≤0.03	>4	≤0.03 – >4	69.9	3.1	27.0
Aztreonam	≤0.12	>16	≤0.12 – >16	78.1	2.8	19.2
Cefepime	≤0.5	>16	≤0.5 – >16	80.4	4.7	14.9
Ceftazidime	0.25	>32	≤0.015 – >32	76.7	5.2	18.1
Ceftriaxone	0.12	>8	≤0.06 – >8	76.1	0.9	23.0
Gentamicin	≤1	>8	≤1 – >8	85.6	0.9	13.5
Meropenem	0.03	0.12	≤0.015 – >32	97.7	0.5	1.8
Piperacillin-tazobactam	2	64	≤0.5 – >64	81.6	2.9	15.5
Tigecycline	0.25	2	≤0.06 – 4	88.7	7.8	3.5
Escherichia coli (262)						
Delafloxacin	0.06	4	0.015 – >4	—	—	—
Levofloxacin	≤0.12	>4	≤0.12 – >4	63.0	2.7	34.4
Moxifloxacin (217)	≤0.25	>4	≤0.25 – >4	58.1		41.9
Ciprofloxacin	0.06	>4	≤0.03 – >4	60.3	5.3	34.4
Aztreonam	≤0.12	>16	≤0.12 – >16	75.2	4.2	20.6
Cefepime	≤0.5	>16	≤0.5 – >16	74.8	6.5	18.7
Ceftazidime	0.25	16	0.03 – >32	76.7	8.0	15.3
Ceftriaxone	≤0.06	>8	≤0.06 – >8	75.6	0.4	24.0
Gentamicin	≤1	>8	≤1 – >8	85.9	0.0	14.1
Meropenem	≤0.015	0.03	≤0.015 – 16	99.6	0.0	0.4
Piperacillin-tazobactam	2	32	≤0.5 – >64	84.7	4.2	11.1
Tigecycline	0.12	0.25	≤0.06 – 1	100.0	0.0	0.0
Pseudomonas aeruginosa (275)						
Delafloxacin	0.5	>4	0.03 – >4	—	—	—
Levofloxacin	0.5	>4	≤0.12 – >4	62.9		37.1
Moxifloxacin (243)	1	>4	≤0.25 – >4	—	—	—
Ciprofloxacin	0.12	>4	≤0.03 – >4	68.0		32.0
Amikacin	4	32	≤0.25 – >32	80.7	4.7	14.5
Aztreonam	8	>16	0.12 – >16	1.8	78.5	19.6
Cefepime	2	16	≤0.12 – >16	80.4		19.6
Ceftazidime	2	32	0.25 – >32	78.9		21.1
Colistin	1	2	≤0.5 – 4	99.6		0.4
Gentamicin	2	>8	≤1 – >8	76.4		23.6
Meropenem	0.5	16	≤0.015 – >32	74.9	12.0	13.1
Piperacillin-tazobactam	4	>64	≤0.5 – >64	73.1		26.9

[a] Criteria as published by EUCAST [2017]
[b] Organisms include *Staphylococcus capitis* (6), *S. caprae* (3), *S. epidermidis* (79), *S. haemolyticus* (18), *S. hominis* (10), *S. lentus* (1), *S. lugdunensis* (33), *S. saprophyticus* (1), *S. sciuri* (1), *S. simulans* (6), *S. warneri* (7)
[c] Organisms include *Staphylococcus epidermidis* (33), *S. haemolyticus* (17), *S. hominis* (1), *S. simulans* (1), *S. warneri* (1)
[d] Organisms include *Staphylococcus epidermidis* (52), *S. haemolyticus* (18), *S. hominis* (4), *S. lugdunensis* (1), *S. saprophyticus* (1), *S. sciuri* (1), *S. warneri* (2)
[e] Organisms include *Streptococcus agalactiae* (57), *S. canis* (2), *S. dysgalactiae* (66), *S. pyogenes* (129)
[f] Organisms include *Streptococcus anginosus* (11), *S. anginosus* group (3), *S. constellatus* (6), *S. gallolyticus* (1), *S. mitis* (1), *S. mitis* group (3), *S. oralis* (1), *S. salivarius/vestibularis* (1)
[g] Uncomplicated UTI only
[h] Organisms include *Citrobacter braakii* (3), *C. freundii* (12), *C. freundii* species complex (11), *C. koseri* (31), *Enterobacter aerogenes* (22), *E. asburiae* (1), *E. cloacae* (82), *E. cloacae* species complex (24), *E. kobei* (2), *Escherichia coli* (262), Gram-negative rods in the family *Enterobacteriaceae* (1), *Hafnia alvei* (2), *Klebsiella oxytoca* (44), *K. pneumoniae* (140), *K. variicola* (2), *Leclercia adecarboxylata* (2), *Morganella morganii* (46), *Proteus mirabilis* (107), *P. vulgaris* (4), *P. vulgaris* group (9), *Providencia rettgeri* (5), *P. stuartii* (4), *Raoultella ornithinolytica* (1), *Serratia liquefaciens* (1), *S. marcescens* (45), *S. rubidaea* (2), unspeciated *Pantoea* (1), unspeciated *Serratia* (1)

Conclusions

- Delafloxacin demonstrated potent *in vitro* activity against fluoroquinolone-susceptible and -resistant Gram-positive ABSSSI pathogens collected in Europe during 2014-2016, including staphylococci (MSSA, MRSA, CoNS, and MR-CoNS), β-haemolytic streptococci, viridans group streptococci, and *E. faecalis*
- Against Gram-negative (*Enterobacteriaceae* and *P. aeruginosa*) ABSSSI isolates from Europe (2014-2016), delafloxacin demonstrated an *in vitro* spectrum of activity comparable to the other fluoroquinolones tested
- Results of this investigation support the continued development of delafloxacin in infections where the above mentioned organisms may be found, including ABSSSI

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