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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 programme

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Background: Delafloxacin is an 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). Delafloxacin has potent activity against Gram-positive and -negative bacterial pathogens frequently associated with skin and skin structure infections (SSSI) 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 SSSI in European medical centres participating in the SENTRY surveillance program during 2014-2016 are presented (Table).

Material/methods: A total of 1,571 staphylococci, 427 β-haemolytic streptococci, 75 viridans group streptococci, 141 *E. faecalis*, 962 Enterobacteriaceae and 264 *P. aeruginosa* isolates collected from patients with SSSI 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 14.6 and 31.3%, respectively. Delafloxacin was highly active against methicillin-resistant *S. aureus* (18.3% MRSA; $MIC_{50/90}$ 0.12/1 mg/L) and CoNS (48.4% MRCoNS; $MIC_{50/90}$ 0.25/1 mg/L) where FQ resistance was 63.9-65.0%. β-haemolytic streptococci were inhibited by low levels of delafloxacin ($MIC_{50/90}$ 0.015/0.03 mg/L; highest MIC 0.12 mg/L) whereas resistance to levofloxacin (96.5% susceptible), erythromycin (81.0% susceptible), clindamycin (89.7% susceptible)

and tetracycline (57.6% 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 98.6% of *E. faecalis* isolates at ≤1 mg/L. Similarly, delafloxacin inhibited 73.3 and 71.2% of Enterobacteriaceae and *P. aeruginosa* at ≤1 mg/L and was comparable in activity to levofloxacin (78.6 and 65.2% inhibited at ≤1 mg/L, respectively).

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

		Delafloxacin MIC (mg/L)		**Levofloxacin MIC (mg/L)**		
Organism	**# tested**	**MIC_{50}**	**MIC_{90}**	**MIC_{50}**	**MIC_{90}**	**%S**
S. aureus	1,325	≤0.004	0.25	0.25	>4	85.3
S. aureus (MRSA)	243	0.12	1	>4	>4	35.0
CoNS	246	0.015	0.5	0.25	>4	64.6
β-haemolytic streptococci	427	0.015	0.03	0.5	1	96.5
Viridans group streptococci	75	0.008	0.03	0.5	1	-
E. faecalis	141	0.12	1	1	>4	75.2
Enterobacteriaceae	962	0.12	4	≤0.12	>4	78.6
E. coli	276	0.06	4	≤0.12	>4	67.0
P. aeruginosa	264	0.5	>4	0.5	>4	65.2