

***In Vitro* Evaluation of Delafloxacin Activity Against Contemporary European Isolates from Community-Acquired Pneumonia and Lower Respiratory Tract Infections: Results from the SENTRY Antimicrobial Surveillance Program (2018-2021)**

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Objective

Delafloxacin is a broad-spectrum fluoroquinolone antibacterial approved by EMA and FDA for treatment of acute bacterial skin and skin structure infections, and community-acquired pneumonia (CAP).

The objective of this study was the analysis of the susceptibilities to delafloxacin for recent European clinical isolates of *Streptococcus pneumoniae*, *Haemophilus influenzae* and methicillin-susceptible *Staphylococcus aureus* (MSSA) from CAP and lower respiratory tract infections (LRTI).

Methods

- CAP and LRTI isolates were consecutively collected at 34 medical centres from 18 European countries participating in the SENTRY Antimicrobial Surveillance Program during 2018-2021.
- Susceptibility testing was performed with CLSI broth microdilution, and EUCAST interpretive criteria were applied.
- Delafloxacin CAP breakpoints were published in the EUCAST rationale document on 2021/04/12.
 - EUCAST delafloxacin CAP breakpoints: MSSA, S ≤ 0.016 /- R > 0.016 mg/L; *S. pneumoniae*, S ≤ 0.06 /- R > 0.06 mg/L; *H. influenzae*, S ≤ 0.004 /- R > 0.004 mg/L.
 - CAP breakpoints for MSSA were also published in EUCAST v12.0 breakpoint tables (1/1/2022).

Results

Table 1. Susceptibilities of delafloxacin and comparators against *S. pneumoniae* and MSSA

Organism/ Antimicrobial agent (number of isolates)	mg/L		EUCAST ^a		
	MIC ₅₀	MIC ₉₀	%S	%I	%R
<i>S. pneumoniae</i> (n = 2,554)					
Delafloxacin	0.015	0.03	98.9 ^b		1.1
Levofloxacin	1	1	^c	98.9	1.1
Moxifloxacin	0.12	0.25	99.0		1.0
Amoxicillin-clavulanic acid (2:1 ratio)	≤0.03	2	81.9 ^d	4.4	13.6
Erythromycin	0.03	>16	77.9	0.3	21.8
MSSA (n = 764)					
Delafloxacin	0.004	0.008	96.5 ^b		4.0
Levofloxacin	0.25	0.5	^c	96.9	3.1
Moxifloxacin	≤0.06	0.12	96.9		3.1

^a Criteria as published by EUCAST (2022). S, susceptible; I, intermediate; R, resistant.

^b EUCAST 2022 CAP breakpoints applied: MSSA, S ≤0.016/ R >0.016 mg/L; *S. pneumoniae*, S ≤0.06/ R >0.06 mg/L; *H. influenzae*, S ≤0.004/ R >0.004 mg/L.

^c An arbitrary susceptible breakpoint of ≤0.001 mg/L has been published by EUCAST indicating that susceptible should not be reported for this organism-agent combination and is interpreted as intermediate, increased exposure.

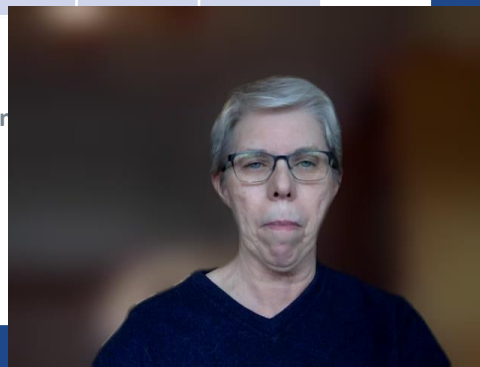
^d Using oral breakpoints.

^e Using non-meningitis breakpoints.

^f The percentage of wild type shown based on the EUCAST epidemiologic cut off.

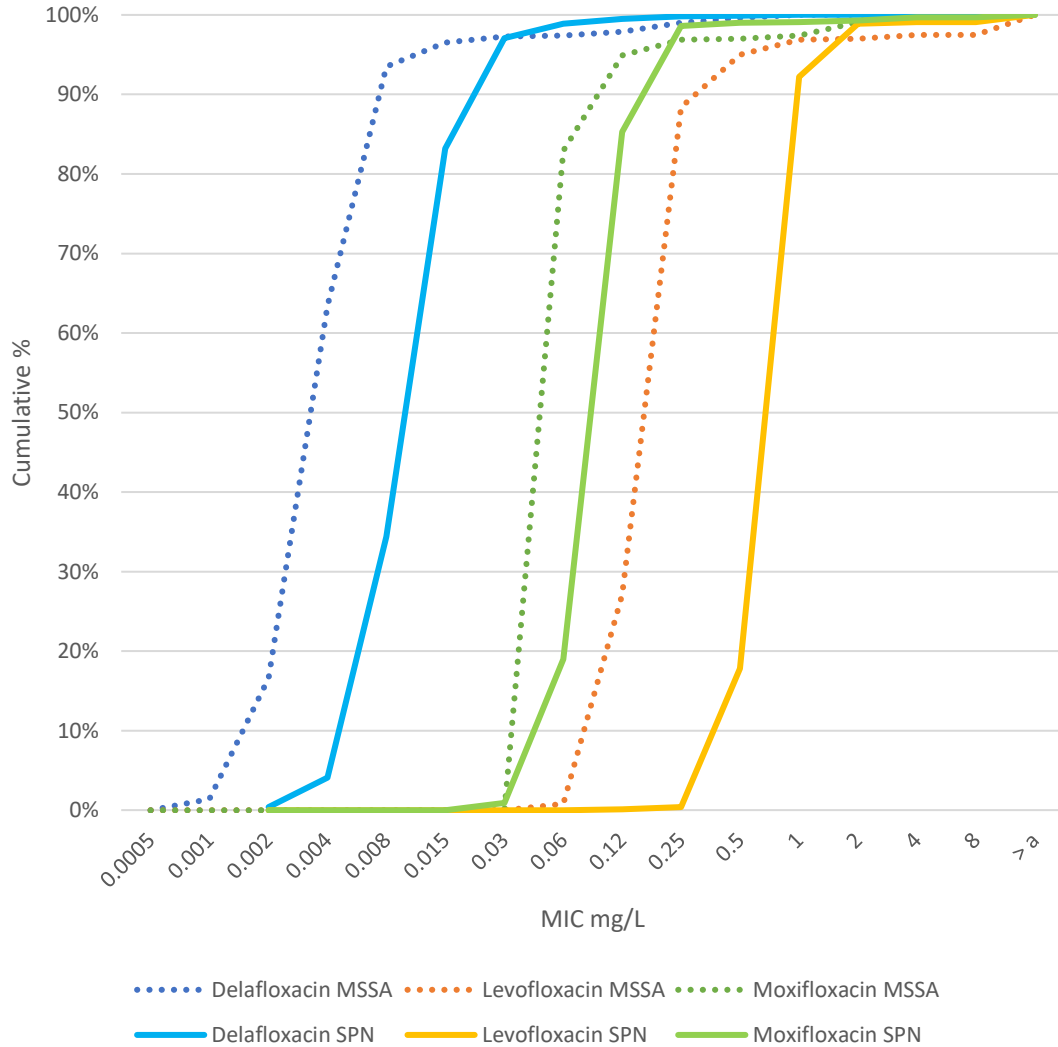
Table 2. Susceptibilities of delafloxacin and comparators against *H. influenzae*

Organism/ Antimicrobial agent (number of isolates)	mg/L		EUCAST ^a		
	MIC ₅₀	MIC ₉₀	%S	%I	%R
<i>H. influenzae</i> (n = 1,503)					
Delafloxacin	0.0005	0.002	96.6 ^b		3.4
Levofloxacin	0.015	0.03	96.3		3.7
Ciprofloxacin	0.008	0.015	96.4		3.6
Moxifloxacin	0.015	0.03	96.8		3.2
Amoxicillin-clavulanic acid (fixed 2)	0.5	2	^{c,d}	95.7	4.3
Ampicillin	0.25	>8	79.7 ^e		20.3
Azithromycin	1	2	98.7 ^f		



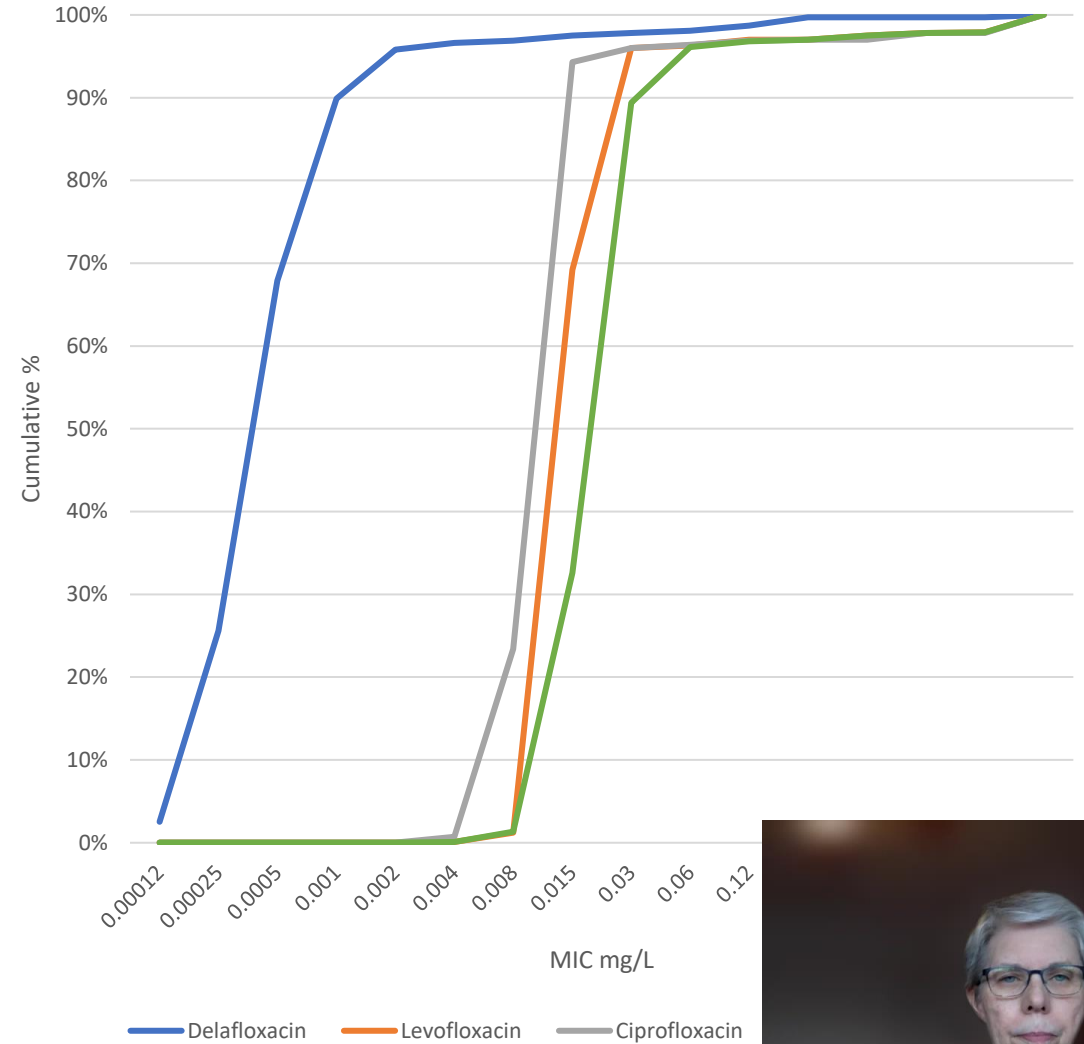
Results

Figure 1. MIC Distributions of MSSA and *S. pneumoniae*



a >, greater than the highest dilution tested.

Figure 2. MIC Distributions of *H. influenzae*



Results

- Delafloxacin was the most active agent tested, with MIC₉₀ values of 0.002 mg/L for *H. influenzae*, 0.008 mg/L for MSSA and 0.03 mg/L for *S. pneumoniae* (Figures 1 and 2).
- Delafloxacin susceptibility was 96.5% and moxifloxacin 96.9% against MSSA (Table 1).
- Levofloxacin was 96.6% intermediate, increased exposure to MSSA.
- *S. pneumoniae* had ≥99.0% susceptibility to delafloxacin and moxifloxacin, and 99.0% intermediate-increased exposure to levofloxacin.
- *H. influenzae* susceptibility was >95% to delafloxacin, moxifloxacin, and levofloxacin (Table 2).
 - Erythromycin had the lowest susceptibility for *S. pneumoniae* (77.9%) while ampicillin had the lowest susceptibility for *H. influenzae* (79.7%).

Conclusions

- Delafloxacin showed potent activity against recent CAP and LRTI isolates from patients in European hospitals.
- Quinolone-resistant MSSA, *S. pneumoniae*, and *H. influenzae* were uncommon. Susceptibilities to other tested oral agents were lower compared to delafloxacin.
- These *in vitro* results suggest that delafloxacin may be a useful therapeutic option for CAP caused by MSSA, *S. pneumoniae*, or *H. influenzae*.

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