IDWeek 2022 | Poster #P2176

In Vitro Evaluation of Delafloxacin Activity Against Contemporary US Isolates from Cystic Fibrosis Patients Hospitalized with Pneumonia: Results from the SENTRY Antimicrobial Surveillance Program (2019–2021)

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Introduction

- Delafloxacin (DLX) is a broad-spectrum fluoroquinolone approved in the US for the treatment of community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections.
- DLX is indicated to treat CABP caused by multiple pathogens, including methicillin-susceptible *Staphylococcus aureus* (MSSA) and *Pseudomonas aeruginosa* (PSA).
  - DLX has increased activity in acidic environments found at infection sites, and is able to penetrate *S. aureus* biofilms (Lemaire et al. 2011, Siala et al. 2014).
  - Fluoroquinolones can be used for oral treatment of PSA infections in cystic fibrosis (CF) patients (Langton Hewer et al. 2020, Millar et al. 2021).
- In this study, the *in vitro* susceptibilities of DLX and comparator quinolones were determined for clinical isolates from US CF patients collected in the SENTRY Antimicrobial Surveillance Program during 2019–2021.

Methods

- Isolates from CF patients hospitalized with pneumonia were consecutively collected from 19 US participating medical centers from all 9 US Census divisions.
  - Only 1 isolate per patient per infection episode was submitted.
- Isolates were identified at each site and confirmed with MALDI-TOF at JMI Laboratories.
- Susceptibility testing was performed according to CLSI broth microdilution methodology (M07, 2018).
  - FDA interpretive criteria for community acquired bacterial pneumonia were used for DLX.
  - CLSI (M100, 2022) criteria were applied to comparators.
  - As MOX does not have CLSI breakpoints for PSA, ciprofloxacin (CIP) was tested.

Results

- A total of 115 *S. aureus* (SA), including 72 MSSA, and 43 methicillin-resistant SA (MRSA), and 67 PSA (25 CIP-R), were tested.
- Susceptibility (%S) to DLX, levofloxacin (LEV), and moxifloxacin (MOX) for SA overall, or MSSA and %S to DLX, LEV, and ciprofloxacin (CIP) for PSA are shown in Table 1.
- Against all SA, DLX was 73.9%S, LEV was 67.0%S, and MOX was 67.0%S.
- DLX had the highest %S against MSSA (94.4%S).
  - Both LEV and MOX were 87.5%S.
- DLX had the highest %S against PSA (68.7%S).
  - LEV was 43.3%S and CIP was 50.7%S.
- The cumulative percent inhibition of SA, MSSA, MRSA, and PSA are shown in Figures 1 and 2.
  - DLX was the most active quinolone against SA, MSSA, and MRSA (Figure 1).
  - DLX %S against MRSA was 39.5%, while LEV %S was 32.6%.
  - DLX and CIP had similar activity against PSA; both were more active than LEV (Figure 2).
  - DLX %S against CIP-R PSA was 36.0% while LEV %S was 4.0%.

Table 1. Susceptibilities of delafloxacin and comparators tested against *S. aureus*, methicillin-susceptible *S. aureus* (MSSA), and *P. aeruginosa* isolates collected from US cystic fibrosis patients hospitalized with pneumonia

		Minimal inhibitory concentrations (MIC) mg/L			CLSI/FDA [a]		
Organism/Antimicrobial agent	No. of isolates	MIC_{50}	MIC_{90}	MIC range	%S	%I	%R
S. aureus							
Delafloxacin	115	0.008	0.5	0.002 to 4	73.9 [b]	9.6	16.5
Levofloxacin	115	0.25	>4	0.06 to >4	67.0	0.0	33.0
Moxifloxacin	115	≤0.06	>4	≤0.06 to >4	67.0	0.9	32.2
MSSA							
Delafloxacin	72	0.004	0.03	0.002 to 1	94.4 [b]	4.2	1.4
Levofloxacin	72	0.25	4	0.06 to >4	87.5	0.0	12.5
Moxifloxacin	72	≤0.06	2	≤0.06 to >4	87.5	0.0	12.5
P. aeruginosa							
Delafloxacin	67	0.5	4	0.015 to 16	68.7 [c]	11.9	19.4
Levofloxacin	67	2	8	0.06 to 32	43.3	17.9	38.8
Ciprofloxacin	67	0.5	4	0.015 to >4	50.7	11.9	37.3

[a] Criteria as published by FDA (2022) for delafloxacin or CLSI (2022) for comparator agents. S susceptible, I intermediate, and R resistant.
[b] Community-acquired bacterial pneumonia breakpoints for MSSA applied for delafloxacin (FDA).
[c] Community-acquired bacterial pneumonia breakpoints applied for delafloxacin (FDA).

Figure 1. Cumulative percent inhibition by delafloxacin (DLX) or levofloxacin (LEV) against all *S. aureus* and MSSA and MRSA phenotypes from cystic fibrosis patients

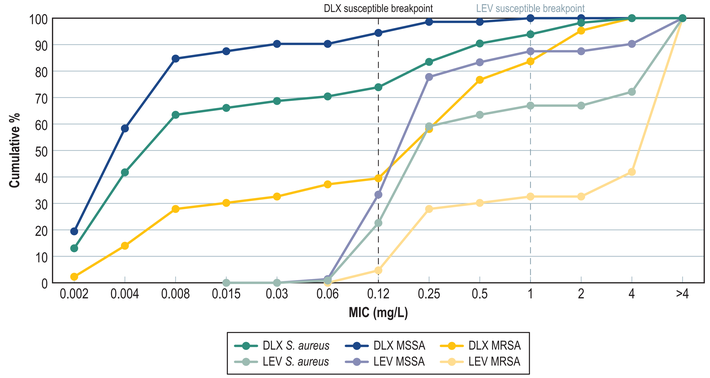
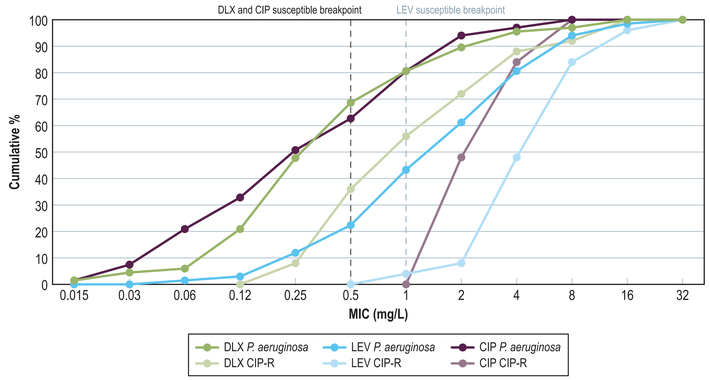


Figure 2. Cumulative percent inhibition by delafloxacin (DLX), levofloxacin (LEV), or ciprofloxacin (CIP) against *P. aeruginosa* and CIP-R *P. aeruginosa* from cystic fibrosis patients



Conclusions

- DLX had good activity against recent MSSA and PSA isolates from US CF patients hospitalized with pneumonia.
- DLX had the highest %S of the fluoroquinolones tested for all organism groups.
  - Due to the increased activity of DLX compared to LEV or CIP, determination of the DLX MIC may be useful if considering a fluoroquinolone.
- These *in vitro* data suggest that DLX could be a useful therapy when both MSSA and PSA coverage is needed in CF patients.

Funding

This study was supported by Melinta Therapeutics.

Authors are employees of JMI Laboratories, which was paid consultant to Melinta Therapeutics in connection with the development of this poster.

Acknowledgments

The authors thank all of the participant centers for the work in providing isolates.

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