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Antimicrobial Activity of DC-159a, a New Fluoroquinolone, against 1,149 Recently Collected Clinical Isolates[▽]

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The activity of DC-159a, a novel orally administered fluorinated quinolone, was evaluated by reference broth microdilution or agar dilution methods against 1,149 recently collected clinical isolates from five continents. Against pathogens associated with community-acquired respiratory tract infections (CA-RTIs), the MIC_{90}s were 0.12 μg/ml for *Streptococcus pneumoniae*, 0.015 to 0.03 μg/ml for *Haemophilus influenzae*, 0.03 μg/ml for *Moraxella catarrhalis*, and 0.12 μg/ml for beta-hemolytic streptococci. Similarly, DC-159a was potent against various types of staphylococci (MIC_{90} range, 0.03 to 2 μg/ml), *Enterococcus faecalis* (MIC_{90}, 4 μg/ml), wild-type isolates of the family *Enterobacteriaceae* (MIC_{90} range, 0.06 to 2 μg/ml), wild-type *Pseudomonas aeruginosa* (MIC_{90}, 2 μg/ml), and *Acinetobacter* spp. (MIC_{90}, 0.12 μg/ml). Fluoroquinolone-nonsusceptible organism subsets usually had elevated DC-159a MICs, but the MICs were often two- to fourfold lower than those of levofloxacin and moxifloxacin. In conclusion, DC-159a appears to possess a balanced broad spectrum of activity that exceeds the activities of the currently marketed fluoroquinolones, especially against pathogens that cause CA-RTIs.

The emergence of resistance among commonly isolated pathogens has compromised the clinical utility of several major antimicrobial classes, including the β-lactams, macrolides, aminoglycosides, glycopeptides, and fluoroquinolones (1, 7, 12, 14). For the fluoroquinolones, the modifications of the DNA gyrase and topoisomerase targets (7) can elevate the gatifloxacin, gemifloxacin, levofloxacin, and moxifloxacin MICs into the resistant ranges for *Streptococcus pneumoniae* isolates and, more rarely, *Haemophilus influenzae* and *Moraxella catarrhalis* isolates. Similarly, important gram-positive pathogens (staphylococci, beta-hemolytic streptococci, enterococci) and gram-negative bacilli (members of the family *Enterobacteriaceae*, *Pseudomonas* spp.) have consistently acquired resistance to the fluoroquinolones by prolonged exposure (1, 13, 14). The need for novel agents in this class has become critical for continued access to agents with clinical activity and for the provision of agents with a balance of potencies against species of emerging pathogens (multidrug-resistant [MDR] *Acinetobacter* spp. and *Stenotrophomonas maltophilia*) while offering continued coverage against pneumococci, *Staphylococcus aureus*, and other community-acquired pathogens (10, 13).

DC-159a is a novel orally administered fluoroquinolone developed by Daiichi Pharmaceutical Co., Ltd. (Tokyo, Japan), and has been reported to have a residual affinity for strains with mutations in the quinolone resistance-determining region (QRDR) (2, 9). Such features (10) provide this agent with a focus of activity against community-acquired pathogens that cause significant occurrences of respiratory tract infections, uncomplicated cutaneous infections, and possibly, other infections caused by wild-type members of the family *Enterobacteriaceae*. To assess this possibility, an international collection of recently collected gram-positive and -negative pathogens (1,149 strains) that contained organisms with well-characterized mechanisms of resistance or with the phenotypic expression of resistance according to the MICs was selected. All tests were performed by reference Clinical and Laboratory Standards Institute (CLSI; formerly NCCLS) methods with appropriate medium supplements for fastidious streptococci (2 to 5% lysed horse blood) and *Haemophilus* sp. strains (*Haemophilus* test medium formulation) (3, 4).

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MATERIALS AND METHODS

Bacterial strains. A total of 1,149 strains recently collected (2005 to 2007) from infected patients worldwide were studied, with a balance of isolates from Europe, the Asia-Pacific, and the Americas (North and South America). The following major species were sampled: *S. pneumoniae* ($n = 112$; 62 penicillin nonsusceptible), *Streptococcus pyogenes* ($n = 30$), *Streptococcus agalactiae* ($n = 30$), *Staphylococcus aureus* ($n = 90$; 60 methicillin-resistant *S. aureus* [MRSA] strains and 30 community-acquired *S. aureus* [CA-MRSA] strains), coagulase-negative staphylococci (CoNS; $n = 60$), enterococci ($n = 173$; 62 vancomycin-resistant enterococci and 10 linezolid-resistant enterococci), *Listeria monocytogenes* ($n = 10$), *H. influenzae* ($n = 80$; 30 β-lactamase-positive strains and 10 β-lactamase-negative and ampicillin-resistant [BLNAR] strains), *Haemophilus parainfluenzae* ($n = 30$), *M. catarrhalis* ($n = 29$; 19 β-lactamase-positive strains), *Bordetella pertussis* ($n = 12$), members of the family *Enterobacteriaceae* ($n = 323$; 38 species), *Pseudomonas aeruginosa* ($n = 40$), *Acinetobacter* spp. ($n = 40$; 5 species), *S. maltophilia* ($n = 30$), and *Neisseria gonorrhoeae* ($n = 60$; 40 ciprofloxacin-nonsusceptible strains). Numerous subsets of wild-type strains and strains with defined resistance mechanisms or phenotypes in each genus or species group were tested.

Susceptibility testing methods. DC-159a and levofloxacin standard powders were supplied by Daiichi Pharmaceutical Co., Ltd. All other agents were obtained from domestic (U.S.) manufacturers. The reference methods described by the CLSI were used throughout the study (3, 4). Gonococci were tested by the agar dilution method on GC agar base with the defined supplement (3, 4). The

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interpretive criteria of CLSI standard M100-S18 (4) were used, where available, to determine the susceptibilities of the isolates to the comparison agents (24 antimicrobials). The PCR methods described by Mutnick et al. (11) were used to determine the 23S rRNA mutations (G2576T) associated with the linezolid resistance found in the enterococci.

Quality control was ensured by the use of the following strains: *S. aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, *Escherichia coli* ATCC 25922 and ATCC 35218, *P. aeruginosa* ATCC 27853, *H. influenzae* ATCC 49247 and ATCC 49766, *S. pneumoniae* ATCC 49619, and *N. gonorrhoeae* ATCC 49226. All quality control test results were within published CLSI ranges (4).

RESULTS

When the 107 pneumococci were subcategorized by their susceptibilities to penicillin (Table 1), the DC-159a MIC_{90} remained unaffected at 0.12 μg/ml. This potency was equal to that of moxifloxacin and eightfold greater than that of levofloxacin. The DC-159a MIC results for the levofloxacin-nonsusceptible *S. pneumoniae* strains were generally increased 8- to 16-fold, but all MICs remained ≤2 μg/ml. Beta-hemolytic streptococci were very susceptible to DC-159a, with MIC_{50}s and MIC_{90}s of 0.12 μg/ml. This potency was slightly greater than that of moxifloxacin and eightfold greater than that of levofloxacin (MIC_{90}, 1 μg/ml).

Most of the antimicrobials tested were active against the *H. influenzae* strains (Table 1). The exceptions were ampicillin against β-lactamase-producing strains, azithromycin (rate of nonsusceptibility, 2.5 to 3.4%), cefuroxime (2.5%), tetracycline (6.7%), and trimethoprim-sulfamethoxazole (20.0 to 22.5%). All fluoroquinolones were very active against *H. influenzae*, with MIC_{90}s ranging from ≤0.015 to ≤0.12 μg/ml. The DC-159a MIC_{90}s for the *H. influenzae* strains were 0.015 and 0.03 μg/ml, with the highest values being for the β-lactamase-positive isolates. The 10 BLNAR strains had very low DC-159a MICs that ranged from 0.008 to 0.015 μg/ml. The *H. parainfluenzae* strains were approximately fourfold less susceptible to DC-159a than the *H. influenzae* strains. This difference was also observed for the other fluoroquinolones tested (Table 1). The *M. catarrhalis* strains were very susceptible to DC-159a, with MIC_{50}s and MIC_{90}s of 0.03 μg/ml, regardless of whether they produced a β-lactamase (Table 1).

Table 2 lists the activity of DC-159a against 150 isolates of staphylococci. DC-159a exhibited potent activity against methicillin (oxacillin)-susceptible *S. aureus* (MSSA) strains, with MIC_{50}s and MIC_{90}s of only 0.03 μg/ml. This level of activity was 16-fold greater than that of ciprofloxacin but 2-fold less than that of gemifloxacin (MIC_{90}, 0.015 μg/ml). MRSA strains derived from patients with nosocomial infections showed the greatest susceptibility to DC-159a (MIC_{90}, 2 μg/ml). However, the range of DC-159a MICs was 32- to 64-fold greater than that for MSSA strains (0.015 to 0.06 μg/ml for MRSA strains versus 0.5 to 4 μg/ml for MSSA strains). None of these MRSA strains were susceptible at the CLSI breakpoint concentrations of the comparison, marketed fluoroquinolones. The activity of DC-159a against 30 well-characterized isolates from patients with CA-MRSA infection (USA300-0114 and its variants) was tested, and the MIC_{50} and MIC_{90} results for these strains were identical to those for the MSSA strains (Table 2). The CA-MRSA strains had a documented virulence island (Panton-Valentine leukocidin positive), staphylococcal chromosomal cassette *mec* type IVa, and *agrI*. Only 30% of the coagulase-negative staphylococcal strains were oxacillin susceptible, and the DC-159a MICs ranged from 0.03 to 0.5 μg/ml (5 $\log_2$ dilutions steps). The activity of DC-159a against a large number of *Staphylococcus saprophyticus* strains ($n = 30$) was tested, with complete activity being achieved at ≤0.5 μg/ml. Overall, among the five groups of staphylococci tested, DC-159a at ≤0.5 μg/ml inhibited all isolates in four of the groups (the exception was the nosocomial MRSA group). DC-159a showed a potency most similar to that of gemifloxacin (MIC_{90} range, 0.016 to 2 μg/ml) and markedly greater than the potencies of the other fluoroquinolones tested.

With one exception, each group of enterococci tested (Table 2) contained a mixture of strains best described as wild type (DC-159a MIC range, ≤0.06 to 0.5 μg/ml) and drug-resistant mutants (DC-159a MIC range, 2 to >8 μg/ml). The DC-159a MIC of 1 μg/ml appears to separate these isolates into two groups that have modal MICs of 0.12 and 4 μg/ml, respectively. Eighty percent of the vancomycin-susceptible *E. faecalis* strains were ciprofloxacin susceptible (wild-type MIC distributions), and among these strains, the potency rank was as follows: gemifloxacin (MIC_{90}, 0.03 μg/ml) > DC-159a (MIC_{90}, 0.12 μg/ml) > gatifloxacin = moxifloxacin (MIC_{90}, 0.25 μg/ml) > ciprofloxacin = levofloxacin (MIC_{90}, 0.5 μg/ml). The largest number of mutant (fluoroquinolone-resistant) enterococcal phenotypes was encountered among the vancomycin-resistant isolates (53 of 62 strains) and the linezolid-resistant isolates (10 of 10 strains).

E. coli wild-type isolates (90% of which were susceptible to ciprofloxacin) were equally susceptible to DC-159a and levofloxacin (MIC_{50}s, 0.03 μg/ml) (Table 3). In contrast, *E. coli* strains producing extended-spectrum β-lactamase (ESBL) enzymes were more likely to be fluoroquinolone resistant, and the DC-159a and levofloxacin MIC_{50}s were 1 doubling dilution higher than those for the wild type (Table 2). The wild-type *Klebsiella* spp. were highly susceptible to ciprofloxacin (90% susceptible; MIC_{50}s, ≤0.03 μg/ml) and DC-159a (MIC_{50} range, 0.03 to 0.5 μg/ml). Ten *K. pneumoniae* strains harboring a KPC-type serine carbapenemase were tested (Table 3), and only two strains had DC-159a MICs of ≤2 μg/ml.

Table 3 also illustrates the activity of DC-159a against 20 *Proteus mirabilis* strains, 2 of which produced a CTX-M-type ESBL, as determined by molecular testing. DC-159a had activity (MIC_{50}, 0.25 μg/ml) equal to the activities of gatifloxacin and moxifloxacin; but it was less active by weight (fourfold) than levofloxacin, gemifloxacin, and ciprofloxacin. With the current CLSI susceptibility breakpoints (4), susceptibilities of the *P. mirabilis* strains to the marketed fluoroquinolones showed marked variations (>20%), with the ranking being as follows: levofloxacin > gatifloxacin > ciprofloxacin > gemifloxacin (moxifloxacin does not have a published breakpoint).

Among the *Citrobacter* spp. (20 of 30 of the strains were *Citrobacter freundii* strains), *Enterobacter* spp. (26 of 33 of the strains were *Enterobacter cloacae*), and the *S. marcescens* strains, significant differences in activity were observed when DC-159a was tested against wild-type strains and various strains with defined mechanisms of resistance (Table 3). The DC-159a MIC_{90}s for the wild-type strains ranged from 0.5 to 2 μg/ml, whereas they ranged from 1 to 8 μg/ml for the resistant subsets of strains. The activity of DC-159a was comparable to the activities of the other fluoroquinolones tested against these isolates of the family *Enterobacteriaceae*, regardless of the core-

TABLE 1. Activity of DC-159a tested by reference CLSI methods against 323 strains of streptococci and gram-negative pathogens associated with respiratory tract infections

Organism (no. of strains tested)/ antimicrobial agent	MIC (μg/ml)			% Susceptible/ % resistant[a]:
	50%	90%	Range	
S. pneumoniae				
Penicillin susceptible (30)				
DC-159a	0.12	0.12	0.06–0.25	−[b]/−
Gatifloxacin	0.25	0.25	0.06–0.5	100.0/0.0
Gemifloxacin	≤0.015	≤0.015	≤0.015–0.03	100.0/0.0
Levofloxacin	1	1	0.5–1	100.0/0.0
Moxifloxacin	0.12	0.12	≤0.03–0.25	100.0/0.0
Ciprofloxacin	1	2	0.25–2	−/−
Erythromycin	≤0.25	≤0.25	≤0.25–>32	96.7/3.3
Clindamycin	≤0.25	≤0.25	≤0.25–>2	96.7/3.3
Penicillin intermediate (30)				
DC-159a	0.06	0.12	0.06–0.12	−/−
Gatifloxacin	0.25	0.25	0.12–1	100.0/0.0
Gemifloxacin	≤0.015	0.03	≤0.015–0.06	100.0/0.0
Levofloxacin	1	1	0.5–1	100.0/0.0
Moxifloxacin	0.12	0.12	0.06–0.5	100.0/0.0
Ciprofloxacin	1	2	0.5–2	−/−
Erythromycin	2	>32	≤0.25–>32	43.3/53.3
Clindamycin	≤0.25	>2	≤0.25–>2	73.3/26.7
Penicillin resistant (32)				
DC-159a	0.12	0.12	0.06–0.12	−/−
Gatifloxacin	0.25	0.5	0.25–1	100.0/0.0
Gemifloxacin	≤0.015	0.03	≤0.015–0.03	100.0/0.0
Levofloxacin	1	1	0.5–2	100.0/0.0
Moxifloxacin	0.12	0.25	0.06–1	100.0/0.0
Ciprofloxacin	1	2	0.5–4	−/−
Erythromycin	4	>32	≤0.25–>32	37.5/62.5
Clindamycin	≤0.25	>2	≤0.25–>2	56.3/43.8
Levofloxacin nonsusceptible (20)				
DC-159a	0.5	1	0.25–2	−/−
Gatifloxacin	4	>4	1–>4	10.0/65.0
Gemifloxacin	0.12	0.25	≤0.06–1	65.0/10.0
Moxifloxacin	2	4	0.25–4	35.0/20.0
Ciprofloxacin	>4	>4	4–>4	−/−
Erythromycin	≤0.25	>2	≤0.25–>8	60.0/40.0
Clindamycin	≤0.25	>2	≤0.25–>2	75.0/20.0
β-Hemolytic streptococci				
Group A (30)				
DC-159a	0.12	0.12	0.06–0.12	−/−
Gatifloxacin	0.25	0.25	0.12–0.5	100.0/0.0
Gemifloxacin	0.015	0.03	0.008–0.06	−/−
Levofloxacin	0.5	1	0.25–2	100.0/0.0
Moxifloxacin	0.12	0.25	0.06–0.25	−/−
Ciprofloxacin	0.5	0.5	0.25–2	−/−
Penicillin	≤0.015	≤0.015	≤0.015	100.0/−
Erythromycin	≤0.06	4	≤0.06–>8	86.7/13.3
Clindamycin	≤0.06	≤0.06	≤0.06–>8	96.7/3.3
Group B (30)				
DC-159a	0.12	0.12	0.06–0.25	−/−
Gatifloxacin	0.25	0.25	0.12–0.5	100.0/0.0
Gemifloxacin	0.015	0.03	0.008–0.06	−/−
Levofloxacin	1	1	0.5–1	100.0/0.0
Moxifloxacin	0.12	0.25	0.06–0.25	−/−
Ciprofloxacin	0.5	1	0.25–1	−/−
Penicillin	0.06	0.12	≤0.015–0.12	100.0/−
Erythromycin	≤0.06	2	≤0.06–>8	76.7/23.3
Clindamycin	≤0.06	≤0.06	≤0.06–>8	90.0/10.0

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TABLE 1—*Continued*

Organism (no. of strains tested)/ antimicrobial agent	MIC (μg/ml)			% Susceptible/ % resistant[a]:
	50%	90%	Range	
H. influenzae				
β-Lactamase negative (40)				
DC-159a	0.008	0.015	0.008–0.015	−/−
Gatifloxacin	≤0.03	≤0.03	≤0.03	100.0/−
Gemifloxacin	≤0.015	≤0.015	≤0.015	100.0/−
Levofloxacin	0.015	0.015	≤0.008–0.03	100.0/−
Moxifloxacin	≤0.03	≤0.03	≤0.03	100.0/−
Ciprofloxacin	≤0.12	≤0.12	≤0.12	100.0/−
Amoxicillin-clavulanic acid	0.5	1	0.25–2	100.0/0.0
Azithromycin	1	2	≤0.5–>16	97.5/−
β-Lactamase positive (30)				
DC-159a	0.015	0.03	≤0.004–0.03	−/−
Gatifloxacin	≤0.03	≤0.03	≤0.03	100.0/−
Gemifloxacin	≤0.015	≤0.015	≤0.015	100.0/−
Levofloxacin	0.015	0.015	≤0.008–0.03	100.0/−
Moxifloxacin	≤0.03	≤0.03	≤0.03–0.06	100.0/−
Ciprofloxacin	≤0.12	≤0.12	≤0.12	100.0/−
Amoxicillin-clavulanic acid	≤1	≤1	≤1	100.0/0.0
Azithromycin	1	2	≤0.5–>4	96.7/−
β-Lactamase negative, ampicillin resistant (10)[c]				
DC-159a	0.015	0.015	0.008–0.015	−/−
Gatifloxacin	≤0.03	≤0.03	≤0.03	100.0/−
Gemifloxacin	≤0.12	≤0.12	≤0.12	100.0/−
Levofloxacin	0.015	0.015	0.015	100.0/−
Moxifloxacin	≤0.03	≤0.03	≤0.03	100.0/−
Ciprofloxacin	≤0.12	≤0.12	≤0.12	100.0/−
Ampicillin	2	2	2–4	0.0/10.0
Amoxicillin-clavulanic acid	4	4	2–8	90.0/10.0
Azithromycin	1	1	0.5–1	100.0/−
H. parainfluenzae (30)				
DC-159a	0.06	0.12	0.008–0.25	−/−
Gatifloxacin	≤0.03	≤0.03	≤0.03–0.12	100.0/−
Gemifloxacin	≤0.12	≤0.12	≤0.12	100.0/−
Levofloxacin	0.03	0.06	0.015–0.12	100.0/−
Moxifloxacin	≤0.03	0.12	≤0.03–0.5	100.0/−
Ciprofloxacin	≤0.25	≤0.25	≤0.25	100.0/−
Ampicillin	≤1	2	≤1–>4	86.7/10.0
Amoxicillin-clavulanic acid	≤2	≤2	≤2–4	100.0/0.0
Azithromycin	0.5	2	0.12–2	100.0/−
M. catarrhalis				
β-Lactamase negative (10)				
DC-159a	0.03	0.03	0.015–0.03	−/−
Gatifloxacin	≤0.03	≤0.03	≤0.03	−/−
Gemifloxacin	≤0.12	≤0.12	≤0.12	−/−
Levofloxacin	0.03	0.03	0.015–0.03	−/−
Moxifloxacin	0.06	0.06	≤0.03–0.06	−/−
Ciprofloxacin	≤0.12	≤0.12	≤0.12	−/−
Penicillin	≤0.03	≤0.03	≤0.03–0.06	−/−
Amoxicillin-clavulanic acid	≤0.06	≤0.06	≤0.06	−/−
Erythromycin	≤0.25	≤0.25	≤0.25	−/−
β-Lactamase positive (19)				
DC-159a	0.03	0.03	0.015–0.03	−/−
Gatifloxacin	≤0.03	≤0.03	≤0.03–0.06	−/−
Gemifloxacin	≤0.12	≤0.12	≤0.12	−/−
Levofloxacin	0.03	0.03	0.015–0.03	−/−
Moxifloxacin	0.06	0.06	≤0.03–0.06	−/−
Ciprofloxacin	≤0.12	≤0.12	≤0.12	−/−

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TABLE 1—*Continued*

Organism (no. of strains tested)/ antimicrobial agent	MIC (μg/ml)			% Susceptible/ % resistant[a]:
	50%	90%	Range	
Penicillin	2	>4	0.25–>4	−/−
Amoxicillin-clavulanic acid	≤0.25	≤0.25	≤0.25	−/−
Erythromycin	≤0.25	≤0.25	≤0.25	−/−
B. pertussis (12)				
DC-159a	0.008	0.015	0.008–0.015	−/−
Levofloxacin	0.06	0.06	0.03–0.06	100.0/0.0
Ciprofloxacin	0.03	0.03	0.015–0.03	100.0/0.0
Azithromycin	0.06	0.12	0.03–0.12	−/−
Clarithromycin	0.06	0.12	0.03–0.25	−/−
Erythromycin	0.12	0.12	0.06–0.25	−/−
Clindamycin	0.25	0.25	0.06–0.5	−/−

[a] Criteria published by the CLSI (4).
[b] −, no breakpoint criteria have been established for this category.
[c] Ampicillin at ≥2 μg/ml, according to the definition of BLNAR.

sistance of the isolates analyzed (Table 3). Only the carbapenems (imipenem) and amikacin showed wider spectra of activity against these groups of the *Enterobacteriaceae*.

DC-159a was active (MIC_{50} and MIC_{90}, 0.06 μg/ml) against all wild-type isolates of *Salmonella* spp. at ≤0.25 μg/ml (Table 3). This level of activity was equal to the levels of activity of all other fluoroquinolones tested. One strain had a CMY-2 β-lactamase that produced resistance to extended-spectrum cephems. Against the more resistant salmonellae, DC-159a MICs were four- to eightfold higher, consistent with a first-step QRDR mutation. All other fluoroquinolone MICs were similarly elevated, but none of the isolates were judged to be resistant according to the CLSI breakpoint criteria (4). The *Shigella* sp. isolates were very susceptible to DC-159a and all fluoroquinolones tested. The test results for strains of five other species of the *Enterobacteriaceae* (*Edwardsiella tarda* [one strain], *Escherichia vulneris* [two strains], *Hafnia alvei* [four strains], *Leclercia adecarboxylata* [one strain], *Pantoea agglomerans* [one strain], and *Serratia plymuthica* [one strain]) showed variable patterns of resistance among the organisms; however, DC-159a inhibited all isolates at ≤1 μg/ml (MIC_{50}, 0.06 μg/ml) (data not shown).

All *P. aeruginosa* isolates (30 strains; Table 3) were ciprofloxacin susceptible, with a single strain having a DC-159a and a gatifloxacin MIC of 4 μg/ml (potential intermediate susceptibility); however, three strains (10% of strains) had moxifloxacin MICs of 4 μg/ml. DC-159a was twofold less active than levofloxacin by use of the MIC_{50} (0.5 μg/ml) and MIC_{90} (2 μg/ml) results. Other than the fluoroquinolones, only the aminoglycosides inhibited more than 90% of the *P. aeruginosa* strains. Against the ciprofloxacin-resistant *P. aeruginosa* strains (10 strains), the DC-159a MICs ranged from 4 to >8 μg/ml. None of the fluoroquinolones tested were active, and only three of the antimicrobials tested (ceftazidime [which was active against 50% of the isolates], imipenem [50%], and amikacin [60%]) were active against ≥50% of these *P. aeruginosa* strains.

The activities of the fluoroquinolones (MIC_{90}s) against the wild-type *Acinetobacter* sp. strains varied over a narrow range from 0.12 μg/ml (DC-159a, gatifloxacin, moxifloxacin) to 0.25 μg/ml (levofloxacin, ciprofloxacin). Acinetobacters resistant to the commonly used fluoroquinolones demonstrated cross-resistance and coresistance to β-lactams (except carbapenems) and some other drug classes. DC-159a was the most active of the agents tested against *S. maltophilia* (30 strains; Table 3).

The activity of DC-159a was compared to the activities of five agents against 60 gonococci with various ciprofloxacin susceptibility categories according to the CLSI (4) breakpoint criteria (Table 4). The DC-159a MICs increased (as did the levofloxacin MICs) as the ciprofloxacin MICs increased. The DC-159a MIC ranges for ciprofloxacin-susceptible, -intermediate, and -resistant strains were 0.008 to 0.015, 0.03 to 0.12, and 0.25 to 1 μg/ml, respectively. The levels of resistance to the β-lactams and tetracycline were also elevated among the ciprofloxacin-resistant strains. Overall, the DC-159a MICs were greater than or equal to eightfold lower than those of ciprofloxacin or levofloxacin against gonococcal strains with mutations in the QRDR.

DISCUSSION

The emergence of resistance to a wide range of antimicrobials among pathogens in medical centers and in the outpatient setting has posed serious therapeutic challenges. Examples of the most problematic pathogens have been (i) CA-MRSA strains, (ii) glycopeptide-nonsusceptible staphylococci, (iii) MDR *P. aeruginosa* and *Acinetobacter* sp. strains, (iv) vancomycin-resistant enterococci, (v) strains with novel β-lactamases with wide substrate affinities, and (vi) MDR *S. pneumoniae* strains (1, 6, 12–14). Concurrent with this resistance has been the introduction of several newer fluoroquinolones (10) primarily directed against community-acquired respiratory tract infections and novel drug classes (oxazolidinones) that are active among resistant gram-positive pathogens (5). These introductions have been associated with evolving resistance due to ribosomal target and QRDR mutations (11, 12). The QRDR mutations in *S. pneumoniae* elevate the MICs of the currently available fluoroquinolone to levels associated with clinical failure (7), and similar QRDR modifications in *S. aureus* (8) present therapeutic obstacles to the use of existing

TABLE 2. Antimicrobial activity of DC-159a against 283 strains of other gram-positive species isolates by CLSI methods

Organism (no. of strains tested)/antimicrobial agent	MIC (μg/ml)			% Susceptible/ % resistant[a]
	50%	90%	Range	
S. aureus				
Oxacillin susceptible (30)				
DC-159a	0.03	0.03	0.015–0.06	−[b]/−
Gatifloxacin	0.06	0.12	≤0.03–0.12	100.0/0.0
Levofloxacin	0.12	0.25	0.06–0.25	100.0/0.0
Moxifloxacin	≤0.03	0.06	≤0.03–0.12	100.0/0.0
Ciprofloxacin	0.25	0.5	0.06–0.5	100.0/0.0
Linezolid	1	2	0.5–2	100.0/−
Tetracycline	≤2	4	≤2–>8	90.0/10.0
Trimethoprim-sulfamethoxazole	≤0.5	≤0.5	≤0.5	100.0/0.0
Clindamycin	0.12	0.12	≤0.06–0.5	100.0/0.0
Erythromycin	0.25	>8	0.25–>8	83.3/16.7
Oxacillin resistant, nosocomial (30)				
DC-159a	1	2	0.5–4	−/−
Gatifloxacin	4	>4	1–>4	0.0/96.7
Levofloxacin	>8	>8	4–>8	0.0/100.0
Moxifloxacin	2	4	1–>4	0.0/83.3
Ciprofloxacin	>4	>4	>4	0.0/100.0
Linezolid	1	2	1–2	100.0/−
Tetracycline	≤2	>8	≤2–>8	80.0/20.0
Trimethoprim-sulfamethoxazole	≤0.5	>2	≤0.5–>2	86.7/13.3
Clindamycin	>8	>8	≤0.06–>8	26.7/70.0
Erythromycin	>8	>8	0.25–>8	6.7/93.3
Oxacillin resistant, community acquired (30)				
DC-159a	0.03	0.03	0.008–0.5	−/−
Gatifloxacin	0.06	0.12	≤0.03–2	93.3/6.7
Levofloxacin	0.12	0.25	0.12–4	93.3/6.7
Moxifloxacin	≤0.03	0.06	≤0.03–1	93.3/0.0
Ciprofloxacin	≤0.25	0.5	≤0.25–>4	93.3/6.7
Linezolid	2	2	1–2	100.0/−
Tetracycline	≤4	≤4	≤4–>8	90.0/10.0
Trimethoprim-sulfamethoxazole	≤0.5	≤0.5	≤0.5	100.0/0.0
Clindamycin	0.12	0.12	≤0.06–0.25	100.0/0.0
Erythromycin	>8	>8	>8	0.0/100.0
CoNS (30)[c]				
DC-159a	0.06	0.5	0.03–0.5	−/−
Gatifloxacin	0.25	2	0.06–4	60.0/16.7
Levofloxacin	0.25	8	0.12–8	60.0/26.7
Moxifloxacin	0.25	2	≤0.03–4	63.3/16.7
Ciprofloxacin	0.5	>4	0.12–>4	56.7/43.3
Linezolid	1	1	0.5–2	100.0/−
Tetracycline	≤2	>8	≤2–>8	86.7/13.3
Trimethoprim-sulfamethoxazole	≤0.5	>2	≤0.5–>2	66.7/33.3
Clindamycin	≤0.06	>8	≤0.06–>8	83.3/16.7
Erythromycin	0.25	>8	≤0.06–>8	53.3/43.3
Oxacillin	2	>2	≤0.25–>2	30.0/70.0
S. saprophyticus (30)				
DC-159a	0.12	0.25	0.03–0.5	−/−
Gatifloxacin	0.25	2	0.06–2	83.3/13.3
Levofloxacin	0.5	2	0.12–8	86.7/10.0
Moxifloxacin	0.12	1	≤0.03–2	83.3/6.7
Ciprofloxacin	0.5	>4	0.12–>4	83.3/16.7
Linezolid	1	2	0.5–2	100.0/−
Tetracycline	≤2	>8	≤2–>8	76.7/23.3
Trimethoprim-sulfamethoxazole	≤0.5	>2	≤0.5–>2	86.7/13.3
Clindamycin	≤0.06	0.5	≤0.06–>8	90.0/10.0
Erythromycin	0.25	>8	0.12–>8	60.0/40.0
Oxacillin	1	>2	0.5–>2	0.0/100.0

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TABLE 2—*Continued*

Organism (no. of strains tested)/antimicrobial agent	MIC (μg/ml)			% Susceptible/ % resistant[a]
	50%	90%	Range	
E. faecalis				
Vancomycin susceptible (30)				
DC-159a	0.12	4	0.06–>8	−/−
Gatifloxacin	0.25	>4	0.12–>4	80.0/20.0
Levofloxacin	0.5	>8	0.25–>8	80.0/20.0
Ciprofloxacin	0.5	>4	0.25–>4	80.0/20.0
Ampicillin	≤1	2	≤1–4	100.0/0.0
Linezolid	1	2	0.5–2	100.0/0.0
Gentamicin-HL	≤500	>1000	≤500–>1000	70.0/30.0
Tetracycline	>8	>8	≤2–>8	23.3/76.7
Erythromycin	2	>8	0.25–>8	13.3/46.7
Vancomycin resistant (30)				
DC-159a	4	4	0.12–8	−/−
Gatifloxacin	>4	>4	0.12–>4	6.7/93.3
Levofloxacin	>8	>8	0.5–>8	6.7/93.3
Ciprofloxacin	>4	>4	0.5–>4	6.7/93.3
Ampicillin	2	4	≤1–16	96.7/3.3
Linezolid	1	2	1–2	100.0/0.0
Gentamicin-HL[c]	>1000	>1000	≤500–>1000	30.0/70.0
Tetracycline	>8	>8	≤2–>8	33.3/66.7
Erythromycin	>8	>8	2–>8	0.0/96.7
Enterococcus faecium				
Vancomycin susceptible (31)				
DC-159a	1	>8	0.06–>8	−/−
Gatifloxacin	2	>4	0.25–>4	51.6/45.2
Levofloxacin	2	>8	0.25–>8	51.6/45.2
Ciprofloxacin	4	>4	0.25–>4	25.8/58.1
Ampicillin	>16	>16	≤1–>16	41.9/58.1
Linezolid	2	2	1–2	100.0/0.0
Gentamicin-HL	≤500	>1000	≤500–>1000	77.4/22.6
Tetracycline	≤2	>8	≤2–>8	58.1/38.7
Erythromycin	>8	>8	0.25–>8	6.5/67.7
Vancomycin resistant (32)				
DC-159a	8	>8	0.25–>8	−/−
Gatifloxacin	>4	>4	0.5–>4	18.8/81.3
Levofloxacin	>8	>8	2–>8	18.8/81.3
Ciprofloxacin	>4	>4	1–>4	3.1/87.5
Ampicillin	>16	>16	2–>16	3.1/96.9
Linezolid	2	2	1–2	100.0/0.0
Gentamicin-HL	≤500	>1000	≤500–>1000	65.6/34.4
Tetracycline	>8	>8	≤2–>8	40.6/59.4
Erythromycin	>8	>8	1–>8	0.0/87.5
Enterococcus spp., linezolid resistant (10)[d]				
DC-159a	4	>8	2–>8	−/−
Gatifloxacin	>4	>4	>4	0.0/100.0
Levofloxacin	>8	>8	>8	0.0/100.0
Ciprofloxacin	>4	>4	>4	0.0/100.0
Ampicillin	≤1	>16	≤1–>16	50.0/50.0
Vancomycin	>16	>16	0.5–>16	40.0/60.0
Gentamicin-HL	≤500	>1000	≤500–>1000	60.0/40.0
Tetracycline	>8	>8	≤2–>8	30.0/70.0
Erythromycin	>8	>8	2–>8	0.0/90.0

[a] Criteria published by the CLSI (4). The determination of β-lactam susceptibility should be directed by the oxacillin test results.
[b] −, no breakpoint criteria have been established for this category.
[c] CoNS include *Staphylococcus auricularis* (four strains), *S. capitis* (three strains), coagulase-negative staphylococcus (one strain), *S. cohnii* (one strain), *S. epidermidis* (five strains), *S. haemolyticus* (three strains), *S. hominis* (two strains), *S. intermedius* (two strains), *S. lugdunensis* (two strains), *S. schleiferi* (one strain), *S. sciuri* (one strain), *S. simulans* (one strain), *S. warnerii* (two strains), and *S. xylosis* (two strains).
[d] Includes *Enterococcus faecalis* (five strains) and *E. faecium* (five strains).
[e] HL, high level.

TABLE 3. Activity of DC-159a against 423 strains of gram-negative bacilli by reference (CLSI) methods

Organism (no. of strains tested)/ antimicrobial agent	MIC (μg/ml)			% Susceptible/ % resistant[a]
	50%	90%	Range	
E. coli				
Wild type (20)				
DC-159a	0.03	0.12	0.015–8	–[b]/–
Gatifloxacin	≤0.03	0.12	≤0.03–>4	90.0/5.0
Gemifloxacin	0.008	0.06	0.004–>2	90.0/10.0
Levofloxacin	0.03	0.25	0.015–8	90.0/5.0
Moxifloxacin	≤0.03	0.25	≤0.03–>4	–/–
Ciprofloxacin	≤0.03	0.12	≤0.03–>4	90.0/10.0
Ceftriaxone	≤0.25	≤0.25	≤0.25–16	95.0/0.0
Imipenem	≤0.5	≤0.5	≤0.5	100.0/0.0
Amikacin	2	2	0.5–4	100.0/0.0
ESBL phenotype (20)[c]				
DC-159a	0.06	>8	0.015–>8	–/–
Gatifloxacin	≤0.03	>4	≤0.03–>4	70.0/20.0
Gemifloxacin	≤0.03	>1	≤0.03–>1	65.0/35.0
Levofloxacin	0.06	>8	0.015–>8	65.0/25.0
Moxifloxacin	0.06	>4	≤0.03–>4	–/–
Ciprofloxacin	≤0.25	>2	≤0.25–>2	65.0/35.0
Ceftriaxone	16	>32	1–>32	40.0/20.0
Imipenem	0.25	0.5	≤0.12–0.5	100.0/0.0
Amikacin	2	16	0.5–16	100.0/0.0
Klebsiella spp.				
Wild type (20)[d]				
DC-159a	0.12	1	0.03–8	–/–
Gatifloxacin	0.06	1	≤0.03–>4	90.0/5.0
Gemifloxacin	0.03	0.5	0.015–>2	85.0/10.0
Levofloxacin	0.06	1	0.03–8	90.0/5.0
Moxifloxacin	0.12	1	0.06–>4	–/–
Ciprofloxacin	≤0.03	0.5	≤0.03–>4	90.0/10.0
Ceftriaxone	≤0.25	32	≤0.25–>32	85.0/10.0
Imipenem	≤0.5	≤0.5	≤0.5	100.0/0.0
Amikacin	1	8	0.5–32	95.0/0.0
ESBL phenotype (20)[e]				
DC-159a	0.5	>8	0.06–>8	–/–
Gatifloxacin	0.5	>4	≤0.03–>4	65.0/20.0
Gemifloxacin	0.25	>1	0.015–>1	55.0/40.0
Levofloxacin	1	>8	0.03–>8	65.0/30.0
Moxifloxacin	0.5	>4	0.06–>4	–/–
Ciprofloxacin	1	>2	≤0.015–>2	55.0/40.0
Ceftriaxone	32	>32	4–>32	15.0/45.0
Imipenem	≤0.5	≤0.5	≤0.5–1	100.0/0.0
Amikacin	16	>32	1–>32	65.0/25.0
KPC producers (10)[f]				
DC-159a	>8	>8	0.06–>8	–/–
Gatifloxacin	>4	>4	≤0.03–>4	20.0/80.0
Gemifloxacin	>2	>2	0.015–>2	10.0/90.0
Levofloxacin	>8	>8	0.03–>8	20.0/80.0
Moxifloxacin	>4	>4	0.06–>4	–/–
Ciprofloxacin	>4	>4	≤0.03–>4	10.0/90.0
Ceftriaxone	>32	>32	16–>32	0.0/80.0
Imipenem	>8	>8	4–>8	10.0/60.0
Amikacin	32	>32	4–>32	30.0/30.0
P. mirabilis (20)[g]				
DC-159a	0.25	>8	0.12–>8	–/–
Gatifloxacin	0.5	>4	0.06–>4	75.0/20.0
Gemifloxacin	0.25	>2	0.03–>2	55.0/45.0
Levofloxacin	0.12	>8	0.03–>8	85.0/15.0
Moxifloxacin	1	>4	0.12–>4	–/–
Ciprofloxacin	0.12	>2	≤0.03–>2	65.0/15.0

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TABLE 3—*Continued*

Organism (no. of strains tested)/ antimicrobial agent	MIC (μg/ml)			% Susceptible/ % resistant[a]
	50%	90%	Range	
Ceftriaxone	≤0.25	32	≤0.25–>32	80.0/10.0
Imipenem	1	2	≤0.5–4	100.0/0.0
Amikacin	4	4	2–>32	95.0/5.0
Citrobacter spp.				
Wild type (20)[h]				
DC-159a	0.06	0.5	0.03–8	−/−
Gatifloxacin	≤0.03	0.5	≤0.03–4	90.0/0.0
Gemifloxacin	0.015	0.25	0.004–>2	90.0/10.0
Levofloxacin	0.03	0.5	0.015–8	90.0/5.0
Moxifloxacin	0.06	1	≤0.03–>4	−/−
Ciprofloxacin	≤0.03	0.5	≤0.03–>4	90.0/10.0
Ceftriaxone	≤0.25	4	≤0.25–8	100.0/0.0
Imipenem	≤0.5	1	≤0.5–1	100.0/0.0
Amikacin	1	2	0.5–4	100.0/0.0
Ceftazidime resistant (10)[i]				
DC-159a	0.12	1	0.06–2	−/−
Gatifloxacin	0.5	4	≤0.03–>4	80.0/10.0
Gemifloxacin	0.03	1	0.008–2	70.0/20.0
Levofloxacin	0.06	1	0.03–4	90.0/0.0
Moxifloxacin	1	>4	0.06–>4	−/−
Ciprofloxacin	0.12	4	≤0.03–>4	80.0/20.0
Ceftriaxone	32	>32	16–>32	0.0/20.0
Imipenem	≤0.5	1	≤0.5–4	100.0/0.0
Amikacin	2	4	1–>32	90.0/10.0
Enterobacter spp.				
Wild type (20)[j]				
DC-159a	0.06	0.5	0.03–>8	−/−
Gatifloxacin	≤0.03	0.12	≤0.03–>4	95.0/5.0
Gemifloxacin	0.015	0.06	0.008–>2	95.0/5.0
Levofloxacin	0.03	0.12	0.015–>8	95.0/5.0
Moxifloxacin	0.06	0.25	≤0.03–>4	−/−
Ciprofloxacin	≤0.03	0.06	≤0.03–>4	95.0/5.0
Ceftriaxone	≤0.25	0.5	≤0.25–>32	95.0/5.0
Imipenem	≤0.5	≤0.5	≤0.5–1	100.0/0.0
Amikacin	1	2	1–16	100.0/0.0
Ceftazidime resistant (13)[k]				
DC-159a	0.5	8	0.06–8	−/−
Gatifloxacin	0.5	>4	≤0.03–>4	69.2/30.8
Gemifloxacin	0.12	>2	0.008–>2	76.9/23.1
Levofloxacin	0.25	>8	0.03–>8	76.9/23.1
Moxifloxacin	0.5	>4	0.06–>4	−/−
Ciprofloxacin	0.25	>4	≤0.03–>4	61.5/30.8
Ceftriaxone	>32	>32	4–>32	23.1/61.5
Imipenem	≤0.5	2	≤0.5–4	100.0/0.0
Amikacin	2	8	0.5–>32	92.3/7.7
Indole-positive *Proteae* (40)[l]				
DC-159a	0.25	8	0.06–>8	−/−
Gatifloxacin	0.12	>4	≤0.03–>4	75.0/20.0
Gemifloxacin	0.06	>2	0.004–>2	70.0/30.0
Levofloxacin	0.06	8	0.03–>8	75.0/20.0
Moxifloxacin	0.25	>4	0.06–>4	−/−
Ciprofloxacin	≤0.03	>4	≤0.03–>4	72.5/27.5
Ceftriaxone	≤0.25	4	≤0.25–32	92.5/0.0
Imipenem	1	2	≤0.5–4	100.0/0.0
Amikacin	2	4	0.5–16	100.0/0.0

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TABLE 3—*Continued*

Organism (no. of strains tested)/ antimicrobial agent	MIC (μg/ml)			% Susceptible/ % resistant[a]
	50%	90%	Range	
S. marcescens				
Wild type (20)				
DC-159a	0.5	2	0.12–8	−/−
Gatifloxacin	0.25	2	0.12–>4	90.0/5.0
Gemifloxacin	0.12	1	0.06–>2	75.0/20.0
Levofloxacin	0.12	1	0.06–4	90.0/0.0
Moxifloxacin	0.5	4	0.25–>4	−/−
Ciprofloxacin	0.06	1	0.06–>4	90.0/10.0
Ceftriaxone	≤0.25	2	≤0.25–>32	90.0/5.0
Imipenem	≤0.5	1	≤0.5–2	100.0/0.0
Amikacin	4	32	1–>32	85.0/5.0
Ceftazidime resistant (10)				
DC-159a	2	8	0.25–8	−/−
Gatifloxacin	2	>4	0.12–>4	50.0/30.0
Gemifloxacin	1	>2	0.03–>2	30.0/60.0
Levofloxacin	1	8	0.12–8	60.0/30.0
Moxifloxacin	2	>4	0.12–>4	−/−
Ciprofloxacin	1	>4	0.06–>4	50.0/50.0
Ceftriaxone	32	>32	16–>32	0.0/50.0
Imipenem	≤0.5	1	≤0.5–1	100.0/0.0
Amikacin	32	>32	2–>32	30.0/30.0
Salmonella spp.				
Wild type (20)[m]				
DC-159a	0.06	0.06	0.015–0.25	−/−
Gatifloxacin	≤0.03	0.06	≤0.03–0.25	100.0/0.0
Gemifloxacin	0.015	0.015	0.004–0.12	100.0/0.0
Levofloxacin	0.03	0.06	0.015–0.25	100.0/0.0
Moxifloxacin	0.06	0.12	≤0.03–0.5	−/−
Ciprofloxacin	≤0.03	≤0.03	≤0.03–0.25	100.0/0.0
Ceftriaxone	≤0.25	≤0.25	≤0.25–16	95.0/0.0
Imipenem	≤0.5	≤0.5	≤0.5	100.0/0.0
Amikacin	1	2	1–4	100.0/0.0
Resistant phenotype (10)[n]				
DC-159a	0.25	0.5	0.06–1	−/−
Gatifloxacin	0.12	0.5	≤0.03–1	100.0/0.0
Gemifloxacin	0.06	0.25	≤0.008–0.25	100.0/0.0
Levofloxacin	0.25	0.5	0.03–1	100.0/0.0
Moxifloxacin	0.25	1	0.03–2	−/−
Ciprofloxacin	0.12	0.25	≤0.03–1	100.0/0.0
Ceftriaxone	≤0.25	32	≤0.25–32	70.0/0.0
Imipenem	≤0.5	≤0.5	≤0.5	100.0/0.0
Amikacin	2	2	1–2	100.0/0.0
Shigella spp. (40)[o]				
DC-159a	0.03	0.06	0.015–0.25	−/−
Gatifloxacin	≤0.03	≤0.03	≤0.03–0.25	100.0/0.0
Gemifloxacin	0.008	0.015	0.004–0.12	100.0/0.0
Levofloxacin	0.03	0.06	0.015–0.25	100.0/0.0
Moxifloxacin	≤0.03	0.06	≤0.03–0.25	−/−
Ciprofloxacin	≤0.03	≤0.03	≤0.03–0.25	100.0/0.0
Ceftriaxone	≤0.25	≤0.25	≤0.25	100.0/0.0
Imipenem	≤0.5	≤0.5	≤0.5	100.0/0.0
Amikacin	4	4	1–8	100.0/0.0
P. aeruginosa				
Wild type (30)				
DC-159a	0.5	2	0.25–4	−/−
Gatifloxacin	0.5	1	0.12–4	96.7/0.0
Levofloxacin	0.25	1	0.12–2	100.0/0.0
Moxifloxacin	1	2	0.25–4	−/−

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TABLE 3—*Continued*

Organism (no. of strains tested)/ antimicrobial agent	MIC (μg/ml)			% Susceptible/ % resistant[a]
	50%	90%	Range	
Ciprofloxacin	0.12	0.25	≤0.03–1	100.0/0.0
Ceftazidime	2	16	≤1–>16	86.7/6.7
Cefepime	2	16	1–>16	86.7/6.7
Imipenem	1	>8	≤0.5–>8	83.3/13.3
Amikacin	2	4	0.5–>32	93.3/3.3
Ciprofloxacin resistant (10)				
DC-159a	>8	>8	4–>8	−/−
Gatifloxacin	>4	>4	4–>4	0.0/90.0
Levofloxacin	>8	>8	8–>8	0.0/100.0
Ciprofloxacin	>4	>4	4–>4	0.0/100.0
Ceftazidime	4	>16	2–>16	50.0/40.0
Cefepime	16	>16	8–>16	40.0/20.0
Imipenem	2	>8	≤0.5–>8	50.0/40.0
Amikacin	8	>32	2–>32	60.0/40.0
Acinetobacter spp.				
Wild type (30)[p]				
DC-159a	0.06	0.12	0.015–1	−/−
Gatifloxacin	≤0.03	0.12	≤0.03–0.5	100.0/0.0
Levofloxacin	0.06	0.25	0.03–0.5	100.0/0.0
Ciprofloxacin	0.12	0.25	0.06–0.5	100.0/0.0
Ceftazidime	4	16	≤1–>16	76.7/10.0
Cefepime	2	16	0.25–>16	86.7/6.7
Imipenem	≤0.5	≤0.5	≤0.5–4	100.0/0.0
Amikacin	2	8	≤0.25–>32	93.3/6.7
Ciprofloxacin and levofloxacin resistant (10)[q]				
DC-159a	8	>8	4–>8	−/−
Gatifloxacin	>4	>4	4–>4	0.0/90.0
Levofloxacin	>8	>8	8–>8	0.0/100.0
Ceftazidime	>16	>16	8–>16	10.0/80.0
Cefepime	16	>16	16–>16	0.0/50.0
Imipenem	1	>8	≤0.5–>8	80.0/20.0
Amikacin	16	>32	4–>32	50.0/40.0
S. maltophilia (30)				
DC-159a	0.12	0.5	0.03–4	−/−
Gatifloxacin	0.5	2	0.12–>4	90.0/6.7
Levofloxacin	0.5	2	0.06–>8	93.3/6.7
Ciprofloxacin	1	4	0.25–>4	53.3/16.7
Ceftazidime	8	>16	≤1–>16	50.0/43.3
Cefepime	>16	>16	4–>16	20.0/56.7
Amikacin	>32	>32	4–>32	6.7/86.7

[a] Criteria published by the CLSI (4).
[b] −, no breakpoint criteria have been established for this category or agent.
[c] Includes strains harboring TEM-1, TEM-3, TEM-4, TEM-5, TEM-6, TEM-7, TEM-8, SHV-5, CTX-M2, CMY-2 (8 strains), or FOX-5 (3 strains).
[d] Includes *Klebsiella oxytoca* (5 strains) and *K. pneumoniae* (15 strains).
[e] Includes *Klebsiella pneumoniae* (20 strains) with mobile AmpC enzymes (9 strains), CTX-M2 (4 strains), SHV-5 (5 strains), SHV-7, and ESBL NOS.
[f] Includes *Klebsiella pneumoniae* (10 strains) harboring KPC NOS (4 strains), KPC-2 (5 strains), or KPC-3 (11 strains).
[g] CTX-M phenotypes (two strains).
[h] Includes *Citrobacter braakii* (1 strain), *C. farmeri* (1 strain), *C. freundii* (11 strains), and *C. koseri* (7 strains).
[i] Includes *Citrobacter freundii* (nine strains), and *Citrobacter* species (one strain).
[j] Includes *Enterobacter aerogenes* (4 strains) and *E. cloacae* (16 strains).
[k] Includes *Enterobacter aerogenes* (1 strain), *E. cloacae* (10 strains), *E. gergoviae* (1 strain), and *Enterobacter* species (1 strain).
[l] Includes *Morganella morganii* (10 strains), *Proteus vulgaris* (11 strains), *Providencia rettgeri* (9 strains), and *Providencia stuartii* (10 strains).
[m] Includes *Salmonella* group B (three strains), *Salmonella* group C (two strains), *Salmonella* group D (two strains), *Salmonella* species (eight strains), *Salmonella enterica* serovar Typhi (two strains), and *S. enterica* serovar Typhimurium (three strains).
[n] Resistance to ampicillin, cephalosporins, tetracyclines, or trimethoprim-sulfamethoxazole. Includes *S. enterica* serovar Enteritidis (one strain), *Salmonella* group B (one strain), *Salmonella* group C (one strain), *S. enterica* serovar Hadar (one strain), *S. enterica* serovar Heidelberg (one strain), *S. enterica* serovar Typhi (one strain), *S. enterica* serovar Typhimurium (three strains), and *S. enterica* serovar Virchow (one strain).
[o] Includes *Shigella boydii* (4 strains), *S. dysenteriae* (3 strains), *S. flexneri* (14 strains), *S. sonnei* (16 strains), and *Shigella* species (3 strains).
[p] Includes *Acinetobacter anitratus* (1 strain), *A. baumannii* (14 strains), *A. calcoaceticus* (3 strains), *A. junii* (2 strains), *A. lwoffii* (8 strains), and *Acinetobacter species* (2 strains).
[q] Includes *Acinetobacter baumannii* (nine strains) and *A. lwoffii* (one strain).

TABLE 4. Activity of DC-159a against 60 *N. gonorrhoeae* strains by the reference agar dilution method

Organism group (no. of strains tested) and antimicrobial agent	MIC (μg/ml)			% Susceptible/ % resistant[a]
	50%	90%	Range	
Ciprofloxacin susceptible (20)				
DC-159a	0.015	0.015	0.008–0.015	−[b]/−
Levofloxacin	0.015	0.03	0.008–0.03	100.0/0.0
Ciprofloxacin	≤0.008	0.015	≤0.008–0.015	100.0/0.0
Ceftriaxone	≤0.008	0.015	≤0.008–0.06	100.0/−
Penicillin	0.25	1	0.015–>4	35.0/10.0
Tetracycline	0.25	1	0.12–2	55.0/10.0
Ciprofloxacin intermediate (25)				
DC-159a	0.12	0.12	0.03–0.12	−/−
Levofloxacin	0.25	0.5	0.12–0.5	0.0/0.0
Ciprofloxacin	0.25	0.5	0.12–0.5	0.0/0.0
Ceftriaxone	0.03	0.06	≤0.008–0.12	100.0/−
Penicillin	2	>4	0.5–>4	0.0/88.0
Tetracycline	1	2	0.5–2	0.0/48.0
Ciprofloxacin resistant (15)				
DC-159a	1	1	0.25–1	−/−
Levofloxacin	4	8	2–8	0.0/100.0
Ciprofloxacin	>4	>4	2–>4	0.0/100.0
Ceftriaxone	0.015	0.06	≤0.008–0.06	100.0/−
Penicillin	2	>4	1–>4	0.0/80.0
Tetracycline	2	>4	0.25–>4	6.7/73.3

[a] Criteria published by the CLSI (4). The criteria for ofloxacin were applied to levofloxacin for comparison purposes only.
[b] −, no breakpoint criteria have been established for this category or drug.

fluoroquinolones for the treatment of CA-MRSA or other MRSA infections. Furthermore, the use of fluoroquinolones as the treatment of choice for uncomplicated gonorrhea has been negated by the high rates of resistance among gonococci in the United States and worldwide (16).

In this study of the activity of DC-159a, DC-159a was shown to possess a combination of antimicrobial qualities that may overcome some of the deficiencies of current fluoroquinolones, confirming the findings of earlier studies (2, 9). Against levofloxacin- or penicillin-resistant *S. pneumoniae* strains, DC-159a had activity (MIC_{90} range, 0.12 to 1 μg/ml) intermediate between that of gemifloxacin (MIC_{90} range, 0.03 to 0.25 μg/ml) and that of moxifloxacin (MIC_{90} range, 0.25 to 4 μg/ml), and DC-159a was also very potent against other species associated with community-acquired respiratory tract infections (MIC range, 0.015 to 0.12; MICs for all strains, ≤0.25 μg/ml). DC-159a was approximately 16-fold more active than ciprofloxacin against staphylococci and showed the potential for use for the treatment of endemic CA-MRSA strains and some mutants with QRDR mutations. Gonococci resistant or intermediately susceptible to ciprofloxacin had DC-159a MICs that ranged from 0.03 to 1 μg/ml. Finally, the overall potency of DC-159a against members of the family *Enterobacteriaceae* (median MIC_{50}, 0.12 μg/ml), *P. aeruginosa* (MIC_{50} for wild-type strains, 0.5 μg/ml), and *Acinetobacter* spp. (MIC_{50} for wild-type strains, 0.06 μg/ml) was most similar to that of levofloxacin, although DC-159a was markedly more active against the *S. maltophilia* strains (MIC_{50}, 0.12 μg/ml). We eagerly await the publication of pharmacokinetic/pharmacodynamic results for DC-159a so that predictive microbiological/clinical breakpoint concentrations can be assigned (4, 15).

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