Venerdì 22 novembre

Sessione 6 | Le nuove armi per la terapia delle infezioni batteriche MDR

Moderatori: *I. Gentile, M. Tumbarello*

DELAFLOXACINA

IVAN GENTILE

Università degli Studi di Napoli 'Federico II'

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DELAFLOXACIN: HISTORICAL PERSPECTIVE

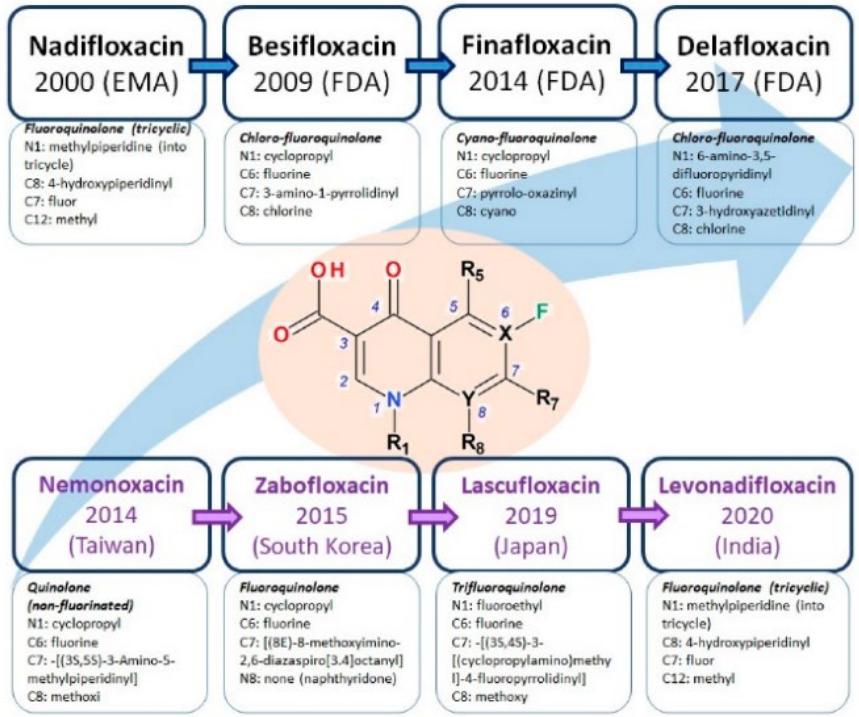


Figure 3. New FQNs chronology in therapy (since 2000) and essential structural characteristics.

pharmaceutics *Pharmaceutics* **2021**, *13*, 1289. https://doi.org/10.3390/pharmaceutics13081289 MDPI

Review

Structural Characterization of the Millennial Antibacterial (Fluoro)Quinolones—Shaping the Fifth Generation

Aura Rusu [1], Ioana-Andreea Lungu [2], Octavia-Laura Moldovan [2], Corneliu Tanase [3,*] and Gabriel Hancu [1]

Generation	Compounds	Antibacterial Spectrum	Therapeutic Indications/Pharmacokinetics, Administration	Ref.
2nd	Nadifloxacin (topical use)	Gram-positive (including methicillin-resistant Staphylococcus aureus (MRSA) and coagulase-negative staphylococci), aerobic Gram-negative, and anaerobic pathogens.	Treatment of acne vulgaris and other skin infections. Topical use, 1% cream.	[26,87–89]
3rd	Levofloxacin	Enterobacteriaceae; Atypical pathogens; Penicillin-resistant Streptococcus pneumoniae.	Acute and chronic bronchitis, exacerbated forms, acquired pneumonia (nosocomial); Oral and parenteral administration, high serum and tissue concentrations, long half-life (6–8 h). Ophthalmic use (0.5% ophthalmic solution).	[29,86,90,91]
3rd	Gatifloxacin (ophthalmic use)	Broad-spectrum including Staphylococcus aureus, Streptococcus species, and Gram-negative pathogens	Bacterial conjunctivitis, ophthalmic use (0.3% or 0.5% ophthalmic solution).	[43]
4th	Moxifloxacin	Enterobacteriaceae; Atypical pathogens; Pseudomonas aeruginosa; Streptococci; MRSA; Anaerobic pathogens. Others: Chlamydophila pneumoniae, Mycoplasma pneumonia	Sexually transmitted diseases, prostatitis, skin and tissue infections, acute and chronic bronchitis, exacerbated forms, acquired pneumonia (nosocomial), intra-abdominal infections, gynecological infections; bacterial conjunctivitis. Oral, parenteral, and ophthalmic administration (0.5%), high serum and tissue concentrations, long half-life (8–16 h). Bacterial skin and skin structure infections.	[34,92,93]
4th	Delafloxacin	Gram-positive (including methicillin-resistant Staphylococcus aureus) and Gram-negative pathogens	Oral and intravenous administration, oral bioavailability 58.8%, plasma protein binding 84%, mean half-life 4.2–8.5 h (oral), and 3.7 h (intravenous)	[39,41,94]
4th	Besifloxacin (topical, ophtalmic administration)	Streptococcus pneumonia, Staphylococcus epidermidis, Staphylococcus aureus, Haemophilus influenza, Moraxella catarrhalis, Corynebacterium spp	Bacterial conjunctivitis. Ophthalmic suspension (0.6%).	[46,95–97]
4th	Finafloxacin (topical, otic administration)	Broad-spectrum activity (very active against Pseudomonas aeruginosa, and Staphylococcus aureus)	Acute otitis externa. Otic suspension (0.3%)	[98–100]

DELAFLOXACIN: CHEMICAL FEATURES

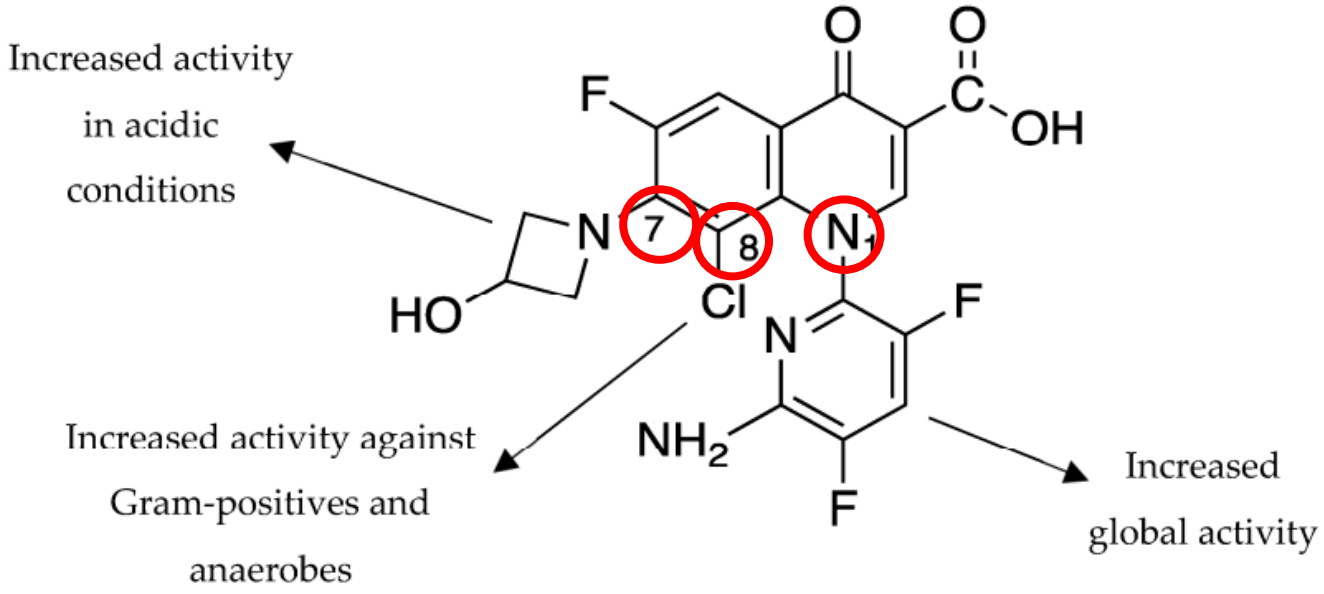
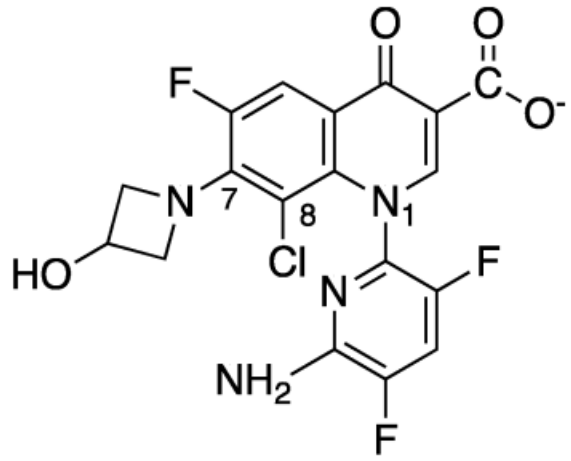


Figure 1. Structure-activity relationships (SAR) of delafloxacin.

pH=5,5

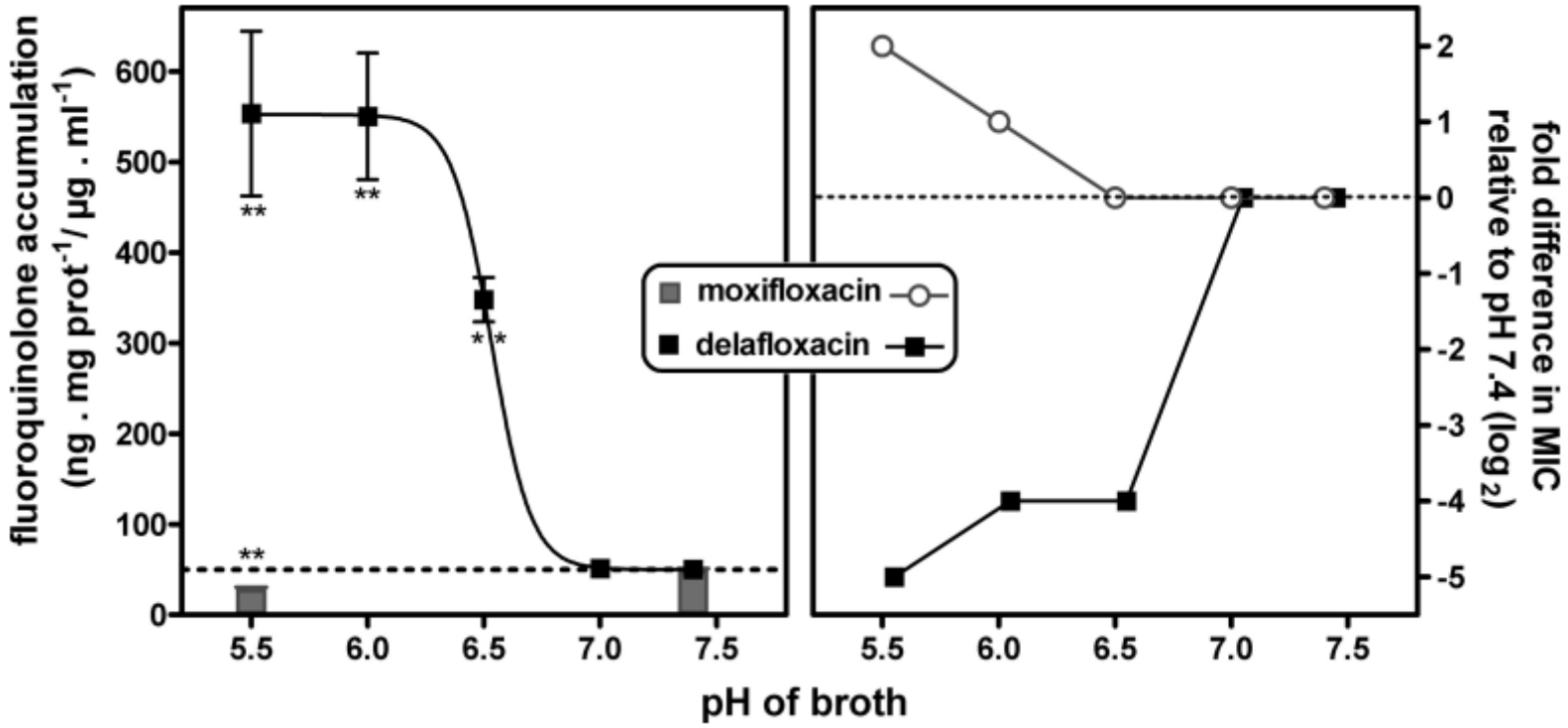
pH=7,4



Turban, Antibiotics 2023

Figure 2. Representation of the non-ionized (**left**) and ionized anionic (**right**) forms of delafloxacin.

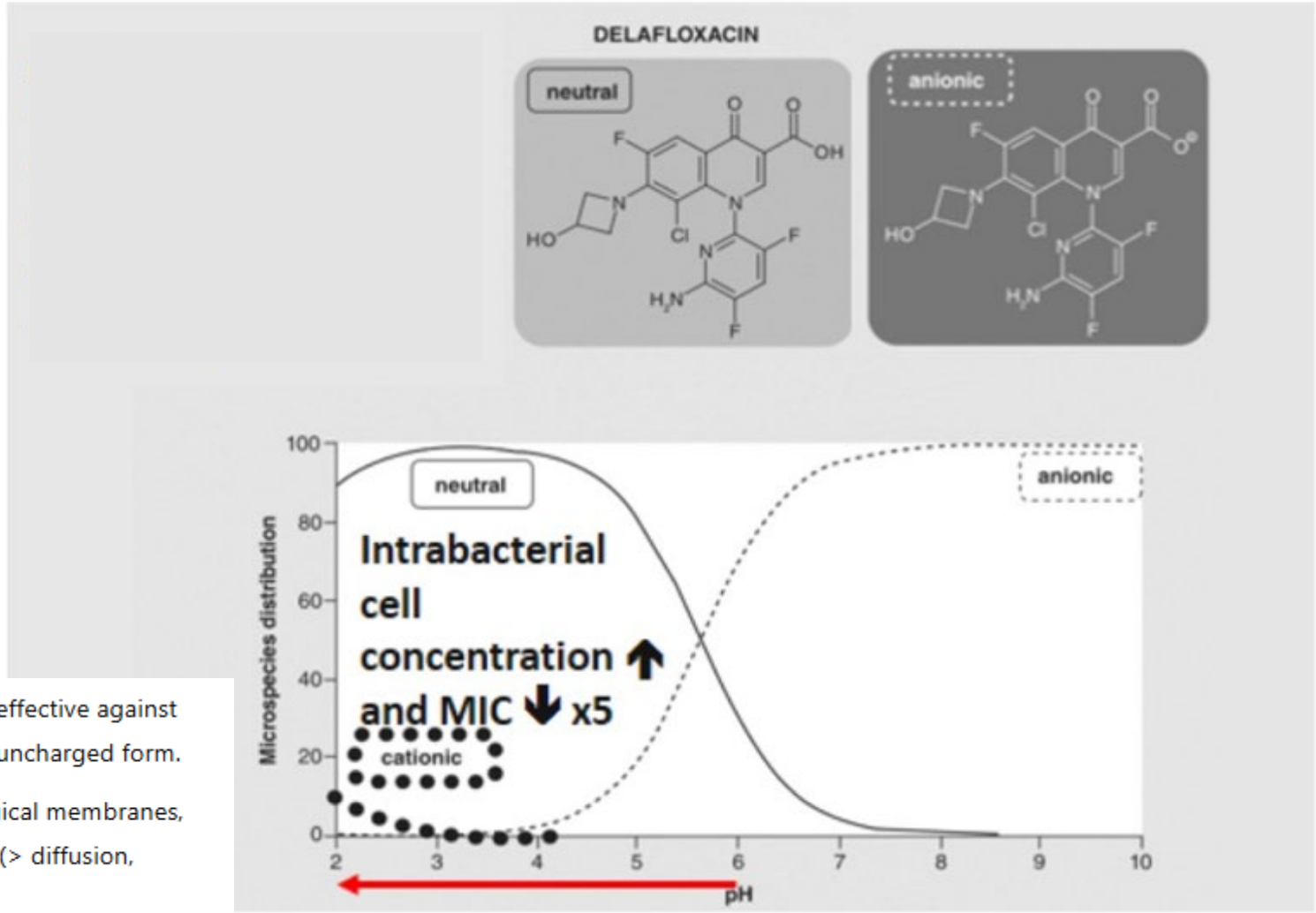
THE IMPORTANCE OF PH



Lemaire, et al. *Antimicrob Agents Chemother.* 2011;55:649-658;

THE IMPORTANCE OF PH

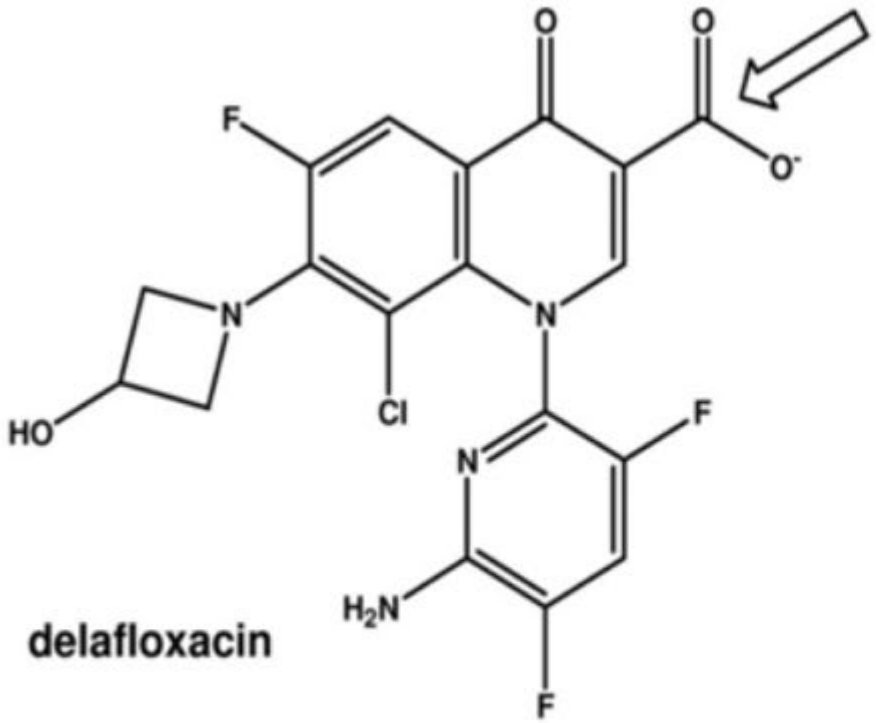
It has **enhanced potency at acid pH relative to other fluoroquinolones** (eg, ciprofloxacin, levofloxacin, moxifloxacin), for which activities decrease (higher MICs) in acidic environments.
This enhanced potency at acid pH likely relates to increased accumulation by S. aureus, whereas lower accumulation was seen with moxifloxacin.
Delafloxacin may therefore fulfill one of the important requisites for enhanced activity in ABSSSI, particularly in infections caused by S. aureus and where high local concentrations are considered

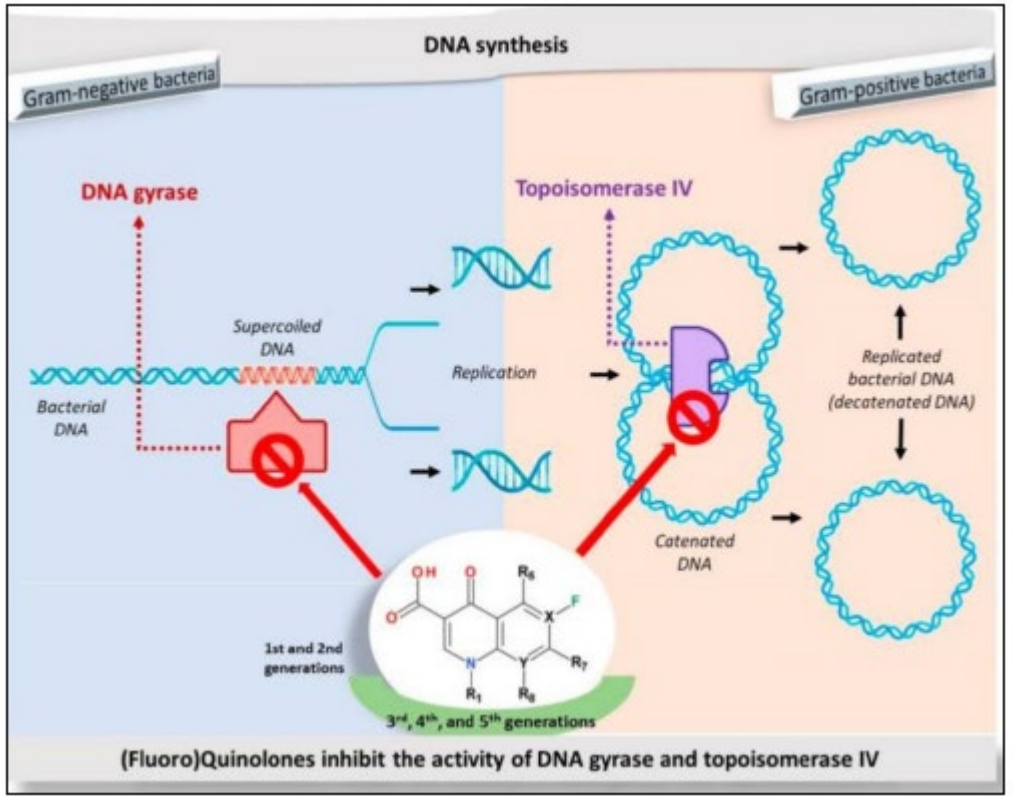


- At physiological pH (~7–7.4), delafloxacin is mainly present as an anion (> effective against Gram-positive bacteria), but at a slightly acidic pH (≤5.5), it is mostly in an uncharged form.
- The non-ionized form of a drug is considered more diffusible across biological membranes, which explains why delafloxacin accumulates more in bacteria at acidic pH (> diffusion, including in the epithelial lining fluid, ELF).

Lemaire, et al. *Antimicrob Agents Chemother.* 2011;55:649-658; Van Bambeke. *Future Microbiology.* 2015;10:1111-1123.

DELAFLOXACIN: DUAL TARGETING





Delafloxacin structural characteristics enable it to target both DNA gyrase and DNA topoisomerase IV from Gram-positive (eg, *S aureus*) and Gram-negative (eg, *E coli*) pathogens with equal affinity and is a poor substrate of efflux pumps (Nor A, B, and C). The dual targeting of gyrase and topoisomerase IV decreases likelihood of resistance, which requires the accumulation of multiple mutations affecting both

Tulkens et al. Clin Infect Dis. 2019

ANTIBIOTIC SPECTRUM

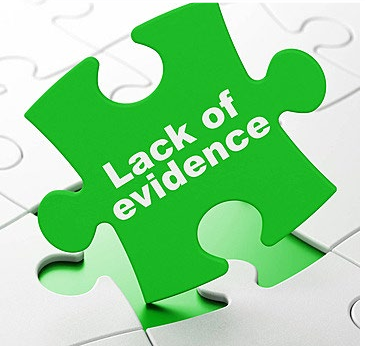
Gram-positive bacteria	Gram-negative bacteria
• *Staphylococcus aureus* (including MRSA) • *Staphylococcus haemolyticus* • *Staphylococcus hominis* • *Staphylococcus lugdunensis* • *Streptococcus agalactiae* • *Streptococcus anginosus group* (including *S. anginosus*, *S. intermedius*, and *S. constellatus*) • *Streptococcus dysgalactiae* • *Streptococcus mitis group* (including *S. cristatus*, *S. gordonii*, *S. oralis*, *S. mitis*, and *S. sanguinis*) • *Streptococcus pyogenes* • *Enterococcus faecalis*	• *Escherichia coli* • *Enterobacter cloacae* • *Klebsiella pneumoniae* • *Pseudomonas aeruginosa*

- **Atypical organisms:** Delafloxacin is effective against atypical bacteria like *Chlamydia pneumoniae*, *Legionella pneumophila*, and *Mycoplasma pneumoniae*.
- **Anaerobes:** Demonstrates good activity against anaerobes such as *Clostridium perfringens*, *Bacteroides fragilis*, *Prevotella* species, *Peptostreptococcus*, *Cutibacterium acnes*, and others, which distinguishes it from some other fluoroquinolones.

Scott. Drugs (2020) 80:1247–1258

EUCAST BREAKPOINTS

	MIC breakpoints (mg/L)		
Pathogens	**S ≤**	**R >**	**Note**
Enterobacterales	0.125	0.125	A disk diffusion test awaits action from the company
S. Aureus (CAP)	0.016	0.016	A disk diffusion test awaits action from the company
S. Aureus (SSTI)	0.25	0.25	A disk diffusion test awaits action from the company
Streptococcus groups A, B, C and G	0.03	0.03	A disk diffusion test awaits action from the company
Viridans group streptococci	0.03	0.03	A disk diffusion test awaits action from the company



Pseudomonas spp.	***Acinetobacter spp.***	***Enterococcus spp.***	***Neisseria gonorrhoeae***
Streptococcus pneumoniae	***Haemophilus influenzae***	***Moraxella catarrhalis***	***Neisseria meningiditis***

IN VITRO ACTIVITY

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

SUSCEPTIBILITY

In Vitro Activity of Delafloxacin against Contemporary Bacterial Pathogens from the United States and Europe, 2014

M. A. Pfaller,[a,b] H. S. Sader,[a] P. R. Rhomberg,[a] R. K. Flamm[a]

JMI Laboratories, North Liberty, Iowa, USA[a]; University of Iowa, Iowa City, Iowa, USA[b]

April 2017 Volume 61 Issue 4 e02609-16

TABLE 1 Cumulative frequency distribution of delafloxacin in MIC results for Europe and the United States[a]

Organism or organism group	Total	No. (%) of isolates for which MIC (μg/ml) was: 0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	>4	MIC_{50} (μg/ml)	MIC_{90} (μg/ml)	%R
Staphylococcus aureus																
US	1,100	666 (60.5)	8 (61.3)	8 (62.0)	38 (65.5)	183 (82.1)	62 (87.7)	63 (93.5)	24 (95.6)	34 (98.7)	0 (98.7)	14 (100.0)	0 (100.0)	≤0.004	0.25	6.6%
EU	250	193 (77.2)	2 (78.0)	1 (78.4)	4 (80.0)	12 (84.8)	13 (90.0)	18 (97.2)	3 (98.4)	3 (99.6)	0 (99.6)	1 (100.0)	0 (100.0)	≤0.004	0.12	2.8%
MSSA																
US	591	515 (87.1)	7 (88.3)	4 (89.0)	10 (90.7)	27 (95.3)	11 (97.1)	8 (98.5)	6 (99.5)	2 (99.8)	0 (99.8)	1 (100.0)	0 (100.0)	≤0.004	0.03	1.5%
EU	186	176 (94.6)	2 (95.7)	1 (96.2)	2 (97.3)	1 (97.8)	2 (98.9)	1 (99.5)	0 (99.5)	1 (100.0)			0 (100.0)	≤0.004	≤0.004	0.5%
MRSA																
US	509	151 (29.7)	1 (29.9)	4 (30.6)	28 (36.1)	156 (66.8)	51 (76.8)	55 (87.6)	18 (91.2)	32 (97.4)	0 (97.4)	13 (100.0)	0 (100.0)	0.06	0.5	12.4%
EU	64	17 (26.6)	0 (26.6)	0 (26.6)	2 (29.7)	11 (46.9)	11 (64.1)	17 (90.6)	3 (95.3)	2 (98.4)	0 (98.4)	1 (100.0)	0 (100.0)	0.12	0.25	9.3%
Coagulase-negative staphylococci																
US	100	51 (51.0)	7 (58.0)	3 (61.0)	1 (62.0)	6 (68.0)	14 (82.0)	4 (86.0)	4 (90.0)	9 (99.0)	1 (100.0)		0 (100.0)	≤0.004	0.5	
EU	100	43 (43.0)	8 (51.0)	1 (52.0)	6 (58.0)	10 (68.0)	10 (78.0)	14 (92.0)	5 (97.0)	3 (100.0)			0 (100.0)	0.008	0.25	

IN VITRO ACTIVITY

Clinical Infectious Diseases

BRIEF REPORT

Emergence of Delafloxacin-Resistant *Staphylococcus aureus* in Brooklyn, New York

Alejandro Iregui, Zeb Khan, Saquib Malik, David Landman, and John Quale

Division of Infectious Diseases, Department of Internal Medicine, State University of New York–Downstate Medical Center, Brooklyn

RESULTS

During the surveillance study performed in 2017, a total of 757 unique patient isolates of *S. aureus* were gathered. Overall, all were susceptible to vancomycin and linezolid, and 99.7% were susceptible to daptomycin. In addition, 63% (n = 478) were susceptible to oxacillin, 85% to clindamycin, 91% to tetracycline, 98% to trimethoprim-sulfamethoxazole, 58% to ciprofloxacin, and 91% (n = 689) to delafloxacin. Among the cases of methicillin-susceptible *S. aureus*, 78% (n = 373) were susceptible to ciprofloxacin (MIC_{50} and MIC_{90} values of 0.25 and >4 mg/L, respectively) and 98% (n = 470) to delafloxacin (MIC_{50} and MIC_{90} values of <0.06 and 0.12 mg/L, respectively). In comparison, among the MRSA isolates, 24% (n = 66) were susceptible to ciprofloxacin (MIC_{50} and MIC_{90} values of >4 and >4 mg/L, respectively) and 78% (n = 219) to delafloxacin (MIC_{50} and MIC_{90} values of 0.12 and 4 mg/L, respectively).

IN VITRO ACTIVITY

JOURNAL ARTICLE

In vitro activity of delafloxacin against clinical levofloxacin-resistant *Helicobacter pylori* isolates

Get access >

Victor Luzarraga, Julie Cremniter, Chloé Plouzeau, Anthony Michaud, Lauranne Broutin, Christophe Burucoa, Maxime Pichon ✉

Journal of Antimicrobial Chemotherapy, Volume 79, Issue 10, October 2024, Pages 2633–2639, https://doi.org/10.1093/jac/dkae269

Results

The estimated ECOFF of delafloxacin was ≤0.125 mg/L. No *H. pylori* isolate showed a levofloxacin-sensitive phenotype with a delafloxacin MIC of >0.125 mg/L. Among the levofloxacin-resistant *H. pylori* isolates, 53.5% had delafloxacin MICs of ≤0.125 mg/L. The N87I mutation was associated with dual levofloxacin/delafloxacin resistance ($P < 0.001$) in contrast to the N87K and D91N mutations ($P > 0.05$). Mutations D91G and D91Y were not associated with a delafloxacin resistance phenotype ($P > 0.05$).

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RESEARCH ARTICLE

In Vitro Activity of Delafloxacin and Finafloxacin against *Mycoplasma hominis* and *Ureaplasma* Species

Yingying Kong,[a,b] Chao Li,[a] Gangfeng Li,[a] Ting Yang,[a,b] Mohamed S. Draz,[c,d] Xinyou Xie,[a,b] Jun Zhang,[a,b] Zhi Ruan[a,b]

[a]Department of Clinical Laboratory, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China
[b]Key Laboratory of Precision Medicine in Diagnosis and Monitoring Research of Zhejiang Province, Hangzhou, China
[c]Department of Medicine, Case Western Reserve University School of Medicine, Cleveland, Ohio, USA
[d]Department of Biomedical Engineering, Cleveland Clinic, Cleveland, Ohio, USA

ABSTRACT The *in vitro* activity of two new fluoroquinolones, delafloxacin and finafloxacin, were evaluated against *M. hominis* and *Ureaplasma* spp. The MICs of delafloxacin, finafloxacin, and two classical fluoroquinolones (moxifloxacin and levofloxacin) were tested against 29 *M. hominis* and 67 *Ureaplasma* spp. isolates using the broth microdilution method. The molecular mechanisms underlying fluoroquinolone resistance were also investigated. Delafloxacin exhibited low MICs against *M. hominis* and *Ureaplasma* spp., including the levofloxacin-resistant isolates. For *M. hominis*, delafloxacin showed low MIC_{90} value of 1 μg/mL (MIC range, <0.031 -1 μg/mL) compared to 8 μg/mL for finafloxacin, 16 μg/mL for moxifloxacin, and 32 μg/mL for levofloxacin. For *U. parvum* and *U. urealyticum*, delafloxacin had low MIC_{90} values (*U. parvum*, 2 μg/mL; *U. urealyticum*, 4 μg/mL) compared to 16 -32 μg/mL for finafloxacin, 16 μg/mL for moxifloxacin, and 32 - >32 μg/mL for levofloxacin. The two mutations GyrA S153L and ParC S91I were commonly identified in fluoroquinolone-resistant *M. hominis*, and ParC S83L was the most frequent mutation identified in fluoroquinolone-resistant *Ureaplasma* spp. Delafloxacin displayed lower MICs against fluoroquinolone-resistant isolates of both *M. hominis* and *Ureaplasma* spp. that have mutations in the quinolone resistance determining regions (QRDRs) than the two classical fluoroquinolones. Delafloxacin is a promising fluoroquinolone with low MICs against fluoroquinolone-resistant *M. hominis* and *Ureaplasma* spp. Our study confirms the potential clinical use of delafloxacin in treating antimicrobial-resistant *M. hominis* and *Ureaplasma* spp. infections.

TABLE 1 MIC distributions of delafloxacin, finafloxacin, moxifloxacin, and levofloxacin against *M. hominis* and *Ureaplasma* species[a]

Organism and antimicrobials	No. of isolates with the indicated MIC (μg/mL)														MIC_{50} (μg/mL)	MIC_{90} (μg/mL)	Resistance %
	<0.031	0.031	0.063	<0.125	0.125	0.25	0.5	1	2	4	8	16	32	>32			
M. hominis (n = 29)																	
Delafloxacin	6		1			3	12	7							0.5	1	NA
Finafloxacin	5						1	1		4	16	2			8	8	NA
Moxifloxacin				5				1	3	1	3	15	1		16	16	24 (82.76%)
Levofloxacin							2		1	2	3	3	17	1	32	32	27 (93.10%)
U. parvum (n = 52)																	
Delafloxacin	5		1		10	2	4	21	6	3					1	2	NA
Finafloxacin							1	7	7	6	20	10	1		8	16	NA
Moxifloxacin							3	6	6	19	8	9	1		4	16	37 (71.15%)
Levofloxacin								5	6	7	11	12	9	2	8	32	41 (78.85%)
U. urealyticum (n = 15)																	
Delafloxacin					1	1		1	7	5					2	4	NA
Finafloxacin									2		1	10	2		16	32	NA
Moxifloxacin								2		1	4	7	1		16	16	13 (86.67%)
Levofloxacin									2			4	6	3	32	>32	13 (86.67%)

[a]For *M. hominis*, the breakpoints were ≥ 2 μg/mL and ≥ 0.5 μg/mL for levofloxacin and moxifloxacin, respectively. For *Ureaplasma* spp., the breakpoints were ≥ 4 μg/mL for levofloxacin and moxifloxacin. NA, not applicable (no CLSI breakpoint).

Pk-Pd: ADME

Infect Dis Ther (2018) 7:197–217
https://doi.org/10.1007/s40121-018-0198-x

REVIEW

Delafloxacin: Place in Therapy and Review of Microbiologic, Clinical and Pharmacologic Properties

Sarah C. J. Jorgensen · Nicholas J. Mercuro · Susan L. Davis · Michael J. Rybak

ADME Criteria	Summary for Delafloxacin
Absorption	Oral bioavailability is approximately 59%. Food intake reduces peak serum concentration (Cmax) by 20% but does not affect total exposure (AUC).
Distribution	Volume of distribution (Vd) ranges from 35 to 48 L. Approximately 84% is protein-bound, primarily to albumin. It has high pulmonary distribution with a 13:1 ratio in epithelial lining fluid versus plasma.
Metabolism	Metabolized mainly through glucuronidation with minimal oxidative metabolism (~1%).
Elimination	Predominantly eliminated through the kidneys (50-65%), with the rest excreted in feces. Half-life (T1/2) ranges from 3.7 hours (IV) to 4.2-8.5 hours (oral). Adjustments are required in severe renal impairment.
Main pK/pD Features	Delafloxacin shows concentration-dependent activity. The key PK/PD parameter is fAUC24/MIC, which is closely linked to its efficacy. It remains potent under acidic conditions, enhancing activity against intracellular pathogens.

Table 3 Pharmacokinetic parameters of delafloxacin and comparator fluoroquinolones. Adapted from references [6, 33–35]

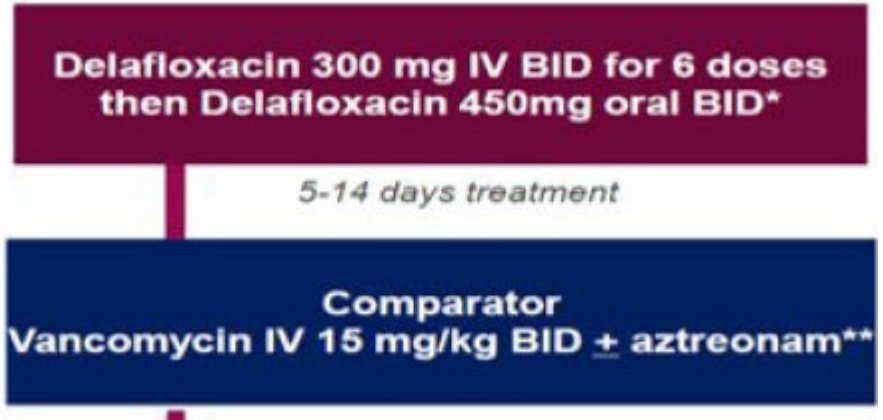
Parameter	Delafloxacin IV (300 mg, every 12 h)	Delafloxacin PO (450 mg, every 12 h)	Levofloxacin PO (750 mg, every 24 h)	Ciprofloxacin PO (500 mg, every 12 h)	Moxifloxacin PO (400 mg, every 12 h)
V_d (l)	35–48		100	84–189[a]	119–189[a]
C_{max} (mg/l)	9.29	7.45	8.6	3.0	4.5
fC_{max} (mg/l)	1.49	1.19	5.3–6.5	1.8–2.4	2.25–3.15
$AUC_{0-\tau}$ (mg h/l)	30.8	23.4	90.7	13.7	48
$fAUC_{0-\tau}$ (mg h/l)	4.93	3.74	56.2–68.9	8.2–11.0	24–33.6
AUC_{24} (mg h/l)	61.6	46.8	90.7	27.4	48
$fAUC_{24}$ (mg h/l)	9.86	7.48	56.2–68.9	16.4–22.0	24–33.6
Protein binding	84%		24–38%	20–40%	30–50%
$T_{1/2}$ (h)	3.7[b]	4.2–8.5	8.8	4–6	10–14
Elimination (urine:feces)	64.5%:28.4%[b]	50.2%:47.7%	87%:4%	57%:20–35%	20%:25%
Oral bioavailability	N/A	58.8%	99%	70%	92%
Metabolism	Glucuronidation[c]		Limited?	Oxidation?	Sulfation, glucuronidation

DELAFLOXACIN: TWO ABSSSI RCTs

A Comparison of the Efficacy and Safety of Intravenous Followed by Oral Delafloxacin With Vancomycin Plus Aztreonam for the Treatment of Acute Bacterial Skin and Skin Structure Infections: A Phase 3, Multinational, Double-Blind, Randomized Study

William O'Riordan, Alison McManus, Juri Teras, Ivan Poromanski, Maria Cruz-Saldariagga, Megan Quintas, Laura Lawrence, ShuJui Liang, Sue Cammarata ✉, PROCEED Study Group Author Notes

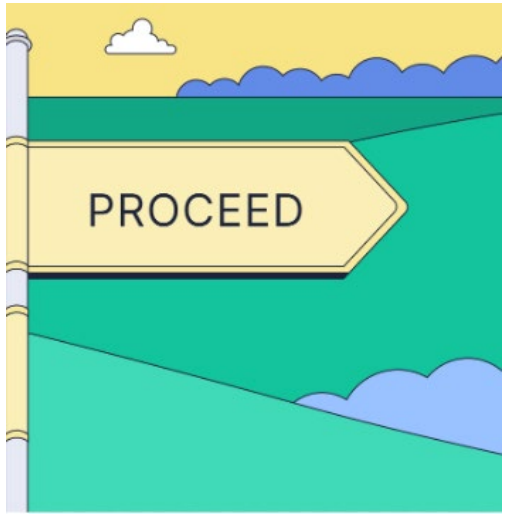
Clinical Infectious Diseases, Volume 67, Issue 5, 1 September 2018, Pages 657–666, https://doi.org/10.1093/cid/ciy165
Published: 06 March 2018 **Article history** ▾

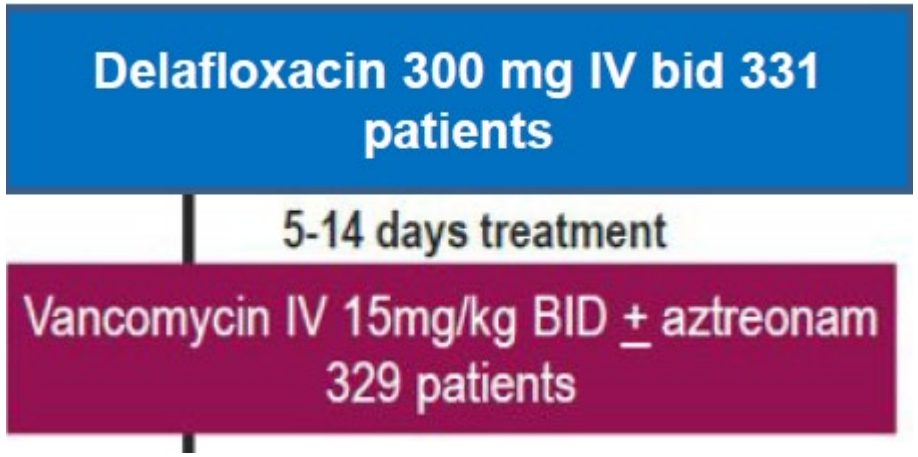


Efficacy and safety of delafloxacin compared with vancomycin plus aztreonam for acute bacterial skin and skin structure infections: a Phase 3, double-blind, randomized study

J Pullman, J Gardovskis, B Farley, E Sun, M Quintas, L Lawrence, R Ling, S Cammarata ✉, PROCEED Study Group Author Notes

Journal of Antimicrobial Chemotherapy, Volume 72, Issue 12, December 2017, Pages 3471–3480, https://doi.org/10.1093/jac/dkx329
Published: 05 October 2017 **Article history** ▾





DELAFLOXACIN: POOLED ANALYSIS - ABSSSIs

Clinical Infectious Diseases

SUPPLEMENT ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Clin Infect Dis. 2019 Apr 8;68(Suppl 3):S223-S232. doi: 10.1093/cid/ciz006.

Analysis of Pooled Phase III Efficacy Data for Delafloxacin in Acute Bacterial Skin and Skin Structure Infections

Philip A. Giordano,[1] Jason M. Pogue,[2] and Sue Cammarata[3]

		RX-3341-302 (Study 302)	RX-3341-303 (Study 303)
Phase; year completed		Phase III; 2014	Phase III; 2016
Population		Adults with ABSSSI (required lesion size ≥75 cm^2) and at least 2 systemic signs of infection	Adults with ABSSSI (required lesion size ≥75 cm^2) and at least 2 systemic signs of infection
Comparator (N)		Vancomycin and aztreonam (329)	Vancomycin and aztreonam (427)
Delafloxacin dose/route (N)		300 mg IV Q12 h (331)	300 mg IV Q12 h for 6 doses with switch to 450 mg oral Q12 h (423)
Duration of therapy		5–14 d	5–14 d
Time points	OR	48–72 h	48–72 h
	EOT	Assessment collected	Assessment collected
	FU	Day 14	Day 14
	LFU	Day 21–28	Day 21–28
	TOC	NA	NA
Stratification factors and enrollment limits at randomization		Infection type enrollment limited to: prior antibiotics – 25%, abscesses – 25%, wounds – 35%	Infection type and BMI (< or ≥ 30 kg/m^2). Enrollment limited to: prior antibiotics – 25%, abscesses – 25%, wounds – 30%, BMI ≥ 30 kg/m^2 – ≤ 50%
Primary endpoint		Objective response at 48–72 h (at least 20% reduction in lesion size, with no non-study medicines, major procedures, or death)	Objective response at 48–72 h (at least 20% reduction in lesion size, with no non-study medicines, major procedures, or death)
Key clinical efficacy secondary endpoint		Investigator assessment of response of signs and symptoms of infection at the FU and LFU visits. Cure was the primary analysis.	Investigator assessment of response of signs and symptoms of infection at the FU and LFU visits. Cure was the primary analysis.

DELAFLOXACIN: POOLED ANALYSIS - ABSSSIs

Table 1. Delafloxacin In Vitro Activity Against *Staphylococcus aureus* in Isolates From Phase III Trials Stratified by Levofloxacin Susceptibility

Organism	N	MIC Range (μg/ml)	MIC_{90}
S. aureus	685	0.002–4	0.25
Levofloxacin–non-susceptible *S. aureus*	232	0.004–4	0.25
MRSA	294	0.002–4	0.25
Levofloxacin–non-susceptible MRSA	195	0.004–4	0.25
MSSA	395	0.002–0.5	0.03
Levofloxacin–non-susceptible MSSA	39	0.004–0.5	0.25

Pooled data for the delafloxacin and comparator treatment arms for the microbiological intent to treat population. N = number of available MIC values from isolates cultured at baseline from primary infection site or blood. If the same pathogen is identified from both the blood and the culture of the acute bacterial skin and skin structure infections, it is counted only once in the summary. Patients with both MRSA and MSSA at baseline are included once in the overall Staphylococcus aureus category.

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.

Clinical Infectious Diseases

SUPPLEMENT ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Clin Infect Dis. 2019 Apr 8;68(Suppl 3):S223-S232. doi: 10.1093/cid/ciz006.

Analysis of Pooled Phase III Efficacy Data for Delafloxacin in Acute Bacterial Skin and Skin Structure Infections

Philip A. Giordano,[1] Jason M. Pogue,[2] and Sue Cammarata[3]

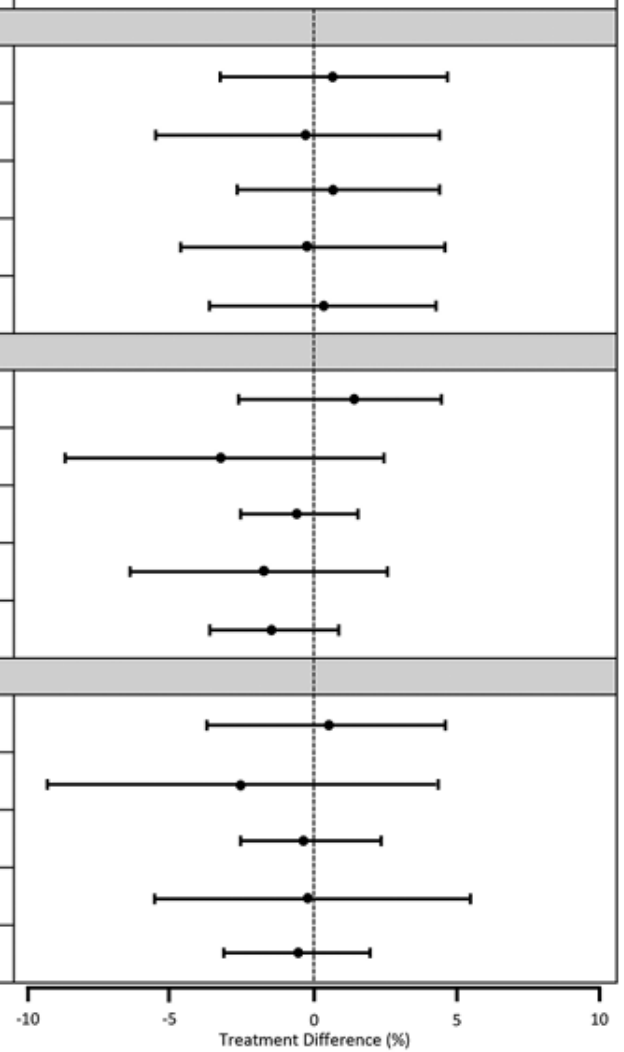
Table 3. Demographics and Baseline Characteristics: Pooled Phase III Analysis Set

	Delafloxacin (n = 754)	Vancomycin + Aztreonam (n = 756)
Age categories (year), n (%)		
≤65	653 (86.6)	661 (87.4)
>65	101 (13.4)	95 (12.6)
Sex, n (%)		
Male	468 (62.1)	485 (64.2)
Female	286 (37.9)	271 (35.8)
Race, n (%)		
American Indian or Alaska Native	17 (2.3)	9 (1.2)
Asian	12 (1.6)	16 (2.1)
Black or African American	40 (5.3)	37 (4.9)
Native Hawaiian or Other Pacific Islander	3 (0.4)	4 (0.5)
White	645 (85.5)	659 (87.2)
Other	37 (4.9)	31 (4.1)
Ethnicity, n (%)		
Hispanic or Latino	233 (30.9)	202 (26.7)
Not Hispanic or Latino	521 (69.1)	554 (73.3)
Region, n (%)		
Asia	9 (1.2)	14 (1.9)
Europe	225 (30.4)	228 (30.4)
Latin America	46 (6.2)	43 (5.7)
North America	461 (62.2)	466 (62.1)
Weight (kg)		
Mean (SD)	85.4 (21.6)	85.8 (22.1)
Median	82.5	82.9
Min, Max	30.8, 198.5	43.8, 185.0
BMI ranges (kg/m^2), n (%)		
BMI <30	414 (55.9)	445 (59.3)
BMI ≥30	327 (44.1)	306 (40.7)
Diabetes, n (%)	84 (11.3)	83 (11.1)
Baseline renal impairment, n (%)	121 (16.3)	121 (16.1)
Patients with history of hepatitis B or C, n (%)	216 (29.1)	217 (28.9)

Abbreviations: BMI, body mass index; SD, standard deviation.

DELAFLOXACIN: POOLED ANALYSIS - ABSSSIs

Study Population	Delafloxacin (% [n/N])	Vancomycin/ Aztreonam (% [n/N])	Treatment Difference (95% CI)
Intent-to-treat Population Analysis Set (ITT)			
Objective Response at 48-72 hours*	81.3 (613/754)	80.7 (610/756)	0.8 (-3.2, 4.7)
Investigator Assessed Cure at FU**	55.2 (416/754)	55.7 (421/756)	-0.5 (-5.5, 4.5)
Investigator Assessed Success at FU**	84.7 (639/754)	84.1 (636/756)	0.8 (-2.8, 4.5)
Investigator Assessed Cure at LFU	69.0 (520/754)	69.0 (522/756)	-0.1 (-4.8, 4.6)
Investigator Assessed Success at LFU	82.0 (618/754)	81.7 (618/756)	0.3 (-3.6, 4.2)
Clinically Evaluable Analysis Set (CE)			
Objective Response at 48-72 hours	86.5 (596/689)	85.4 (584/684)	1.2 (-2.6, 4.9)
Investigator Assessed Cure at FU	61.0 (362/593)	63.9 (366/573)	-3.1 (-8.6, 2.5)
Investigator Assessed Success at FU	96.6 (573/593)	97.2 (557/573	-0.6 (-2.7, 1.6)
Investigator Assessed Cure at LFU	80.2 (467/582)	82.5 (468/567)	-1.9 (-6.4, 2.6)
Investigator Assessed Success at LFU	96.0 (559/582)	97.2 (551/567)	-1.4 (-3.6, 0.8)
Microbiologically Evaluable Analysis Set (ME)			
Objective Response at 48-72 hours	87.8 (425/484)	87.4 (415/475)	0.5 (-3.8, 4.7)
Investigator Assessed Cure at FU	59.8 (245/410)	61.9 (245/396)	-2.5 (-9.2, 4.2)
Investigator Assessed Success at FU	97.8 (401/410)	98.0 (388/396)	-0.2 (-2.5, 2.2)
Investigator Assessed Cure at LFU	81.0 (332/410)	81.1 (321/396)	0.1 (-5.3, 5.5)
Investigator Assessed Success at LFU	97.1 (398/410)	97.5 (386/396)	-0.5 (-3.1, 2.0)



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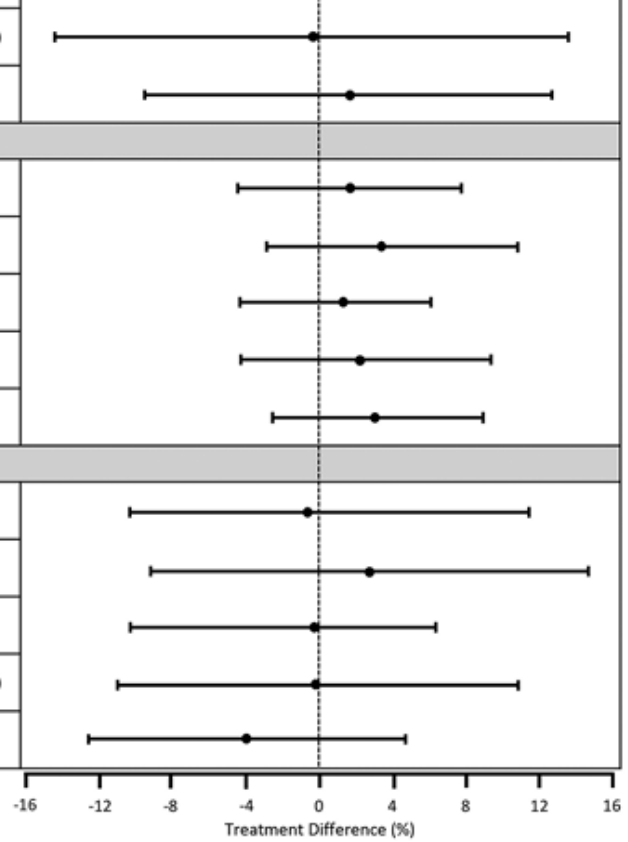
DELAFLOXACIN: POOLED ANALYSIS - ABSSSIs

Study Population	Delafloxacin (% [n/N])	Vancomycin/ Aztreonam (% [n/N])	Treatment Difference (95% CI)
Diabetes			
Objective Response at 48-72 hours*	75.9 (63/83)	77.8 (63/81)	-1.4 (-14.4, 11.6)
Investigator Assessed Cure at FU**	53.0 (44/83)	51.9 (42/81)	1.3(-13.7, 16.3)
Investigator Assessed Success at FU**	85.5 (71/83)	84.0 (68/81)	2.2 (-9.2, 13.6)
Investigator Assessed Cure at LFU	67.5 (56/83)	67.9 (55/81)	-0.3 (-14.6, 13.9)
Investigator Assessed Success at LFU	85.5 (71/83)	85.2 (69/81)	1.7(-9.5, 12.9)
Patient Body Mass Index ≥ 30 kg/M²			
Objective Response at 48-72 hours	80.4 (266/331)	79.2 (244/308)	1.7 (-4.5, 7.9)
Investigator Assessed Cure at FU	58.0 (192/331)	54.9 (169/308)	3.5 (-4.1, 11.1)
Investigator Assessed Success at FU	86.1 (285/331)	85.1 (262/308)	1.3 (-4.2, 6.8)
Investigator Assessed Cure at LFU	69.5 (230/331)	66.9 (206/308)	2.6 (-4.6, 9.8)
Investigator Assessed Success at LFU	84.0 (278/331)	81.2 (250/308)	3.1 (-2.9, 9.0)
Presence of Renal Impairment (CrCl < 90 mL/min)			
Objective Response at 48-72 hours	76.2 (93/122)	75.4 (92/122)	0.7 (-10.2, 11.5)
Investigator Assessed Cure at FU	64.8 (79/122)	61.5 (75/122)	2.8 (-9.1, 14.7)
Investigator Assessed Success at FU	87.7 (107/122)	88.5 (108/122)	-0.2 (-10.3, 6.3)
Investigator Assessed Cure at LFU	74.6 (91/122)	74.6 (91/122)	-0.1 (-11.0, 10.9)
Investigator Assessed Success at LFU	85.2 (104/122)	88.5 (108/122)	-4.0 (-12.7, 4.8)



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DELAFLOXACIN: POOLED ANALYSIS - ABSSSIs

Table 5. Per-pathogen Microbiological Response Rate at Follow-up: Microbiologically Evaluable Population

n/N1[b]	Per-pathogen Microbiological Response (Documented or Presumed Eradication)[a] ME at FU Analysis Set	
	Delafloxacin (n = 410)	Vancomycin + Aztreonam (n = 396)
S. aureus	244/248 (98.4%)	233/239 (97.5%)
MRSA	106/108 (98.1%)	97/99 (98.0%)
MSSA	140/142 (98.6%)	136/140 (97.1%)
S. anginosus[c]	47/47 (100.0%)	34/35 (97.1%)
S. pyogenes	18/19 (94.7%)	15/15 (100.0%)
K. pneumoniae	17/17 (100.0%)	17/17 (100.0%)
P. aeruginosa	11/11 (100.0%)	10/10 (100.0%)
E. coli	11/11 (100.0%)	16/17 (94.1%)
S. haemolyticus	12/12 (100%)	7/7 (100%)
E. cloacae	11/12 (91.7%)	9/10 (90.0%)
S. agalactiae	11/11 (100%)	11/12 (91.7%)
E. faecalis	9/10 (90.0%)	12/13 (92.3%)
S. lugdunensis	10/10 (100%)	7/7 (100%)

If the same pathogen is identified from both the blood and the culture of the ABSSSI, it is counted only once in the summary. Patients with both MRSA and MSSA at baseline are included once in the overall *Staphylococcus aureus* category. The overall count of patients with *Staphylococcus aureus* includes patients whose isolates were not tested for susceptibility and, therefore, do not contribute to either the MRSA or MSSA counts.

Abbreviations: ABSSSI, acute bacterial skin and skin structure infections; FU, follow-up; ME, microbiologically evaluable; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.

[a]Investigator-assessed response in ME at FU analysis set was the same as per-pathogen microbiological response.

[b]N1 = number of patients who have the given target pathogen at baseline from the ABSSSI or blood culture; n = success, which is defined as documented or presumed eradication.

[c]The *Staphylococcus anginosus* group includes *S. anginosus*, *S. intermedius*, and *S. constellatus*.

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Philip A. Giordano,[1] Jason M. Pogue,[2] and Sue Cammarata[3]

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In Vitro Activity of Delafloxacin and Microbiological Response against Fluoroquinolone-Susceptible and Nonsusceptible *Staphylococcus aureus* Isolates from Two Phase 3 Studies of Acute Bacterial Skin and Skin Structure Infections

S. McCurdy,[a] L. Lawrence,[a] M. Quintas,[a] L. Woosley,[b] R. Flamm,[b] C. Tseng,[c] S. Cammarata[a]

Melinta Therapeutics, New Haven, Connecticut, USA[a]; JMI Laboratories, North Liberty, Iowa, USA[b]; H20 Clinical, Hunt Valley, Maryland, USA[c]

TABLE 3 Microbiological response at follow-up for subjects with *S. aureus* isolates from primary infection site or blood cultures by levofloxacin susceptibility and nonsusceptibility by delafloxacin MIC[a]

Organism	Baseline delafloxacin MIC (μg/ml)	*N*1	No. (%) of subjects with: Eradicated/presumed eradicated infection	Persisted/presumed persisted infection
Levofloxacin-susceptible *S. aureus*			165	3
	0.002	15	15 (100.0)	0
	0.004	44	44 (100.0)	0
	0.008	101	98 (97.0)	3 (3.0)
	0.015	7	7 (100.0)	0
	0.06	1	1 (100.0)	0
Levofloxacin-nonsusceptible *S. aureus*			80	1
	0.03	3	3 (100.0)	0
	0.12	38	38 (100.0)	0
	0.25	36	35 (97.2)	1 (2.8)
	0.5	3	3 (100.0)	0
	4	1	1 (100.0)	0
Levofloxacin-susceptible MRSA			36	1
	0.004	3	3 (100.0)	0
	0.008	30	29 (96.7)	1 (3.3)
	0.015	3	3 (100.0)	0
	0.06	1	1 (100.0)	0
Levofloxacin-nonsusceptible MRSA			70	1
	0.12	32	32 (100.0)	0
	0.25	36	35 (97.2)	1 (2.8)
	0.5	2	2 (100.0)	0
	4	1	1 (100.0)	0
Levofloxacin-susceptible MSSA			130	2
	0.002	15	15 (100.0)	0
	0.004	41	41 (100.0)	0
	0.008	72	70 (97.2)	2 (2.8)
	0.015	4	4 (100.0)	0
Levofloxacin-nonsusceptible MSSA			10	0
	0.03	3	3 (100.0)	0
	0.12	6	6 (100.0)	0
	0.5	1	1 (100.0)	0

[a]Results are from pooled data for the MEFUI population. Percentages were calculated as 100 × (*n*/*N*1), where *n* is the number of subjects and *N*1 is the number of subjects for each MIC value. If multiple MIC values were reported per subject per pathogen, the highest value was used. MRSA, methicillin-resistant *Staphylococcus*

DELAFLOXACIN: SAFETY IN ABSSSI

Clinical Trial › Clin Infect Dis. 2019 Apr 8;68(Suppl 3):S233-S240. doi: 10.1093/cid/ciy1080.

Analysis of Pooled Phase 3 Safety Data for Delafloxacin in Acute Bacterial Skin and Skin Structure Infections

Matteo Bassetti [1], David Hooper [2], Glenn Tillotson [3]

	AESI (All Cause)		AESI (Related)	
Special Interest Preferred Term	Delafloxacin (N = 741) n (%)	VAN/AZ (N = 751) n (%)	Delafloxacin (N = 741) n (%)	VAN/AZ (N = 751) n (%)
Subjects with at least one TEAE of special interest	52 (7.0)	69 (9.2)	25 (3.4)	43 (5.7)
Hepatic related events	23 (3.1)	30 (4.0)	16 (2.2)	20 (2.7)
Increased ALT	14 (1.9)	14 (1.9)	10 (1.3)	10 (1.3)
Increased AST	10 (1.3)	14 (1.9)	6 (0.8)	10 (1.3)
Increased transaminases	3 (0.4)	5 (0.7)	3 (0.4)	2 (0.3)
Increased hepatic enzyme	2 (0.3)	2 (0.3)	1 (0.1)	2 (0.3)
Liver function test abnormal	0	2 (0.3)	0	2 (0.3)
Hypertransaminasaemia	2 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)
Increased gamma-glutamyltransferase	1 (0.1)	1 (0.1)	0	0
Hepatic cirrhosis	0	1 (0.1)	0	0
Potential myopathy	15 (2.0)	34 (4.5)	7 (0.9)	20 (2.7)
Increased blood creatinine Phosphokinase	8 (1.1)	15 (2.0)	3 (0.4)	7 (0.9)
Increased blood creatinine	2 (0.3)	4 (0.5)	1 (0.1)	4 (0.5)
Myalgia	1 (0.1)	2 (0.3)	0	1 (0.1)
Renal impairment	2 (0.3)	1 (0.1)	2 (0.3)	0
Renal failure – acute	1 (0.1)	7 (0.9)	1 (0.1)	3 (0.4)
Musculoskeletal pain	1 (0.1)	2 (0.3)	0	1 (0.1)
Renal failure	0	3 (0.4)	0	3 (0.4)
Decreased creatinine renal clearance	0	1 (0.1)	0	1 (0.1)

DELAFLOXACIN: SAFETY (SUMMARY) IN ABSSSI

Adverse Event	Delafloxacin N = 741 (%)	VAN/AZT N = 751 (%)
Hepatic events	2.2	2.7
Myopathy	0.9	2.7
Hyperglycemia	0.3	0.1
Peripheral neuropathy	0.1	0.3
QT prolongation	0	0.1
Tendon disorder	0	0
Hypoglycemia	0.1	0.3
C difficile diarrhea	0.1	0
Convulsions	0	0.1
Phototoxicity	0	0

Clinical Trial > Clin Infect Dis. 2019 Apr 8;68(Suppl 3):S233-S240. doi: 10.1093/cid/ciy1080.

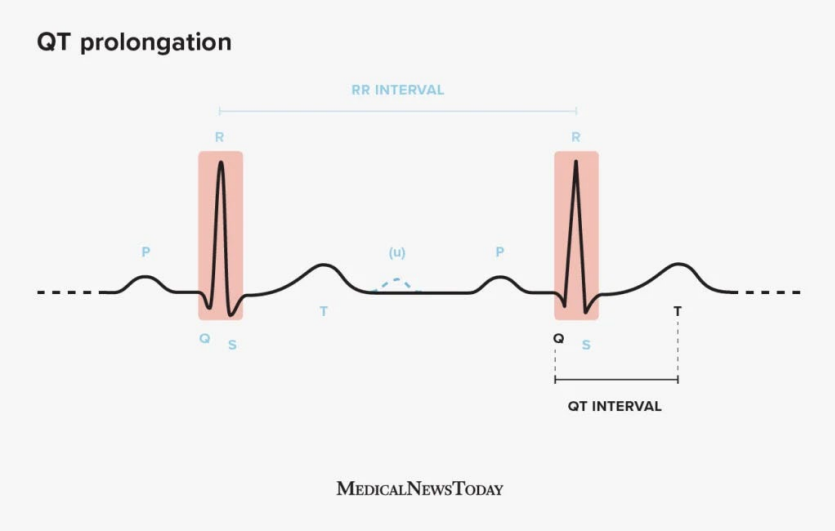
Analysis of Pooled Phase 3 Safety Data for Delafloxacin in Acute Bacterial Skin and Skin Structure Infections

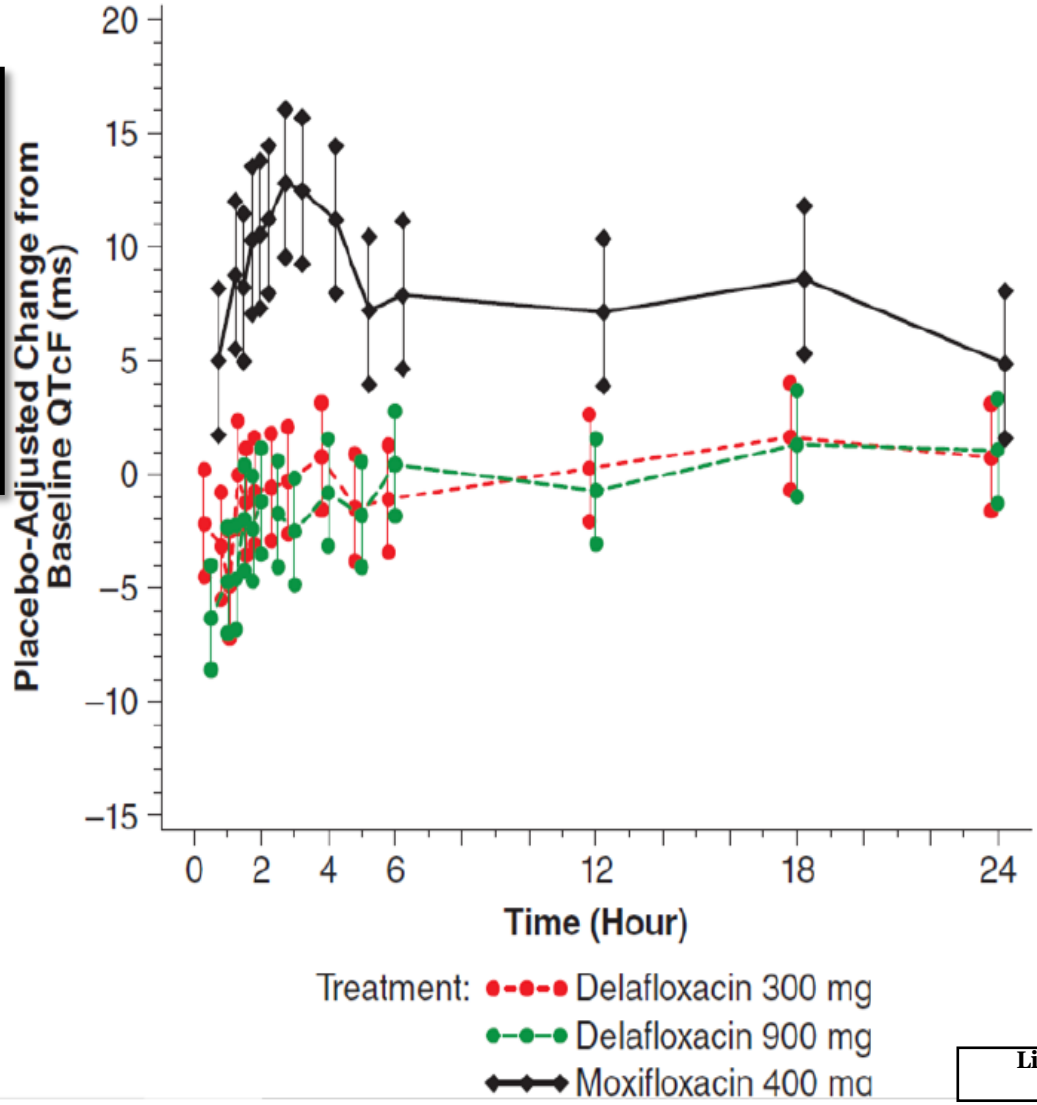
Matteo Bassetti [1], David Hooper [2], Glenn Tillotson [3]

DELAFLOXACIN AND QTc

A randomized crossover study, double-blind, placebo-controlled, with four periods, involving 52 healthy adults evaluated the effect of delafloxacin on the corrected QT interval (QTc).

- Delafloxacin at 300 mg intravenously (i.v.; therapeutic dose), delafloxacin at 900 mg i.v. (supratherapeutic dose), moxifloxacin at 400 mg orally (p.o.; positive control), and placebo were compared.
- At each time point evaluated after the administration of delafloxacin, the upper limit of the 90% confidence interval (CI) for the placebo-corrected change from baseline in the QTcF (QT corrected using Fridericia's formula) was less than 10 ms (maximum of 3.9 ms at 18 hours post-administration), indicating the absence of a clinically significant increase in the QTc interval.





Litwin et al. Antimicrob Agents Chemother. 2015;

DELAFLOXACIN: AIFA INDICATIONS

Condizioni cliniche e criteri di rimborsabilità

Diagnosi: infezioni complicate della cute o dei tessuti molli negli adulti con identificazione batterica al baseline (terapia mirata)

Si ☐ Specificare l'agente eziologico: _____

Specificare se l'uso di altri agenti antibatterici comunemente raccomandati per il trattamento iniziale di tali infezioni è considerato inappropriato, in particolare per ragioni legate a resistenza, scurezza, allergia o metodo di somministrazione

resistenza

mancata tollerabilità e/o controindicazione per ragioni di sicurezza

metodo di somministrazione non compatibile con la gestione ottimale del paziente.

PROGRAMMA TERAPEUTICO

	P.A.	Farmaco	Specialità	Dosaggio
☐	Delafloxacina	Quofenix	300 mg polvere per concentrato per soluzione per infusione	☐ 300 mg di delafloxacina ogni 12 ore somministrati in 60 minuti mediante infusione endovenosa
			OPPURE	
☐	Delafloxacina	Quofenix	450 mg per via orale ogni 12 ore	☐ 450 mg per via orale ogni 12 ore per una durata totale compresa tra 5 e 14 giorni

Per i dosaggi e le modalità di somministrazione si vedano i corrispondenti RCP

Formulazione endovenosa

La dose raccomandata è di 300 mg di delafloxacina ogni 12 ore somministrati in 60 minuti mediante infusione endovenosa. Il passaggio a delafloxacina 450 mg compresse per via orale ogni 12 ore è possibile a discrezione del medico. La durata totale del trattamento è compresa tra 5 e 14 giorni per le ABSSSI.

Formulazione in compresse

Il regime raccomandato di delafloxacina è di 450 mg per via orale ogni 12 ore per una durata totale compresa tra 5 e 14 giorni, a discrezione del medico. Le compresse di delafloxacina possono essere assunte con o senza cibo.

DELAFLOXACIN: DOSAGE ADJUSTMENTS

Route of administration	Recommended dosing regimen[b]	Recommended dosing regimens for renal impairment based on eGFR (mL/min/1.73 m^2)[b]	
		30–89	15–29
iv[a]	300 mg iv every 1 h	no dosage adjustment	200 mg iv every 12 h
po	450 mg po every 12 h	no dosage adjustment	no dosage adjustment
iv[a] to po	300 mg iv every 12 h then switch to 450 mg po every 12 h	no dosage adjustment	200 mg iv every 12 h then switch to 450 mg po every 12 h

[a]Infusion administered over 60 min.
[b]Total duration 5–14 days.

J Antimicrob Chemother 2018; **73**: 1439–1451
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Journal of Antimicrobial Chemotherapy

Clinical review of delafloxacin: a novel anionic fluoroquinolone

Bryan T. Mogle[1], Jeffrey M. Steele[1,2], Stephen J. Thomas[3,4], KarenBeth H. Bohan[5] and Wesley D. Kufel[1,5,6]*

SSTI: RISK FACTORS FOR MRSA

Clinical approach

Current approach to skin and soft tissue infections. Thinking about continuity of care

Rev Esp Quimioter 2023; 36 (Suppl. 1): 37-45

Table 2 Risk factors associated with methicillin-resistant *Staphylococcus aureus* (MRSA) skin and soft tissue infections (SSTI)

Risk Factors Associated with MRSA SSTI (including CA-MRSA)
Ethnicity (African Americans, Hispanic compared with Caucasian); recent travel (in Africa, Latin America or South East Asia)
Socioeconomic lower quintile, poor hygienic conditions, overcrowded housing, incarceration
Previous antibiotic therapy; recent (last three previous months)
History of MRSA: Previous colonization or *S. aureus* infection
Exposure: hospitalization in the previous 12 months, ICU admission, residence of long-term care facility, household contacts
Previous minor or major surgery
Intensive procedures and other instrumental techniques (e.g. image or radiological studies, central vascular catheters, implantable device)
Contact activities, such as daycare young children, contact sports activities, military service, contact with farm animals, insect bite injuries
Presence of underlying comorbidities: diabetes mellitus, peripheral vascular disease, cardiovascular disease, chronic wounds on extremities (often open), chronic renal disease, dialysis dependence, intravenous drug use,
Preexisting skin lesions (burns, eczematous dermatitis, etc.)
Purulent cellulitis
Hereditary (primary or congenital immunodeficiencies) or iatrogenic neutrophil disorder; immunosuppression

Methicillin-resistant *Staphylococcus aureus*: MRSA; skin and soft tissue infections: SSTI; Intensive care unit: UCI; Community-acquired methicillin-resistant *Staphylococcus aureus*: CA-MRSA.

DELAFLOXACIN: PLACE IN THERAPY (SSTI)

Clinical approach

Current approach to skin and soft tissue infections. Thinking about continuity of care

Rev Esp Quimioter 2023; 36 (Suppl. 1): 37-45

Table 3 Potentially relevant factors to be balanced on a case-by-case basis for optimizing the use of antibiotics (either already available or future new-generation) in patients with SSTI at moderate or high risk of MRSA infection

Antibiotic	Switch to oral therapy and early discharge	Useful if poor adherence factors to outpatient therapy (oral treatment at home)	Avoidance (no need) of hospitalization	Significant Drug interactions	Use in kidney dysfunction or renal failure	Coverage of GNB	Low risk of CDI	Use if Allergy to β-lactams
New anti-MRSA cephalosporins: Ceftaroline, Ceftobiprole	-	-	-	-	(+)*	+	-	-
Tedizolid	+	-	+	+	+	-	+	+
Long-acting lipoglycopeptides: Dalbavancin, Oritavancin	-	+	+	-	(+/-)*	-	+	+
Telavancin	-	-	-	-	-	-	+	+
Delafloxacin	+	-	+	(-)*	(+/-)*	+	-	+
Omadacycline	+	-	+	+	+	+	-	+

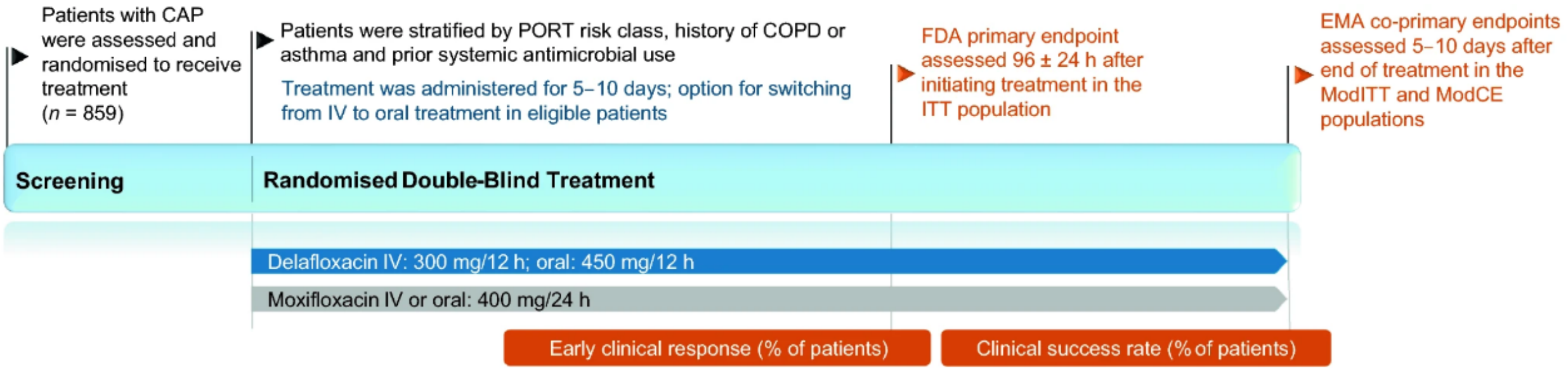
Skin and soft tissue infections (SSTI); methicillin-resistant *Staphylococcus aureus* (MRSA); *Clostridioides difficile* infection (CDI); Gram-negative bacilli (GNB). (+)*: Dosage adjustments adapted to creatinine clearance are necessary. (-)*: Less common and relevant than in older quinolones. (+/-)*: Still with little experience and few data.

TAKE-HOME MESSAGE FOR SSTI

Delafloxacin is indicated in community-acquired mono or polymicrobial (Gram-positive/Gram-negative) SSTI with particular advantages when:		
S aureus is the major pathogen (including MRSA)	Location of the infection is in an acidic environment (not or partially drained abscess, ischemia, biofilm)	Switch to oral therapy is desired for early discharge

Scott. Drugs. 2020

FDA/EMA BUT NON AIFA-APPROVED: CAP



Trial design of the randomised, double-blind, multinational phase III DEFINE-CABP trial in adults with CAP [22]. Efficacy results are reported in the animated figure (available online). *CAP* community-acquired pneumonia, *COPD* chronic obstructive pulmonary disease, *ModCE* modified clinically evaluable, *(Mod)ITT* (modified) intent-to-treat, *IV* intravenous, *PORT* Patient Outcomes Research Team

Delafloxacin: A Review in Community-Acquired Pneumonia

Adis Drug Evaluation | Published: 16 June 2022

Volume 82, pages 913–923, (2022) Cite this article

Open Forum Infectious Diseases

MAJOR ARTICLE

A Phase 3 Study to Compare Delafloxacin With Moxifloxacin for the Treatment of Adults With Community-Acquired Bacterial Pneumonia (DEFINE-CABP) *Open Forum Infectious Diseases*, Volume 7, Issue 1, January 2020, ofz514

Juan P. Horcajada,[1] Robert A. Salata,[2] Rodolfo Álvarez-Sala,[3] Floarea Mimi Nitu,[4] Laura Lawrence,[5] Megan Quintas,[5] Chun-Yen Cheng,[6] and Sue Cammarata[5,©]; for the DEFINE-CABP Study Group*

DEFINE-CAPB: POPULATION

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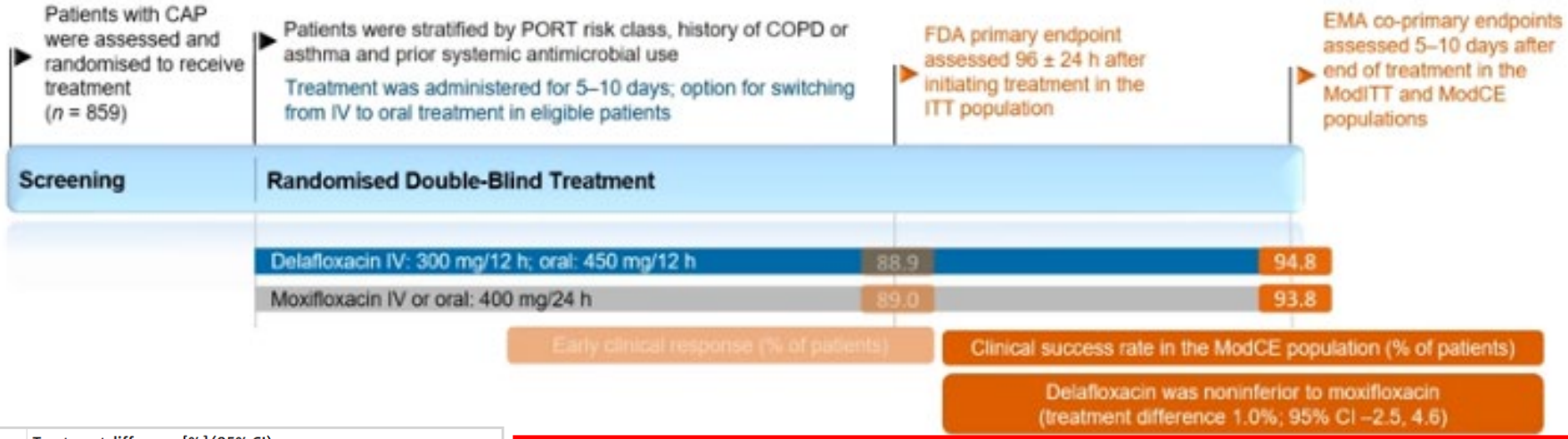
Table 1. Subject Demographics and Baseline Characteristics (ITT Population)

Characteristic	Delafloxacin (n = 431)	Moxifloxacin (n = 428)	Total (n = 859)
Age, y			
Mean (SD)	60.7 (16.06)	59.3 (16.58)	60.0 (16.33)
Median	63.0	61.0	62.0
PORT risk class, No. (%)			
II	54 (12.5)	57 (13.3)	111 (12.9)
III	258 (59.9)	260 (60.7)	518 (60.3)
IV	115 (26.7)	103 (24.1)	218 (25.4)
V	4 (0.9)	8 (1.9)	12 (1.4)
Sex, No. (%)			
Male	251 (58.2)	253 (59.1)	504 (58.7)
Female	180 (41.8)	175 (40.9)	355 (41.3)
Race, No. (%)			
White	398 (92.3)	388 (90.7)	786 (91.5)
Bacteremia, No. (%)			
Yes	5 (1.2)	8 (1.9)	13 (1.5)
BMI category, No. (%)			
<30 kg/m^2	328 (76.1)	316 (73.8)	644 (75.0)
≥30 kg/m^2	103 (23.9)	112 (26.2)	215 (25.0)
Diabetes, No. (%)			
Yes	70 (16.2)	61 (14.3)	131 (15.3)
COPD/asthma, No. (%)			
Yes	61 (14.2)	56 (13.1)	117 (13.6)

DEFINE-CAPB: MAIN RESULTS

Delafloxacin: Clinical Considerations
Anionic fluoroquinolone with a unique chemical structure; targets both DNA gyrase and topoisomerase IV
Noninferior to moxifloxacin in a phase III trial with respect to clinical response rates
Generally well tolerated, with a tolerability profile generally consistent with that established for patients with bacterial skin infections
Not associated with QT prolongation or phototoxicity
Suitable for intravenous or oral administration, with switching from intravenous to oral possible



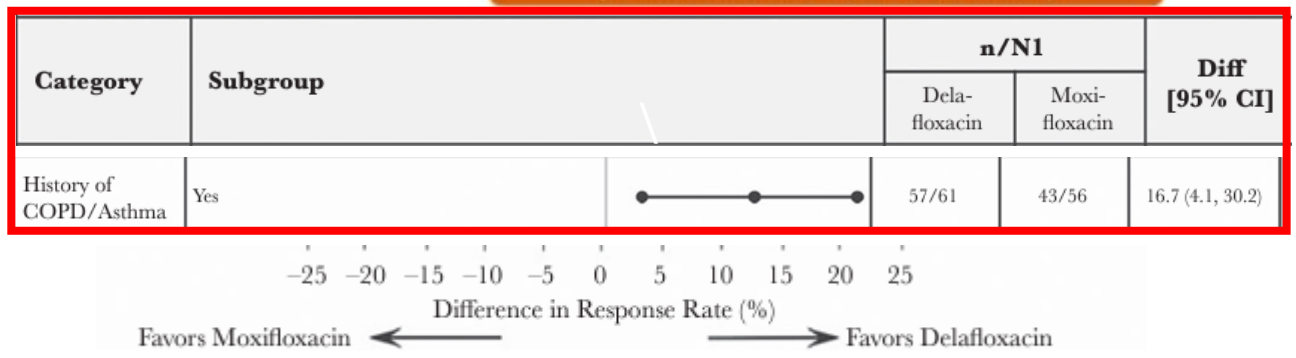
Populations	Delafloxacin	Moxifloxacin	Treatment difference [%] (95% CI)
	n/N (%)	n/N (%)	
ECR rates [22, 23]			
ITT[a]	383/431 (88.9)	381/428 (89.0)	−0.2 (−4.4, 4.1) NI
MITT	236/257 (91.8)	233/263 (88.6)	3.2 (−1.9, 8.5)
CE	381/418 (91.1)	380/414 (91.8)	−0.6 (−4.5, 3.2)
ME	235/253 (92.9)	233/256 (91.0)	1.9 (−3.0, 6.8)
TOC clinical success rates [22, 23]			
ModITT[b]	342/376 (91.0)	330/370 (89.2)	1.1 (−3.2, 5.5) NI
ModCE[b]	331/349 (94.8)	320/341 (93.8)	1.0 (−2.5, 4.6) NI
ITT	390/431 (90.5)	384/428 (89.7)	0.8 (−3.3, 4.8)

ECR was evaluated 96 ± 24 h after initiating treatment (see Sect. 3 for details). TOC endpoints were evaluated by the investigator 5–10 days after end of treatment

CE clinically evaluable, *ECR* early clinical response, *ITT* intent-to-treat, *ME* microbiologically evaluable, *MITT* microbiological ITT, *ModCE* modified CE, *ModITT* modified ITT, *NI* noninferior, *TOC* test of cure

[a]FDA-defined primary endpoint (12.5% noninferiority margin)

[b]EMA-defined co-primary endpoints (10% noninferiority margin)



Responder rates were similar between the delafloxacin and moxifloxacin groups for all subgroups analyzed, except for subjects with COPD or asthma, where delafloxacin was significantly better than moxifloxacin (93.4% vs 76.8%; difference, 16.7%; 95% CI, 4.1% to 30.2%) (Figure 2).

Delafloxacin: A Review in Community-Acquired Pneumonia

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DEFINE-CAPB: MICROBIOLOGICAL SUCCESS

Table 2. Pathogens Identified at Baseline in >1% of Subjects (MITT Population)

Baseline Pathogens	No. (%) of Subjects Total (n = 520)
Streptococcus pneumoniae	226 (43.5)
PSSP	102 (19.6)
PISP	25 (4.8)
PRSP	19 (3.7)
MDRSP	12 (2.3)
MRSP	35 (6.7)
Haemophilus parainfluenzae	76 (14.6)
Mycoplasma pneumoniae	65 (12.5)
Legionella pneumophila	62 (11.9)
Haemophilus influenzae	62 (11.9)
Staphylococcus aureus	57 (11.0)
MRSA	2 (0.4)
MSSA	55 (10.6)
Chlamydia pneumoniae	41 (7.9)
Klebsiella pneumoniae	33 (6.3)
Escherichia coli	27 (5.2)
Pseudomonas aeruginosa	24 (4.6)
Klebsiella oxytoca	10 (1.9)
Moraxella catarrhalis	12 (2.3)

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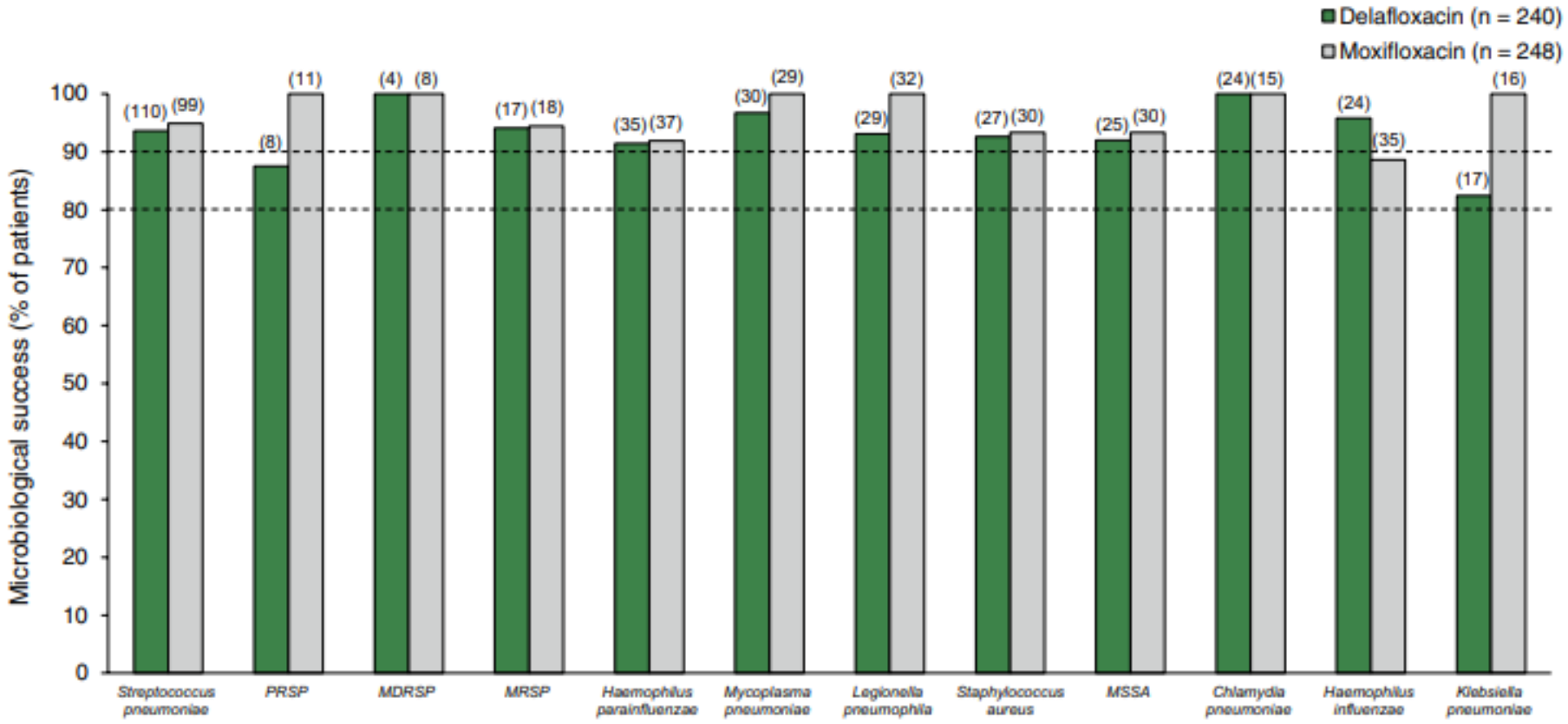

Fig. 2 Microbiological success (documented or presumed eradication) rates at test of cure in microbiologically evaluable patients during the DEFINE-CABP phase III trial [22]. The numbers within brackets indicate the number of evaluable patients. Dashed lines show 80% and 90% microbiological success rates for clarity. *MDRSP* multidrug-resistant *S. pneumoniae*, *MRSP* macrolide-resistant *S. pneumoniae*, *MSSA* methicillin-susceptible *S. aureus*, *PRSP* penicillin-resistant *S. pneumoniae*

DEFINE-CAPB: SAFETY (GENERAL)

Category	Delafloxacin	Moxifloxacin
Total TEAEs	30.5% of subjects	26.2% of subjects
Related TEAEs	15.2% of subjects	12.6% of subjects
Severe TEAEs	4.4% of subjects	3.3% of subjects
SAEs (Severe Adverse Events) Possibly Related to Treatment	0.5% (hypersensitivity, C. difficile colitis)	0%
TEAEs Leading to Discontinuation	3.5%	1.6%
Deaths Due to TEAEs	2.1% (none related to the drug)	1.6% (none related to the drug)
Common TEAEs	Diarrhea, increased transaminases, headache	Diarrhea, increased transaminases, headache
Hepatic TEAEs	5.1% of subjects (mild to moderate)	2.8% of subjects (mild to moderate)
QT Prolongation	0 cases	2 cases (0.5%)
Other AESIs (Adverse Events of Special Interest)	No cases of phototoxicity, tendon disorders, or peripheral neuropathy	Potential myopathy and QT prolongation

Journal of Global Antimicrobial Resistance 32 (2023) 72–73

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journal homepage: www.elsevier.com/locate/jgar

Letter to the Editor

Postoperative linezolid-resistant methicillin-resistant *Staphylococcus epidermidis* mediastinitis in a heart transplant patient: first case of therapeutic success with delafloxacin

Editor: Stefania Stefani

At 47 d post-transplant, the patient's case was discussed in a multidisciplinary meeting, and it was decided to modify the antibiotic therapy to limit exposure to ceftaroline, a broad-spectrum cephalosporin with potential toxicity, and to simplify the treatment with oral administration.

THERAPEUTIC ADVANCES in
Infectious Disease

Case Report

'TAVR Infected Pseudomonas Endocarditis': a case report

Francis Essien, Shane Patterson, Fernando Estrada, Timothy Wall, John Madden and Michael McGarvey

Ther Adv Infect Dis
2022, Vol. 9: 1–8
DOI: 10.1177/20499361221138459

Hindawi
Case Reports in Pulmonology
Volume 2022, Article ID 1008330, 5 pages
https://doi.org/10.1155/2022/1008330

Hindawi

Case Report

Ciprofloxacin-Resistant *Pseudomonas aeruginosa* Lung Abscess Complicating COVID-19 Treated with the Novel Oral Fluoroquinolone Delafloxacin

The American Journal of the Medical Sciences
Volume 363, Issue 4, April 2022, Pages 359-363

Patient-Centered Focused Review

Early Clinical Experience with Delafloxacin: A Case Series

J. Patrik Hornak MD [1], David Reynoso MD, PhD [1 2]

Results

Five patients were prescribed DLX (median age 59 years, 40% female, 100% outpatient) with a median treatment duration of seven days. Prescriptions were initiated by infectious diseases specialists (2/5, 40%), emergency medicine physicians (2/5, 40%), and ophthalmologists (1/5, 20%). The most common conditions treated were prosthetic joint infections (PJI) and acute skin and soft tissue infections (each n=2). Both PJIs were caused by multi-drug-resistant

Annals of Case Reports
D'Introno A, et al. Ann Case Rep: 9: 101859
www.doi.org/10.29011/2574-7754.101859
www.gavinpublishers.com

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GAVIN PUBLISHERS

Case Report

Long-Time Conservative Treatment and Off-Label Use of Delafloxacin in Abdominal Aortic Graft Infection: Case Report

Alessia D'Introno[1*], Marialuisa Cavallo[1], Francesca Loparco[1], Lorena Quarato[1], Lauretana Perrone[1], Valeria Rollo[1], Artor Niccoli Asabella[2], Alessandro Anglani[3], Cinzia Anna Pennetta[4], Emanuela Ciracì[1]

[1]Internal Medicine Unit, Ostuni Hospital, Ostuni, Brindisi, Italy
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[4]Hospital Pharmacy, Ostuni Hospital, Ostuni, Brindisi, Italy.

THE HYPOCRISY OF ID SPECIALISTS

Clinical Infectious Diseases

EDITORIAL COMMENTARY

Another New Antibiotic for Skin Infections and Why Infectious Disease Specialists Are Hypocrites

Loren G. Miller[1,2]

The article critiques infectious disease specialists' perceived **"hypocrisy"** in their approach to new antibiotics. This term describes the **paradoxical behavior** of these specialists: they **advocate strongly for the development** of new antibiotics to combat rising resistance, but once these drugs are available, they **actively discourage widespread use**.

This cautious approach is rooted in the principle of **antibiotic stewardship**. Specialists aim to **conserve the efficacy** of new antibiotics for severe cases where alternative treatments fail or for patients with infections resistant to existing drugs. By limiting the use of newer antibiotics, they seek to **delay resistance development**, which can occur rapidly with overuse. This protective approach means that, although they have advocated for these drugs, they appear **"hypocritical"** by advising restraint once the medications reach the market.

This caution is influenced by **past experiences** where initially promising new antibiotics quickly saw **reduced effectiveness** as resistance developed. For example, antibiotics like **ciprofloxacin and levofloxacin**, once effective against skin infections caused by *S. aureus*, saw **significant reductions in efficacy** due to resistance from overuse. Specialists understand that once a new antibiotic becomes widely used, resistance often emerges, potentially **rendering it ineffective** for future patients.

In essence, while this cautious approach may seem **contradictory or "hypocritical"**, it is a strategy aimed at the **long-term preservation of antibiotic efficacy**, ultimately benefiting **future patients** and **public health** on a larger scale.

Comment on

A Comparison of the Efficacy and Safety of Intravenous Followed by Oral Delafloxacin With Vancomycin Plus Aztreonam for the Treatment of Acute Bacterial Skin and Skin Structure Infections: A Phase 3, Multinational, Double-Blind, Randomized Study.

O'Riordan W, McManus A, Teras J, Poromanski I, Cruz-Saldariagga M, Quintas M, Lawrence L, Liang S, Cammarata S; PROCEED Study Group.

Clin Infect Dis. 2018 Aug 16;67(5):657-666. doi: 10.1093/cid/ciy165.

PMID: 29518178 Free PMC article. Clinical Trial.

DELAFLOXACIN: CONCLUSIONS

Antibiotic with in vitro activity against methicillin-resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa.
Potential for polymicrobial diabetic foot infections and osteoarticular infection: In scenarios where polymicrobial diabetic foot infections are suspected, current international guidelines recommend combining an anti-MRSA agent with another agent such as a FQ.
Empirical (as monotherapy) and targeted treatment of community-acquired bacterial pneumonia.
Because of delafloxacin's spectrum of activity and enhanced activity in acidic environments due to its anionic chemical structure, perhaps a more suitable role for delafloxacin would be for the management of abscesses where multidrug-resistant organisms are more commonly found.