

Once-Daily Oral Gatifloxacin versus Oral Levofloxacin in Treatment of Uncomplicated Skin and Soft Tissue Infections: Double-Blind, Multicenter, Randomized Study

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This was a double-blind, multicenter study in which 410 adults (≥18 years of age) with uncomplicated skin and soft tissue infections (SSTIs) were randomized to receive either 400 mg of gatifloxacin orally once daily or 500 mg of levofloxacin orally once daily for 7 to 10 days. The study protocol called for four assessments—before and during treatment, at the end of treatment, and posttreatment. Efficacy evaluations included clinical response and bacterial eradication rates. Of 407 treated patients, 202 (108 women, 94 men) received gatifloxacin and 205 (111 women, 94 men) received levofloxacin. For clinically evaluable patients, the cure rates were 91% for gatifloxacin and 84% for levofloxacin (95% confidence interval [CI] for the difference, –2.0 to 15.2%). Clinical cure rates for microbiologically evaluable patients were 93% for gatifloxacin and 88% for levofloxacin (95% CI for the difference, –6.5 to 16.8%). The bacterial eradication rate was 92% for each group, with gatifloxacin eradicating 93% of the methicillin-susceptible *Staphylococcus aureus* isolates and levofloxacin eradicating 91% of them. Both drugs were well tolerated. Most of the adverse events were mild to moderate, and nausea was the most common adverse event in each treatment arm. Once-daily oral gatifloxacin (400 mg) is clinically efficacious and well tolerated compared with once-daily levofloxacin (500 mg) for the treatment of patients with uncomplicated SSTIs.

Uncomplicated skin and soft tissue infections (SSTIs) are commonly encountered in medical practice (3). These infections include impetigo, erysipelas, cellulitis, folliculitis, postoperative wound infections, and simple abscesses. The most common pathogens implicated in uncomplicated SSTIs are *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Streptococcus agalactiae*, and less often involved are gram-negative organisms (e.g., *Pseudomonas aeruginosa* and *Escherichia coli*) (24). Postoperative wound infections are often due to a combination of exogenous staphylococci and streptococci and endogenous enteric organisms. Because uncomplicated SSTIs seldom lead to the destruction of skin structures and consequent septicemia, they can generally be treated with an oral antibiotic with good activity against gram-positive pathogens. Local measures, such as debridement or incision and drainage, are also employed in select cases to facilitate and speed curing.

Many traditional antimicrobial agents, such as β -lactams, provide excellent coverage of methicillin-sensitive *S. aureus* and streptococci. Among the oral β -lactams demonstrating good clinical efficacy are, for example, cefprozil, cefpodoxime proxetil, cefuroxime axetil, cephalexin, cefadroxil, and penicillin- β -lactamase inhibitor combinations such as amoxicillin-clavulanate (17, 23, 25, 26). Depending on the drug, clinical efficacy rates with these agents for mild-to-moderate SSTIs range from approximately 78 to 100% (17, 23, 25, 26). Traditional macrolides, such as erythromycin, as well as the newer agents azithro-

mycin and clarithromycin, have also been used extensively to treat SSTIs. Reported clinical efficacy rates for these drugs range from 74 to 96% (20, 25).

Although traditional agents generally offer effective therapy for uncomplicated SSTIs, many have shortcomings that may limit their utility. For example, allergy to β -lactams is fairly common and, depending on the drug, traditional agents may need to be administered two to four times per day, which may adversely impact compliance. Furthermore, significant pretherapy resistance to older macrolides has been reported (1) and is beginning to be reported for the newer macrolides (25). Finally, macrolide-associated gastrointestinal side effects may limit the use of these agents.

Gatifloxacin [1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-(3-methyl-1-piperazinyl)-4-oxo-3-quinolinecarboxylic acid] is a new 8-methoxy fluoroquinolone possessing broad-spectrum activity against gram-positive bacteria (including methicillin-susceptible *S. aureus*, some strains of methicillin-resistant *S. aureus*, *S. pyogenes*, *S. agalactiae*, pneumococci, and enterococci), and gram-negative bacteria (most members of the family *Enterobacteriaceae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Neisseria gonorrhoeae*) (3, 5, 6, 11, 19). This expanded-spectrum fluoroquinolone has several favorable structure-activity characteristics. The methoxy group at the C-8 position is thought to lessen the likelihood of antimicrobial resistance by requiring bacteria to acquire two topoisomerase mutations to express high-level resistance (6, 27).

The clinical trial described here was conducted to compare the safety and efficacy of gatifloxacin to those of levofloxacin in patients with uncomplicated SSTIs and to evaluate the eradi-

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cation rates of bacterial pathogens commonly associated with these infections.

MATERIALS AND METHODS

Study design and ethics. This was a double-blind, multicenter, randomized study. The study protocol and conduct followed guidelines established by the Infectious Disease Society of America and the Food and Drug Administration for the evaluation of anti-infective agents used for this indication. In addition, the Institutional Review Board or Independent Ethics Committee of each site approved the study protocol and all participating patients or their legal guardians provided written informed consent prior to enrollment.

Eligibility and accrual. The protocol called for the enrollment of 380 adult (≥ 18 -year-old) men and women to be divided equally between treatment groups. Patients were stratified by study site and diagnosis (impetigo, cellulitis-erysipelas, wound infection, or abscess-folliculitis), and the target for each treatment group was 30 patients per diagnosis. Diagnoses were made within the 2 days before randomization and were based on the assessment of clinical signs and symptoms by the investigator. Women with childbearing potential were required to provide a documented negative serum or urine pregnancy test within 72 h of starting administration of the study drug and to sign an agreement pledging to use effective contraception throughout the study. In addition to pregnancy or lactation, study exclusion criteria included findings of a complicated SSTI, immediate need for surgical intervention, concomitant treatment with topical antimicrobials or corticosteroids at the target site, concomitant osteomyelitis or another bacterial infection, a deep venous thrombosis, receipt of another systemic antibiotic within 7 days of randomization or likely receipt of such during the study period, a previously diagnosed immune disease(s), a history of significant hypersensitivity reactions to fluoroquinolones, known renal insufficiency (serum creatinine of ≥ 1.5 mg/dl), and clinically significant hepatic disease (alanine aminotransferase and/or aspartate aminotransferase and/or total bilirubin levels that were equal to or greater than three times the upper normal limit).

Patients were randomized by using a dynamic balancing algorithm (21) designed to minimize the imbalance between inequalities within the treatment arms for each study site, for each diagnosis, and for the overall study.

Treatment. Both study drugs were given orally on a once-daily basis for 7 to 10 days, with patients receiving either 400 mg of gatifloxacin (Tequin; Bristol-Myers Squibb Company, Princeton, N.J.) or 500 mg of levofloxacin (Levaquin; Ortho-McNeil Pharmaceutical, Inc., Raritan, N.J.). Therapy was administered in a double-blind, "double-dummy" fashion. Local adjunctive measures, such as dressing changes, were permitted as long as they did not include the application of topical antimicrobial agents.

Study procedures. The clinical status of patients was evaluated during clinic visits conducted at regular intervals throughout the study, i.e., (i) within the 48 h before the start of drug administration, (ii) after 3 to 5 days of therapy, and (iii) 7 to 14 days after the completion of treatment (this was considered the test-of-cure visit). In addition, immediately following the completion of study drug administration (i.e., 3 to 5 days posttreatment), patients were contacted by telephone to assess compliance, safety, and the response to therapy and if the patient's symptoms had not improved at that time, a clinic visit was to be scheduled.

Pretreatment cultures were obtained by swab (wound infection, impetigo, spontaneously draining abscess, folliculitis) or needle aspiration (cellulitis, erysipelas, and some cases of abscess-folliculitis). Isolated aerobes were tested for susceptibility to gatifloxacin and levofloxacin by using disk diffusion and MIC determination procedures approved by the NCCLS. In addition, isolates of *S. aureus* were tested for susceptibility to methicillin. Although anaerobic cultures were permitted if the potential existed for anaerobic infection (e.g., perirectal lesions or a foul-smelling discharge from a surgical wound), no susceptibility testing of these isolates was done. Testing for β -lactamase was performed only if *H. influenzae* was isolated.

Outcome measures. (i) **Efficacy.** Clinical and bacteriologic responses were assessed at the test-of-cure visit. Patients were deemed clinically cured if their pretreatment signs and symptoms of infection had improved or resolved and they did not need additional antibiotic therapy. Patients were deemed to have clinically failed if they experienced either persistent or worsening signs and symptoms, developed new signs and symptoms of infection, or needed debridement or incision and drainage.

Bacteriologic responses were classified as follows: documented eradication, no growth of the pretreatment pathogen in a culture taken at the test-of-cure visit; presumed eradication, lack of culturable material in a clinically cured patient; documented persistence, growth of the pretreatment pathogen in a culture taken at the test-of-cure visit; presumed persistence, lack of culturable material in a patient who had clinically failed. New infections were any in which a new patho-

gen was isolated and/or clinical signs and symptoms indicative of a new infection occurred during or after receipt of the study drug.

(ii) **Safety.** Patients were closely monitored for clinically adverse events, as well as clinically significant changes from the baseline laboratory indices, vital signs, and physical examination findings. The severity of clinically adverse events was categorized by the investigators as mild, moderate, or severe. The investigators also classified the relationship of adverse events to the study drugs as either certainly, probably, or possibly drug related; not drug related; or with an unknown relationship to the study drug.

Statistical methods. Assuming equivalent response rates of 80% for the two study drugs, it was estimated that 150 evaluable patients per arm would provide a study with 90% power ($\alpha = 0.05$, two sided) to declare gatifloxacin and levofloxacin equivalent within 15%. Based on an anticipated evaluability rate of 80%, 190 patients per arm was the target sample size.

Patient evaluability was assessed under blinded conditions. In order to be considered clinically evaluable, patients were required to meet the study entry criteria, to have received at least 5 days of their prescribed study regimen (or at least 3 days if the patient was determined to have clinically failed), to have had a pretreatment culture performed, to have had a test-of-cure assessment, and to have not received any other presumably effective antimicrobial agent concomitantly with the study drug. Patients who discontinued the study drug due to a treatment-related adverse event(s) or lack of efficacy were considered to have clinically failed. Clinically evaluable patients with pretreatment cultures positive for a bacterial pathogen that was susceptible to both study drugs were classified as microbiologically evaluable.

The primary efficacy variable, clinical response, was assessed in clinically evaluable patients. A 95% confidence interval (CI) for the difference in the clinical cure rate between the treatment arms was computed by using an exact method (Stat Xact-3). Gatifloxacin and levofloxacin were deemed equivalent if the lower confidence limit for the difference between cure rates was greater than or equal to -15% . A lower confidence limit of greater than 0 was considered to indicate a superior gatifloxacin cure rate. The bacterial eradication rates of the two drugs were compared by pathogen.

Safety data were assessed for all patients who received at least one dose of a study drug. The primary endpoints were the incidence of drug-related adverse events and the frequency of abnormal posttreatment laboratory events (in the direction of toxicity) in patients with normal baseline values. For statistical analysis, adverse events that were certainly, probably, or possibly drug related were grouped together as drug related.

RESULTS

Patient characteristics. The all-treated (intent-to-treat) patient population ($n = 407$) comprised 202 recipients of gatifloxacin and 205 recipients of levofloxacin. The two groups were well matched in terms of demographic traits and types of infection (Table 1). Cellulitis, abscess, wound infections, and folliculitis accounted for more than two-thirds of the infections. Pretreatment signs and symptoms included some combination of erythema, pain, tenderness, and warmth for the majority of patients.

Extent of exposure. Treatment compliance was monitored by a review of the patient's medication diary and by retrieval of unused drug at the last clinic or office visit. Rates of compliance with the study medication regimen were comparable in both treatment arms. Ninety percent of all gatifloxacin patients ($n = 181$) and 92% of all levofloxacin patients ($n = 189$) completed therapy, with 93% in each group receiving 7 to 10 doses of medication.

The frequencies of premature discontinuation of medication were comparable in the two groups (10% [21] of the patients in the gatifloxacin group versus 8% [16] of the patients in the levofloxacin group). The reasons for patients discontinuing a study drug prematurely were adverse events (6 gatifloxacin patients [2 due to drug-related adverse events] and 10 levofloxacin patients [9 due to drug-related adverse events]), loss to follow-up (impossible to assess compliance; 11 and 2 patients in the respective groups), patient decision (3 patients in the

TABLE 1. Demographics, baseline characteristics, and concomitant antimicrobials of all treated patients^a

Parameter	Gatifloxacin	Levofloxacin
Ratio of men to women	94:108	94:111
Mean age, range (yr)	39, 18–85	40, 18–90
No. (%):		
White	162 (80)	165 (80)
Hispanic	26 (13)	23 (11)
Black	10 (5)	11 (5)
Other race	4 (2)	6 (3)
No. (%) with diagnosis of:		
Abscess	45 (22)	59 (29)
Cellulitis	53 (26)	50 (24)
Wound infection	48 (24)	48 (23)
Folliculitis	44 (22)	34 (17)
Impetigo	12 (6)	13 (6)
Erysipelas	0 (0)	1 (<1)
No. (%) of patients with pathogen	120 (59)	104 (51)

^a The group of all treated patients includes all of the individuals who received at least one dose of gatifloxacin ($n = 202$) or levofloxacin ($n = 205$).

gatifloxacin group), protocol violation (2 patients in the levofloxacin group), poor clinical response (1 patient in each group), and administration of another antibiotic (1 patient in the levofloxacin group took azithromycin for sinusitis).

Patient disposition. Of the 407 treated patients, 333 (82%) were clinically evaluable (161 in the gatifloxacin group and 172 in the levofloxacin group) and 180 (44%) were microbiologically evaluable (95 and 85, respectively) (Table 2). The primary reasons why patients were classified as clinically unevaluable were the absence of a test-of-cure assessment of response in the gatifloxacin group and that the patient received less than 5 days of therapy (excluding those classified as having clinically failed) in the levofloxacin group. In both treatment groups, the primary reason for patients being classified as microbiologically unevaluable was lack of pretreatment isolation of a pathogen.

Pretreatment pathogens. One or more pretreatment pathogens were obtained from 224 patients. A total of 308 pathogens (197 [64%] gram positive, 106 [34%] gram negative, and 5 [2%] unidentified) were isolated—155 from gatifloxacin-treated patients and 153 from levofloxacin-treated patients. The most common gram-positive aerobes ($n = 183$) were *S. aureus* (147 [80%] of 183), *S. pyogenes* (15 [8%] of 183), *S. agalactiae* (11 [6%] of 183), and *Bacillus* spp. (6 [3%] of 183). The most common gram-negative aerobes ($n = 93$) were *Acinetobacter lwoffii* (14 [14%] of 93), *Acinetobacter baumannii* (9 [10%] of 93), *P. aeruginosa* (9 [10%] of 93), and *E. coli* (8 [9%] of 93). A total of 32 anaerobes (10% of all pathogens) were isolated.

Susceptibility testing revealed no gatifloxacin-resistant isolates, although intermediate susceptibility (MIC of 4 μ g/ml) was noted in one isolate each of *S. aureus* and *P. aeruginosa*. One *S. aureus* isolate was resistant to levofloxacin (MIC of 8 μ g/ml), and one isolate each of *Enterococcus raffinosus* and *Pseudomonas* sp. showed intermediate susceptibility to this agent (MIC of 4 μ g/ml in both cases).

Overall clinical response. The treatment groups were comparable based on the clinical cure rates among clinically evaluable patients (91% [146 of 161] for the gatifloxacin group and 84% [145 of 172] for the levofloxacin group; 95% CI for the

TABLE 2. Disposition of patients

Study population or reason for exclusion	No. (%) of patients treated with:	
	Gatifloxacin	Levofloxacin
All treated	202 (100)	205 (100)
Clinically evaluable	161 (80)	172 (84)
Clinically unevaluable	41 (20)	33 (16)
Reason why unevaluable		
No test-of-cure visit	12 (6)	5 (2)
No pretreatment culture	8 (4)	8 (4)
Received <5 days of study drug therapy (excluding failures)	6 (3)	8 (4)
Received systemic antimicrobial with study drug	3 (1)	1 (<1)
Did not meet entry criteria	2 (1)	2 (1)
Other	10 (5)	9 (4)
Microbiologically evaluable	95 (47)	85 (42)
Microbiologically unevaluable	107 (54)	120 (59)
Reason why unevaluable		
No pretreatment pathogen isolated	85 (42)	101 (49)
Clinically unevaluable	14 (7)	10 (5)
Pathogen resistant	0 (0)	1 (<1)
Other	8 (4)	8 (4)

difference, -2 to $+15\%$) (Table 3). Across the infection diagnoses, the cure rates for gatifloxacin were consistently numerically higher but not statistically significantly different from those for levofloxacin: cellulitis, 98 versus 83%, respectively; wound infection, 95 versus 88%, respectively; abscess, 80 versus 78%, respectively. All patients with impetigo were clinically cured by the fluoroquinolone they received. In all cases, cure rates were independent of the duration of therapy. For patients who received 7 days of therapy, the cure rates for gatifloxacin and levofloxacin were 97% (32 of 33) and 84% (21 of 25), respectively; for those who received 10 days of therapy, the respective rates were 91% (108 of 119) and 86% (115 of 134).

Persistence or worsening of primary signs and symptoms was the main reason why patients in both treatment groups were classified as having clinically failed (gatifloxacin, 12 patients; levofloxacin, 21 patients). The next most common reason for clinical failure was the need for incision and drainage of the infected site (three gatifloxacin patients [two with abscesses and one with folliculitis] and four levofloxacin patients [three with abscesses and one with a wound infection]).

TABLE 3. Clinical cure rates of clinically evaluable patients by infection diagnosis

Diagnosis	No. cured/total no. (%) of patients who received:	
	Gatifloxacin	Levofloxacin
All	146/161 (91) ^a	145/172 (84) ^a
Cellulitis	39/40 (98)	35/42 (83)
Abscess	28/35 (80)	37/47 (78)
Wound infection	35/37 (95)	35/40 (88)
Folliculitis	34/39 (87)	26/31 (84)
Impetigo	10/10 (100)	11/11 (100)
Erysipelas		1/1 (100)

^a 95% CI for difference, -2 to $+15\%$.

TABLE 4. Clinical cure and bacterial eradication by pretreatment pathogen

Pathogen(s)	No./total no. (%) of:			
	Clinically evaluable patients with clinical cure		Microbiologically evaluable patients with bacterial eradication	
	Gatifloxacin	Levofloxacin	Gatifloxacin	Levofloxacin
Total	93/103 (90)	80/94 (85)	107/116 (92)	113/123 (92)
Gram-positive aerobes	75/82 (91)	70/81 (86)	74/81 (91)	71/78 (91)
<i>Staphylococcus aureus</i> ^a	66/69 (96)	54/62 (87)	64/69 (93)	56/61 (92)
<i>Streptococcus pyogenes</i>	4/6 (67)	4/5 (80)	4/6 (67)	5/5 (100)
<i>Streptococcus agalactiae</i>	1/2 (50)	8/9 (89)	2/2 (100)	7/9 (78)
<i>Bacillus</i> spp.	3/3 (100)	2/3 (67)	3/3 (100)	1/1 (100)
Other	1/2 (50)	2/2 (100)	1/1 (100)	2/2 (100)
Gram-negative aerobes	32/37 (86)	41/47 (87)	33/35 (94)	42/45 (93)
<i>Acinetobacter lwoffii</i>	5/6 (83)	4/7 (57)	6/6 (100)	7/7 (100)
<i>Acinetobacter baumannii</i>	3/3 (100)	6/6 (100)	3/3 (100)	6/6 (100)
<i>Pseudomonas aeruginosa</i>	0/1 (0)	5/6 (83)	1/1 (100)	5/6 (83)
<i>Escherichia coli</i>	2/2 (100)	3/4 (75)	2/2 (100)	3/4 (75)
<i>Pseudomonas</i> spp.	1/1 (100)	3/3 (100)	1/1 (100)	2/2 (100)
<i>Flavimonas oryzihabitans</i>	2/3 (67)	1/1 (100)	2/3 (67)	1/1 (100)
<i>Serratia marcescens</i>	2/2 (100)	1/2 (50)	2/2 (100)	1/2 (50)
<i>Klebsiella pneumoniae</i>	1/2 (50)	2/2 (100)	2/2 (100)	2/2 (100)
<i>Klebsiella oxytoca</i>	2/2 (100)	1/1 (100)	2/2 (100)	1/1 (100)
<i>Proteus mirabilis</i>	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)
Other	13/14 (93)	14/14 (100)	11/12 (92)	13/13 (100)

^a Includes isolates that are methicillin susceptible, methicillin resistant, and of unspecified susceptibility.

Clinical response by pathogen. The cure rates in those from whom a pretreatment pathogen was isolated were 90% (93 of 103) for gatifloxacin and 85% (80 of 94) for levofloxacin among the clinically evaluable patients (Table 4) and 93% (88 of 95) and 88% (75 of 85), respectively, among the microbiologically evaluable patients. For clinically evaluable patients infected with *S. aureus*, the predominant pathogen in this study, the clinical cure rates were 96% (66 of 69) and 87% (54 of 62) for gatifloxacin and levofloxacin, respectively.

Microbiological response. Bacterial eradication rates were largely consistent with clinical responses. Therapy with either gatifloxacin or levofloxacin eradicated 92% of all of the pathogens isolated from the microbiologically evaluable patients in this study (Table 4). The eradication rates for gatifloxacin and levofloxacin were 91% each for patients infected with gram-positive aerobes and 94 and 93%, respectively, for patients infected with gram-negative aerobes.

Posttherapy cultures documented the persistence of three isolates in each treatment arm, none of which had become resistant to the study drugs.

New infections. Fourteen patients in each treatment group developed a new infection(s). There were seven cases of vaginitis (five of them in patients taking gatifloxacin), three cases each of cellulitis and upper respiratory tract infection, two cases each of folliculitis and sinusitis, and single cases of various other skin ($n = 6$) and non-skin ($n = 7$) infections.

Safety. Drug-related adverse events are summarized in Table 5. The most common adverse events were nausea (8% for gatifloxacin and levofloxacin), diarrhea (6% for each drug), vaginitis (8 and 4%, respectively), and headache (3 and 5%, respectively). A minority of patients discontinued the study drug prematurely due to a drug-related adverse event (two gatifloxacin-treated and nine levofloxacin-treated patients).

Laboratory abnormalities. Alterations in laboratory values in patients with normal pretreatment measurements were generally mild (grade 1), clinically nonsignificant, and comparable between gatifloxacin- and levofloxacin-treated patients.

DISCUSSION

Uncomplicated SSTIs are increasingly viewed as appropriate infections for treatment with the newer fluoroquinolones (7, 8, 12, 13, 18). These agents have activity against the major gram-positive and gram-negative pathogens associated with SSTIs (9, 19). Moreover, their expanded gram-positive activity, ability to achieve adequate concentrations in tissue at skin sites, suitability for once-daily dosing, and proven tolerability suggest that these agents are good alternatives to agents traditionally used for empirical therapy (8, 12, 15, 16).

Findings from this multicenter study indicate that once-daily 400-mg doses of gatifloxacin are as well tolerated, safe, and efficacious, both clinically and microbiologically, as once-daily 500-mg doses of levofloxacin when given for 7 to 10 days to patients with uncomplicated SSTIs. The cure rates among clinically evaluable patients were 91% for gatifloxacin and 84% for levofloxacin and were comparable whether patients received 7 or 10 days of treatment. Except for erysipelas, all major forms of uncomplicated SSTI were well represented in this study. For patients infected with *S. aureus*, the predominant pathogen in both serious and uncomplicated SSTIs (7, 12, 13, 15, 16), the cure rates were 96 and 87% for the respective treatment groups.

Pretreatment microbiologic findings in this study were characteristic of uncomplicated SSTIs; the predominant isolates were *S. aureus* (66%) and streptococci (11%). This study also yielded a number of *Acinetobacter* species (11%). Gatifloxacin and levofloxacin were equally effective in eradicating isolated pathogens. None of the three persistent *S. aureus* isolates detected in each study group had become resistant to gatifloxacin or levofloxacin.

The most common drug-related adverse events for gatifloxacin and levofloxacin were nausea, headache, vaginitis, and diarrhea; the majority were mild to moderate in severity. Drug-related discontinuations were relatively rare at <1% (2 of 202

TABLE 5. Drug-related adverse events of all treated patients

Clinical adverse event	No. (%) of patients treated ^b with:	
	Gatifloxacin	Levofloxacin
Nausea	16 (8)	16 (8)
Diarrhea	12 (6)	12 (6)
Vaginitis ^a	9 (8)	4 (4)
Dizziness	7 (3)	4 (2)
Abdominal pain	6 (3)	4 (2)
Headache	6 (3)	10 (5)
Pruritus	5 (2)	4 (2)
Asthenia	5 (2)	0 (0)
Rash	4 (2)	3 (1)
Nervousness	3 (1)	1 (<1)
Eructation	2 (1)	5 (2)
Pain	2 (1)	5 (2)
Taste perversion	1 (<1)	3 (1)
Insomnia	1 (<1)	3 (1)

^a Percentage calculated for female patients only.

^b There were 202 patients in the gatifloxacin group and 205 in the levofloxacin group.

patients) for gatifloxacin versus 4% (9 of 205 patients) for levofloxacin.

In both in vitro and in vivo studies, gatifloxacin has been shown to be highly active against the gram-positive and gram-negative organisms frequently encountered in patients with SSTIs (6, 11, 19). It has been found to be more active than trovafloxacin and sparfloxacin against ciprofloxacin-resistant *S. aureus* and coagulase-negative staphylococci (11). The concentration of gatifloxacin achieved in skin tissue (tissue-to-plasma concentration ratio of >1 from 2 to 24 h after dosing) (19) surpasses by severalfold the MICs for 90% of the strains of *S. aureus* (0.12 µg/ml) and *S. pyogenes* (0.5 µg/ml) tested (3; E. Huczko, L. Valera, B. Conetta, T. Stickle, A. Macko, and J. Fung-Tomc, Abstr. 39th Intersci. Conf. Antimicrob. Agents Chemother., abstr. 351, 1999). Moreover, its in vitro activity against pathogens implicated in animal and human bite wound infections—including various *Pasteurella* species, anaerobic veterinary species, and atypical pathogens, such as fastidious aerobic bacteria—has been shown to be comparable to that of other available quinolones (10). In the case of *Pasteurella* species, gatifloxacin showed activity better than that of amoxicillin-clavulanate; for the majority of aerobes, the MIC of gatifloxacin for 90% of the strains tested was 0.016 µg/ml (10).

Chemical modifications are notable for improving the tolerability of gatifloxacin and optimizing its pharmacokinetics. Specifically, the addition of a methoxy group at the C-8 position is believed to minimize the potential for phototoxicity, a problem seen with other fluoroquinolones, e.g., sparfloxacin and lomefloxacin (2, 22), but not seen to date with gatifloxacin. As with most fluoroquinolones, gatifloxacin exhibits concentration-dependent bactericidal activity and a long postantibiotic effect (4). Moreover, its long serum half-life of 8 h allows once-daily administration (14). Since intravenous and oral doses of the drug are bioequivalent, the two formulations are interchangeable. This feature may be of chief import to patients with surgical wound infections who could be started on the intravenous formulation and then switched to the same dose of the oral form when it is clinically appropriate.

Summary. The desire for improved treatment outcomes, safety, and patient convenience continues to drive the development of improved and more potent fluoroquinolones for use in a variety of infections. As a group, the newer fluoroquinolones provide improved coverage against gram-positive organisms and offer the convenience of once-daily oral administration. Findings from this study indicate that gatifloxacin is at least as clinically and microbiologically effective as levofloxacin for the treatment of patients with uncomplicated SSTIs, including those whose infections are due to *S. aureus* or *S. pyogenes*.

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