

Efficacy of Lomefloxacin as Compared to Norfloxacin in the Treatment of Uncomplicated Urinary Tract Infections in Adults

ABDOLLAH IRAVANI, M.D., Orlando, Florida

The efficacy and safety of 7–10-day courses of lomefloxacin (single daily dose of 400 mg) or norfloxacin (twice-daily doses of 400 mg) for the treatment of uncomplicated urinary tract infections were compared in two large, multicenter, randomized trials. This article presents the combined results of these trials, which were conducted in a total of 27 centers throughout the United States. A total of 727 adults, mostly women, with symptoms of acute urinary tract infection were enrolled; 370 patients were randomized to lomefloxacin treatment, and 357 received norfloxacin. The bacteriologic cure rate at 5–9 days post-therapy was 98.2% in the lomefloxacin group and 96.3% in the norfloxacin group ($p = \text{nonsignificant}$). The clinical success rate of 99.1% in the lomefloxacin group was significantly higher than the success rate of 93.5% in the norfloxacin group ($p = 0.002$). Adverse events were reported by 157 lomefloxacin-treated patients and 129 patients receiving norfloxacin. Adverse events attributable to drug treatment occurred in 41 patients (11.1%) in the lomefloxacin group and 27 (7.6%) in the norfloxacin group. Eight lomefloxacin (2.2%) and three norfloxacin patients (0.8%) were withdrawn from treatment because of adverse events probably attributable to the drug. The incidence of dizziness, tremor, and photosensitivity rash was higher in the lomefloxacin group than in the norfloxacin group, while the incidence of nausea was higher in the norfloxacin group. The results of these trials demonstrate that once-daily administration of 400 mg lomefloxacin is as safe and effective clinically as, and superior bacteriologically to, twice-daily administration of 400 mg norfloxacin in the treatment of acute uncomplicated urinary tract infections in adult patients.

From the University of Florida, Gainesville, Florida (previous affiliation; retired 1991); the Orlando Regional Medical Center; and the Central Florida Research Center (current affiliation).

Requests for reprints should be addressed to Abdollah Iravani, M.D., Department of Pediatrics and Medical Education, Division of Nephrology, 85 West Miller Street, Suite 203, Orlando, Florida 32806.

Lomefloxacin, a new orally administered difluoroquinolone, has a broad antibacterial spectrum of activity against gram-negative and gram-positive organisms, including Enterobacteriaceae, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. Lomefloxacin possesses in vitro antibacterial activity comparable to that of ofloxacin, norfloxacin, and fleroxacin, but is less active than ciprofloxacin [1–4]. Lomefloxacin is absorbed rapidly from the gastrointestinal tract and attains peak plasma concentrations in approximately 1 hour. It has a plasma half-life of 7–8 hours [5], significantly longer than norfloxacin and ciprofloxacin (4 hours) [6].

Lomefloxacin penetrates well and develops prolonged high tissue levels. Over 70% of the oral dose is excreted in the active form in the urine. Urine concentrations 24 hours after dosing exceed the minimum inhibitory concentration for 90% (MIC_{90}) of urinary tract pathogens [5,6].

The objective of these prospective, single-blind (investigator-blinded), randomized, multicenter trials was to compare the safety and efficacy of a 7–10-day course of lomefloxacin 400 mg once daily to norfloxacin 400 mg twice daily in the treatment of acute uncomplicated urinary tract infections in adults.

PATIENTS AND METHODS

This article presents the results of two randomized, multicenter studies that were conducted according to similar protocols. The protocols were approved by the institutional review boards at each participating center. All patients provided written informed consent prior to enrollment.

Adult outpatients with clinical signs and symptoms of uncomplicated urinary tract infection were enrolled and assigned, using a 1:1 computer-generated randomization, to receive 7–10 days of treatment with either once-daily lomefloxacin 400 mg (two 200 mg capsules; Searle, Chicago, Illinois) or twice-daily norfloxacin 400 mg (400 mg tablets; Merck, Sharp, and Dohme, West Point, Pennsylvania). The drugs were dispensed by an independent third party to ensure investigator blinding. The duration of treatment and dosage of norfloxacin

was based on the approved therapy for uncomplicated urinary tract infections, as described in the product prescribing information for norfloxacin in the United States.

Patient Selection

The criteria for patient inclusion in the study were as follows: male or female outpatients, age ≥ 18 years; signs and symptoms of urinary tract infection, such as dysuria, frequency, hematuria, suprapubic or loin pain and tenderness; bacteriuria found on microscopic examination of urine sediment within 48 hours prior to treatment; bacteriuria documented by $\geq 10^5$ colony-forming units (CFU) of a bacterium per mL in two consecutive urine cultures if the patient was asymptomatic; women of child-bearing age must have used a barrier or hormonal method of contraception, or have been surgically sterilized. Pregnant or lactating women, patients who had complicated urinary tract infections (by history or previous radiologic findings), patients with baseline pathogens resistant to either study drug, impaired renal or liver function, convulsive disorders, and hypersensitivity to quinolones or azaquinolones were excluded. Patients who had received an investigational drug within the previous 4 weeks, antimicrobial therapy within 72 hours of enrollment, or those expected to consume systemic antimicrobial agents, theophylline, phenytoin, warfarin, or antacids during the study period were excluded.

Patient Evaluation

Prior to enrollment, a complete medical history and a general physical examination were obtained for each patient. In addition, the type, duration, and severity of symptoms were assessed. Clinical laboratory evaluation included hematology, serum chemistries, and urinalysis of a clean-catch mid-stream or straight catheter urine specimen within 48 hours prior to therapy. Clinical and bacteriologic evaluations were repeated 2–4 days after the start of therapy, and 5–9 days post-therapy.

Bacteriologic Techniques

All urine specimens were collected and handled in accordance with accepted laboratory procedures and cultured according to standard laboratory practices [7,8]. Bacterial colony counts and susceptibility to lomefloxacin and norfloxacin were determined for each isolated pathogen, using either the disk diffusion or the microbroth dilution method [9]. Lomefloxacin 10 μg and norfloxacin 10 μg susceptibility disks were used. Pathogens were considered resistant to lomefloxacin or norfloxacin if they had zone diameters of ≤ 15 mm or ≤ 12 mm, respectively. Organisms with MIC values ≥ 16 $\mu\text{g/mL}$

were considered resistant to lomefloxacin, and organisms with MIC values ≥ 32 $\mu\text{g/mL}$ were considered resistant to norfloxacin.

Efficacy Assessment

Bacteriologic results were defined as: "cure," sterile urine culture (containing $\leq 10^4$ CFU/mL of the baseline pathogen) after 2–4 days of therapy that remained sterile at 5–9 days post-therapy; "cure with superinfection," elimination of the original pathogen ($\leq 10^4$ CFU/mL) at days 2–4 during therapy and 5–9 days post-therapy, with appearance of a different pathogen; or "persistence," original pathogen $> 10^4$ CFU/mL at days 2–4 during therapy or at 5–9 days post-therapy. Both "cure" and "cure with superinfection" were considered bacteriologic "eradication."

Assessment of clinical outcome was based on comparison of the severity grade of signs and symptoms before therapy and 5–9 days post-therapy. Results were defined as: "cure," resolution of all baseline signs and symptoms; "improvement," decrease of at least one severity grade in one or more baseline signs or symptoms with none worsening; or "failure," no change or worsening of baseline signs and symptoms. Both "cure" and "improvement" were considered "success."

Safety Assessment

In order to monitor patient safety, blood chemistry analyses, complete blood cell counts, and urinalysis were performed at each visit, and physical examination was repeated at the end of the study. Patients were monitored for the development of adverse events. Patients at 13 of 27 study sites kept diaries of adverse events. All treatment-emergent events were reported with the investigator's assessment of drug attribution.

Statistical Methodology

Statistical analyses were performed using SAS version 5.18 [10] and BMDP 1988 version [11]. Statistical significance was set at the 0.05 level. The Cochran-Mantel-Haenszel test was used to determine whether differences between treatments in clinical success rates and bacteriologic eradication rates exist when treatment effects are adjusted for study effects [12]. Logistic regression analyses were performed to analyze further study effect, treatment effect, age and sex effects, and study-by-treatment interaction on the bacteriologic outcome results.

RESULTS

Study Population

A total of 727 patients were enrolled in the study at 27 sites throughout the United States. Of these,

370 (51%) received lomefloxacin (350 female, 20 male) and 357 (49%) received norfloxacin (339 female, 18 male). The median age of the patients was 33 years (range, 17–87) in the lomefloxacin group and 32 years (range, 18–96) in the norfloxacin group. Each patient presented with various combinations of dysuria, frequency, suprapubic pain, loin pain, pyuria, and hematuria. Patient demographic characteristics and baseline clinical and laboratory findings are shown in **Table I**. There were no statistically significant differences in demographic characteristics, clinical presentation, urinary findings, or the severity of the clinical symptoms between the two treatment groups.

Patient Evaluability

Of the 727 patients enrolled and randomized to treatment groups, 264 in the lomefloxacin group and 249 in the norfloxacin group had significant pretherapy bacteriuria ($\geq 10^5$ CFU/mL of urine). Of these, 220 patients in the lomefloxacin group and 216 in the norfloxacin group returned for the 5–9 day post-therapy evaluation, met all the evaluability criteria, and were thus considered evaluable for determination of bacteriologic and clinical efficacy. Reasons for patient unevaluability are shown in **Table II**.

Baseline Pathogens

All pathogens isolated at baseline were susceptible in vitro to both drugs except for two strains of Group D streptococci resistant to lomefloxacin, and one strain resistant to norfloxacin. Four lomefloxacin and nine norfloxacin patients each had more than one pretherapy isolate ($\geq 10^5$ CFU/mL of urine); thus, the number of isolates reported may exceed the number of patients in a given group. From the evaluable lomefloxacin and norfloxacin patients, 225 and 224 bacterial strains, respectively, were isolated prior to therapy. The most common isolates were *Escherichia coli* (78.0%), *Proteus mirabilis* (8.0%), *Staphylococcus saprophyticus* (4.9%), and *Klebsiella pneumoniae* (2.9%).

Bacteriologic Efficacy

At 5–9 days post-therapy, eradication (defined as cure or cure with superinfection) of the baseline pathogens occurred in 98.2% of evaluable patients in the lomefloxacin group and 96.4% of the norfloxacin group. In the lomefloxacin group, 174 of 177 *E. coli* (98.3%), two of three *Enterobacter* spp. (66.7%), and 100% of the remaining urinary isolates were eradicated. In the norfloxacin group, the eradication rates were 97.1% (168/173) for *E. coli*, 85.7% (6/7) for *K. pneumoniae*, 83.3% (5/6) for *Staphylococcus* spp., 50% (1/2) for *Serratia* spp.,

TABLE I

Patient Demographics and Baseline Clinical and Laboratory Findings

	Lomefloxacin 370 Patients	Norfloxacin 357 Patients
Age (years)		
Median (range)	33 (17–87)	32 (18–96)
Weight (kg)		
Median (range)	64 (42.2–154.9)	64 (35.4–169.2)
Race		
Caucasian	331 (89%)	324 (91%)
Black	16 (4%)	19 (5%)
Other	23 (7%)	14 (4%)
Sex		
Female	350 (95%)	339 (95%)
Male	20 (5%)	18 (5%)
Signs and symptoms		
Suprapubic tenderness	221 (60%)	213 (60%)
Costovertebral angle tenderness	65 (18%)	82 (23%)
Pyuria*	295 (80%)	286 (80%)
Hematuria*	152 (41%)	150 (42%)
Severity of symptoms†		
Mild	122 (33%)	121 (34%)
Moderate	233 (63%)	226 (63%)
Severe	15 (4%)	10 (3%)

* >1 white or red blood cell count/high-power field unspun urine or >5 white or red blood cell count/high-power field spun urine.

†Symptoms graded as mild if usual activities not limited, moderate if usual activities somewhat limited, and severe if usual activities precluded.

TABLE II

Reasons for Patient Failure to Meet Evaluability Criteria

	Lomefloxacin 370 Patients	Norfloxacin 357 Patients
Patients with pretherapy urine culture $\geq 10^5$ CFU/mL	264	249
Evaluable patients	220	216
Nonevaluable patients	150	141
Primary reason for unevaluability		
No growth, low counts or missing baseline culture	106	108
Drug not started within 48 hours of baseline culture; 5–9 day post-therapy evaluation not done or not performed on time; concomitant antimicrobial	35	28
Bacteria resistant or not tested*	9	5

CFU = colony-forming units.

*Pathogen resistant to lomefloxacin ($n = 2$) or norfloxacin ($n = 1$), or not tested ($n = 11$).

and 100% for the remaining urinary isolates (**Table III**). The difference in bacteriologic eradication rates for the lomefloxacin and norfloxacin groups was not statistically significant (**Table IV**). Superinfection occurred in two patients in the lomefloxacin group (with *Staphylococcus* spp. and *Streptococcus agalactiae*), and in six patients in the norfloxacin group (with Group D *Streptococcus*, *Streptococcus* spp., and *Acinetobacter calcoaceticus*). Of the strains causing superinfection, the *S. agalactiae* isolate was resistant to lomefloxacin, and the *A. calcoaceticus* isolate was resistant to norfloxacin. The differences between the two groups were not statistically significant.

TABLE III

Eradication of Baseline Pathogens at 5–9 Days Post-therapy in Evaluable Patients

Organism	Lomefloxacin 220 Patients		Norfloxacin 216 Patients	
	Pretherapy Isolates n	Eradicated n (%)	Pretherapy Isolates n	Eradicated n (%)
<i>Escherichia coli</i>	177	174 (98.3)	173	168 (97.1)
<i>Proteus mirabilis</i>	20	20 (100)	16	16 (100)
<i>Staphylococcus saprophyticus</i>	9	9 (100)	13	13 (100)
<i>Klebsiella pneumoniae</i>	6	6 (100)	7	6 (85.7)
<i>Citrobacter</i> species	4	4 (100)	2	2 (100)
Other <i>Staphylococcus</i> species	2	2 (100)	6	5 (83.3)
<i>Enterobacter</i> species	3	2 (66.7)	3	3 (100)
Enterococci	1	1 (100)	2	2 (100)
<i>Pseudomonas aeruginosa</i>	1	1 (100)	0	0
<i>Serratia</i> species	2	2 (100)	2	1 (50)
Total	225*	221 (98.2)	224*	216 (96.4)

*Multiple pretherapy isolates in some patients (see text).

Clinical Efficacy

At 5–9 days post-therapy, clinical success was noted in 99.1% of the lomefloxacin group and in 93.5% of the norfloxacin group (Table IV). The difference in clinical success rates for lomefloxacin and norfloxacin patients was statistically significant ($p = 0.002$).

Outcome in Men

Men comprised 5% of each treatment group. The median age of men was 53 (range, 18–79) years and 45 (range, 20–74) years in the lomefloxacin and norfloxacin groups, respectively. The bacteriologic eradication rates in men were 100% (10/10) for lomefloxacin-treated patients and 90.9% (10/11) for patients treated with norfloxacin, and the clinical success rate was 100% for each group.

TABLE IV

Clinical and Bacteriologic Responses at 5–9 Days Post-therapy in Evaluable Patients

Therapeutic Outcome	Lomefloxacin 220 Patients n (%)	Norfloxacin 216 Patients n (%)
Bacteriologic		
Eradication*	216 (98.2)	208 (96.3)
Cure	214 (97.3)	202 (93.5)
Cure with superinfection	2 (0.9)	6 (2.8)
Persistence	4 (1.8)	8 (3.7)
Clinical†		
Success‡	218 (99.1)	202 (93.5)
Cure	194 (88.2)	176 (81.5)
Improvement	24 (10.9)	26 (12.0)
Failure	2 (0.9)	13 (6.0)

*Eradication = cure + (cure with superinfection).

†Clinical outcome data missing for one norfloxacin patient.

‡Success = cure + improvement.

Bacteriologic and Clinical Results in "Intent-to-Treat" Patients

An additional analysis of treatment results included patients who did not meet all evaluability criteria described previously. The results for these intent-to-treat patients are reported in Table V. At 5–9 days post-therapy, bacteriologic cure and eradication rates were 96.8% and 98.0%, respectively, in the lomefloxacin group and 93.8% and 96.3%, respectively, in the norfloxacin group (p values not calculated). The logistic regression analyses (Cochran-Mantel-Haenszel test) showed that there was no statistically significant contribution to the bacteriologic outcome for the pooled data made by age ($p = 0.86$) or sex ($p = 0.75$). At 5–9 days post-therapy, clinical cure and success were achieved in 83.6% and 97.5%, respectively, of the lomefloxacin group, and in 77.0% and 92.8%, respectively, of the norfloxacin group (p values not calculated). The overall bacteriologic and clinical outcomes of the "intent-to-treat" patients were comparable to those achieved for the evaluable patients in each treatment group.

Adverse Events

Adverse events were reported by 157 of 370 patients in the lomefloxacin group and in 129 of 357 patients in the norfloxacin group. The number of patients with adverse events probably attributable to drug treatment was 41 (11.1%) in the lomefloxacin group and 27 (7.6%) in the norfloxacin group. The most commonly reported adverse events were nausea, headache, dizziness, photosensitivity reactions, and diarrhea. Adverse events occurring in >1% of the patients are shown in Table

TABLE V

Clinical and Bacteriologic Response at 5–9 Days Post-therapy in "Intent-to-Treat" Patients

Therapeutic Outcome	Lomefloxacin n (%)	Norfloxacin n (%)
Bacteriologic		
Number of patients with known outcome	252 (100)	242 (100)
Eradication*	247 (98.0)	233 (96.3)
Cure	244 (96.8)	227 (93.8)
Cure with superinfection	3 (1.2)	6 (2.5)
Persistence	5 (2.0)	9 (3.7)
Clinical		
Number of patients with known outcome	324 (100)	305 (100)
Success†	316 (97.5)	283 (92.8)
Cure	271 (83.6)	235 (77.0)
Improvement	45 (13.9)	48 (15.7)
Failure	8 (2.5)	22 (7.2)

*Eradication = cure + (cure with superinfection).

†Success = cure + improvement.

VI. The incidence of dizziness, tremor, and photosensitivity was higher in the lomefloxacin group, whereas the incidence of nausea was higher in the norfloxacin group. Adverse events were generally mild to moderate, innocuous, and transient. The majority of them subsided while the medication was continued or soon after therapy was completed. Treatment was discontinued in eight lomefloxacin (2.2%) and three norfloxacin (0.8%) patients for adverse events probably attributable to the study drugs. The most common adverse events resulting in withdrawal of patients from study participation were dizziness, nausea, and rash (Table VII).

A number of statistically significant changes from baseline were observed in each treatment group for the laboratory parameters tested. However, they were either not clinically significant or were consistent with amelioration of an acute infection.

COMMENT

The results of the multicenter trials reported here demonstrate that a 7–10 day course of lomefloxacin (400 mg once daily) compares favorably with norfloxacin (400 mg twice daily) in the treatment of urinary tract infections in adult outpatients. The diversity of the patient population in these studies reflects the wide variety of sites enrolling patients (student health care centers, university-affiliated clinics, Veterans Administration hospitals, nonacademic health facilities, and private practices) and permits extrapolation of the results to the wide range of patients likely to be treated for urinary tract infections in general practice. The overall results of the present study are excellent and corroborate recent clinical studies conducted in adult outpatients with uncomplicated urinary tract infections [13–22].

TABLE VI

Comparison of Adverse Events with Incidence of >1% (Regardless of Attribution to Study Drug)

	Lomefloxacin 370 Patients n (%)	Norfloxacin 357 Patients n (%)
Gastrointestinal system		
Nausea	26 (7.0)	34 (9.5)
Diarrhea	10 (2.7)	8 (2.2)
Abdominal pain	8 (2.2)	7 (2.0)
Dyspepsia	4 (1.1)	6 (1.7)
Constipation	4 (1.1)	3 (0.8)
Vomiting	2 (0.5)	4 (1.1)
Central/peripheral nervous system		
Headache	33 (8.9)	29 (8.1)
Dizziness	26 (7.0)	6 (1.7)
Tremor	8 (2.2)	—
Leg cramps	4 (1.1)	2 (0.6)
Skin and appendages		
Photosensitivity	18 (4.9)	—
Pruritus, genital	10 (2.7)	6 (1.7)
Increased sweating	4 (1.1)	—
Rash	4 (1.1)	4 (1.1)
Whole body		
Back pain	4 (1.1)	9 (2.5)
Asthenia	4 (1.1)	1 (0.3)
Respiratory system		
Upper respiratory tract infection	7 (1.9)	6 (1.7)
Psychiatric		
Nervousness	6 (1.6)	—
Somnolence	2 (0.5)	4 (1.1)
Reproductive (female)		
Vaginitis	6 (1.6)	6 (1.7)
Dysmenorrhea	—	4 (1.1)
Liver		
SGPT increase	—	7 (2.0)
SGOT increase	1 (0.3)	5 (1.4)
Resistance mechanism disorder		
Moniliasis	5 (1.4)	3 (0.8)

SGOT = serum glutamic oxaloacetic transaminase; SGPT = serum glutamic pyruvic transaminase.

TABLE VII

Adverse Events with Probable Attribution to Study Drug in Patients Withdrawn from Treatment

	Lomefloxacin 370 Patients n (%)	Norfloxacin 357 Patients n (%)
Number of patients withdrawn		
For any adverse event	15 (4.1)	5 (1.4)
For adverse event probably attributable to study drug	8 (2.2)	3 (0.8)
Number of adverse events*		
Dizziness	4	—
Nausea	2	1
Nervousness	1	—
Headache	1	1
Respiratory disorder	1	—
Abdominal pain	1	—
Photosensitivity reaction (one bullous eruption)	2	—
Pruritus	1	—
Edema	1	1
Depression	1	—
Rash	1	2
Insomnia	1	—
Increased sweating	1	—
Abnormal vision	1	—
Vomiting	—	1

*Some patients experienced more than one adverse event.

The types of urinary isolates were in agreement with those previously reported for acute uncomplicated urinary tract infections in adults [14–16,18,23]. The most common urinary pathogens in evaluable patients were *E. coli* (78.0%), *P. mirabilis* (8.0%), *S. saprophyticus* (4.9%), and *K. pneumoniae* (2.9%). Except for two streptococcal isolates, all baseline pathogens were susceptible in vitro to both lomefloxacin and norfloxacin.

The clinical success rate for the evaluable patients in the lomefloxacin group (99.1%) was significantly higher than that in norfloxacin group (93.5%; $p = 0.002$). The bacteriologic eradication rate for evaluable patients in the lomefloxacin group (98.2%) was comparable to that in the norfloxacin group (96.3%; $p = \text{nonsignificant}$). Therapeutic efficacy was similarly achieved in both treatment groups regardless of patient age or sex. The bacteriologic outcome and clinical response of the intent-to-treat patients in both treatment groups were comparable to those of the evaluable patients. The overall results of the present study compared favorably with those reported for new quinolones, cephalosporins, and trimethoprim/sulfamethoxazole [14–16,18,19,21,22,24,25].

Both drugs were generally well tolerated. Adverse events considered by the investigators to be probably attributable to the study drugs occurred in 11.1% of lomefloxacin-treated patients and 7.6% of the norfloxacin group. The adverse event profiles for lomefloxacin and norfloxacin were similar and in agreement with those associated with newer quinolones [13,16,20,24–27]. These events were generally mild to moderate, transient, did not require remedial medications, and disappeared during therapy or when therapy was stopped. The difference in the percentage of patients who discontinued therapy because of adverse events probably related to the study drug (2.2% and 0.8%, respectively, in the lomefloxacin and norfloxacin groups) and changes in the safety laboratory tests were not clinically significant between the two treatment groups.

Because of increasing bacterial resistance to the more commonly used antimicrobials, quinolones may well prove to be effective and useful agents for the treatment of urinary tract infections. Lomefloxacin's safety profile, broad spectrum of antibacterial activity, and prolonged half-life confirm the potential value of lomefloxacin as a new oral antimicrobial agent. Lomefloxacin, with a once-daily regimen, should improve patient compliance, thus increasing treatment success.

ACKNOWLEDGMENT

These multicenter trials were conducted by the following principal investigators: Paul Black, M.D. (San Diego, California), Kim Burch, M.D. (Menomonee Falls, Wisconsin),

sin), Dave Colan, M.D. (Grand Island, Nebraska), Harry Collins, M.D. (Edison, New Jersey), Kathie Cronin, M.D. (Modesto, California), R. Whitney Curry, M.D. (Gainesville, Florida), Linda Dorzab, M.D. (Kansas City, Missouri), David Faust, D.O. (Oconomowoc, Wisconsin), Lawrence Ferraro, D.O. (Bridgewater, New Jersey), Larry I. Gilderman, D.O. (North Miami, Florida), David Ginsberg, D.O. (Harleysville, Pennsylvania), Leonard Goldberg, M.D. (Sunnyvale, California), Stephen F. Gordon, M.D. (Atlanta, Georgia), Claude B. Goswick, M.D. (College Station, Texas), Michael Grossman, M.D. (Phoenix, Arizona), Kenneth R. Hutchins, M.D. (Charlotte, North Carolina), Abdollah Iravani, M.D. (Gainesville, Florida), Merlin Kampfer, M.D. (Phoenix, Arizona), Christopher Koeppl, M.D. (Rhineland, Wisconsin), Sergio Mather, M.D. (Fort Myers, Florida), Mila Means, M.D. (Wichita, Kansas), Benjamin G. Newman, M.D. (Altamonte Springs, Florida), Robert K. NimLos, M.D. (Sun City West, Arizona), Michael I. Opiari, D.O. (Warren, Michigan), Mark Rubright, M.D. (Longmont, Colorado), Gilbert Solomon, M.D. (Tarzana, California), and Michael Wood, M.D. (Aurora, Illinois).

The author would like to thank Lisa Duncanson, Lee Stutevoss, and Elizabeth Patrick for their technical assistance and help in the preparation of this manuscript.

REFERENCES

1. Wise R, Andrews JM, Ashby JP, Matthews RS. In vitro activity of lomefloxacin, a new quinolone antimicrobial agent, in comparison with those of other agents. *Antimicrob Agents Chemother* 1988; 32: 617–22.
2. Hirose T, Okezaki E, Kato H, Ito Y, Inoue M, Mitsuhashi S. In vitro and in vivo activity of NY-198, a new difluorinated quinolone. *Antimicrob Agents Chemother* 1987; 31: 57–62.
3. Chin N-X, Novelli A, Neu HC. In vitro activity of lomefloxacin (SC-47111; NY-198), a difluoroquinolone 3-carboxylic acid, compared with those of other quinolones. *Antimicrob Agents Chemother* 1988; 32: 656–62.
4. Clarke AM, Zemcov SJV. Comparative in vitro activity of lomefloxacin, a new difluoroquinolone. *Eur J Clin Microbiol Infect Dis* 1989; 8: 164–8.
5. Morrison PJ, Mant TGK, Norman GT, Robinson J, Kunka RL. Pharmacokinetics and tolerance of lomefloxacin after sequentially increasing oral doses. *Antimicrob Agents Chemother* 1988; 32: 1503–7.
6. Schentag JJ, Nix DE, Wise R. Pharmacokinetics and tissue penetration of the quinolones. In: Siporin C, Heifetz CL, Domagala JM, eds. *The new generation of quinolones*. New York: Marcel Dekker, 1990; 189–222.
7. Edwards PR, Ewing WH. *Identification of Enterobacteriaceae*, 3rd ed. Minneapolis: Burgess Publishing Co., 1972; 3: 7–47.
8. Schoenkecht FD, Sabath LD, Thornsberry C. In: *Manual of clinical microbiology*, 4th ed. Washington, DC: American Society for Microbiology, 1985; 1000–4.
9. Bauer ACO, Kirby WMM, Sherry JL, Turck M. Antibiotic susceptibility testing by a standardized single dose method. *Am J Clin Pathol* 1966; 45: 493–6.
10. SAS Institute. *SAS user's guide: statistics*, 5th ed. Cary, North Carolina: SAS Institute, 1985; 956.
11. BMDP Statistical software manual and software release. Berkeley: University of California Press, 1988; 605–10.
12. Fleiss J. *Statistical methods for rates and proportions*. 2nd ed. New York: John Wiley & Sons, 1981; 119–23.
13. Goldstein EJ, Kahn RM, Alpert ML, Ginsberg BP, Greenway FL, Citron DM. Ciprofloxacin versus cinoxacin in therapy of urinary tract infections. *Am J Med* 1987; 82(4A): 284–7.
14. Iravani A, Richard GA. Amoxicillin-clavulanic acid versus cefaclor in the treatment of acute urinary tract infections and their effect on the urogenital and rectal flora. *Antimicrob Agents Chemother* 1986; 29: 107–11.
15. Iravani A, Richard GA, Baer H. Treatment of uncomplicated urinary tract infections with trimethoprim versus sulfisoxazole, with special reference to antibody-coated bacteria and fecal flora. *Antimicrob Agents Chemother* 1981; 19: 842–50.
16. Childs SJ. Tissue penetration and clinical efficacy of enoxacin in urinary tract infections. *Clin Pharmacokinet* 1989; 16 (Suppl 1): 32–7.
17. Selin LK, Godfrey KM, Thomson MJ, Kennedy JK, Urias BA, Ronald A. Comparison of norfloxacin versus nalidixic acid in therapy of acute urinary tract infections. *Can J Infect Dis* 1990; 1: 35–40.
18. Iravani A, Richard GA, Johnson D, Bryant A. A double-blind, multicenter comparative study of the safety and efficacy of cefixime versus amoxicillin in the treatment of acute urinary tract infection in adult patients. *Am J Med* 1988; 85 (Suppl 3A): 17–25.
19. Haase DA, Harding GKM, Thomson MJ, Kennedy JK, Urias BA, Ronald AR. Comparative trial of norfloxacin and trimethoprim-sulfamethoxazole in the treatment of women with localized, acute, symptomatic urinary tract infections and antimicrobial effect on periurethral and fecal microflora. *Antimicrob Agents Chemother* 1984; 26: 481–4.

20. Monk JP, Campoli-Richards DM. Ofloxacin. A review of its antibacterial activity, pharmacokinetic properties and therapeutic use. *Drugs* 1987; 33: 346-91.
21. Malinverni R, Glauser MP. Comparative studies of fluoroquinolones in the treatment of urinary tract infections. *Rev Infect Dis* 1988; 10: S153-3.
22. Sabbaj J, Hoagland VL, Shih WJ. Multiclinic comparative study of norfloxacin and trimethoprim-sulfamethoxazole for treatment of urinary tract infections. *Antimicrob Agents Chemother* 1985; 27: 297-301.
23. Iravani A. Urinary tract infections: epidemiology and therapeutic approaches. Royal Society of Medicine Services Limited. ICSS 1987; 127: 25-33.
24. Iravani A, Richard G. A double blind comparison of ciprofloxacin (BAY O9867) and cinoxacin in treatment of acute urinary tract infections (UTIs) [Abstract]. 27th Interscience Conference on Antimicrobial Agents and Chemotherapy 1987; 148; A296.
25. Iravani A. Safety and efficacy of oral temafloxacin compared to trimethoprim-sulfamethoxazole in patients with uncomplicated urinary tract infections [Abstract No. 68]. Seventh Mediterranean Congress of Chemotherapy, May 1990, Barcelona, Spain.
26. Boyko EJ, Iravani A, Silverman MH, Schelling DJ, Wright RA. A randomized, controlled trial of a 10-day course of amifloxacin versus trimethoprim-sulfamethoxazole in the treatment of acute, uncomplicated urinary tract infection. *Antimicrob Agents Chemother* 1990; 34: 665-8.
27. Hooton TM, Latham RH, Wong ES, Johnson C, Roberts PL, Stamm WE. Ofloxacin versus trimethoprim-sulfamethoxazole for treatment of acute cystitis. *Antimicrob Agents Chemother* 1989; 33: 1308-12.