Clinical Perspectives on New Antimicrobials: Focus on Fluoroquinolones

David A. Talan

Department of Medicine, Divisions of Emergency Medicine and Infectious Diseases, University of California, Los Angeles, and Olive View–UCLA Medical Center, Sylmar, California

Respiratory tract infections are the most common infectious presentation in the community and hospital settings and are a major cause of morbidity and mortality worldwide. Recently, newer fluoroquinolones have been recommended for the treatment of these infections. Among them, moxifloxacin shows improved activity against gram-positive pathogens, has maintained potency against gram-negative organisms, and shows activity against atypical pathogens and anaerobes. Moxifloxacin also has excellent in vitro activity against strains resistant to penicillin, erythromycin, and other fluoroquinolones, such as levofloxacin. Moxifloxacin has demonstrated clinical efficacy rates of 90%–95% in clinical trials in community-acquired pneumonia, acute exacerbations of chronic bronchitis, and acute sinusitis. In these trials, moxifloxacin demonstrated no serious or unexpected adverse effects. Development of resistance appears to be slower for moxifloxacin than for several other fluoroquinolones, making moxifloxacin a good treatment choice. The pharmacodynamics of moxifloxacin support once-daily oral therapy of short duration, providing convenience, compliance, and safety advantages.

Acute respiratory tract infections (ARTIs) are a major cause of death globally and are responsible for 8% of the total burden of disability and premature death worldwide [1]. ARTIs kill 4 million children annually in developing countries [1], and in developed countries, respiratory infections place heavy demands on health care services and are also a leading cause of morbidity. Changing demographics in the United States, such as mobile and aging populations, shifting immigration patterns, and a growing pool of immunodeficient hosts (patients with HIV infection, patients with cancer who are undergoing chemotherapy, and transplant patients), have resulted in a high prevalence of ARTIs. They account for 20% of medical consultations, 30% of absences from work, and 75% of all antibiotic prescriptions [1]. Among ARTIs, pneumonia is a major cause of morbidity and mortality in the United States. Four million cases are estimated to occur annually, the majority of which are acquired in the community. Mortality is 10%–25% for community-acquired pneumonia (CAP) and approaches 50% for hospital-acquired pneumonia (HAP) [2, 3].

The economic cost of respiratory infections is high, taking into account physician and hospital visits, time lost at work, the impact on normal daily activities, and the cost of treatment. Treatment costs for CAP in the United States in 1998 were $8.4 billion [4], and predicted current treatment costs for acute exacerbations of chronic bronchitis (AECB) in 1999 are $1.2 billion [5]. The most recent reliable data on the treatment costs associated with sinusitis come from 1996, when overall health care expenditures were $5.8 billion, with the primary diagnosis of chronic or acute sinusitis accounting for $3.5 billion (59%) [6].

BACTERIAL PATHOGENS IN ARTIs AND ANTIMICROBIAL TREATMENT

A variety of bacterial species are associated with ARTIs, including gram-positive, gram-negative, and atypical...
The most common pathogens in CAP, HAP, AECB, and sinusitis include *Streptococcus pneumoniae*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, Legionella species, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* [7–9]. The flora in HAP changes with length of hospitalization and can include enteric gram-negative bacteria. The most common cause of pneumonia is *S. pneumoniae*; this pathogen is also commonly found in patients with AECB and sinusitis [10, 11]. *H. influenzae* is the most prevalent bacterial pathogen in AECB, and, together with *S. pneumoniae* and *M. catarrhalis*, it accounts for >80% of all bacterial exacerbations [11].

Because of cost considerations and specimen collection difficulties, primary care physicians seldom attempt to identify the causative pathogen in AECB and sinusitis. In CAP, bacteriological identification of the etiologic agent is not always performed, and even if aggressive diagnostic testing is carried out, a pathogen may not always be isolated. Treatment is therefore necessarily empiric. Guidance in empiric management is provided in statements released by various bodies such as the American Thoracic Society [12] and the Infectious Diseases Society of America [13, 14]. However, these guidelines are not always consistent and are based on national trends in resistance, whereas local resistance rates may be very different from the national average.

### ANTIMICROBIAL RESISTANCE

One of the difficulties in establishing treatment guidelines is the growing problem of antimicrobial resistance. Resistance to β-lactam drugs is widespread both in gram-positive and gram-negative bacteria, with resistance to macrolides, tetracycline, and trimethoprim-sulfamethoxazole (TMP-SMX) increasing and resistance to some fluoroquinolones emerging. In 1998, in the United States, the overall rate of *S. pneumoniae* strains showing resistance to penicillin was 29.5%, with 19 of 24 study centers showing increased resistance rates of 2.9% over the previous 3-year interval to 39.2%. Similar increases in rates of resistance were observed with other antimicrobial agents [15]. Multidrug resistance (defined as lack of susceptibility to penicillin and at least 2 other non-β-lactam classes of agents) was observed in 16% of *S. pneumoniae* strains [15]. The rates of penicillin resistance in *S. pneumoniae* have been shown to vary significantly from state to state, with 38% of strains showing reduced susceptibility in Tennessee versus 15% in Maryland [16]. Recently, reduced susceptibility to ciprofloxacin and other fluoroquinolones was also reported in *S. pneumoniae* strains isolated in Canada [17]. Other respiratory pathogens show similar trends. Almost 40% of *H. influenzae* strains collected from across the United States are resistant to ampicillin, with a growing number (4.5%) also insensitive to clavulanic acid [18], indicating that in addition to β-lactamases, alterations in penicillin-binding proteins contribute to resistance. In recent surveys in the United States, >90% of *M. catarrhalis* strains were found to produce β-lactamases [19–21].

Whether or not resistance has an impact in the clinical setting and at what point empiric treatment becomes ineffective are key issues. Successful treatment of resistant pathogens appears to be related to the ability to achieve high drug levels in the serum and at the site of infection. Penicillin or ampicillin is likely to be ineffective for penicillin-resistant pneumococcal infections of the central nervous system because of the low drug concentrations achieved at this site, and the same holds true for chloramphenicol [22]. However, penicillin concentrations achievable in serum are much higher, and intermediate resistant pneumococci are likely to be successfully eradicated [23]. Patients with bacteremic pneumococcal pneumonia have been shown to be effectively treated with β-lactam agents [24]. Recent data from Garau et al. [25] have shown that macrolide therapy has failed in 20 cases of macrolide-resistant *S. pneumoniae* infections, leading to pneumococcal bacteremia.

Resistance in vitro may not preclude usage of a drug for treatment. However, treatment failures with various antimicrobial agents have been reported in a variety of bacterial infections caused by resistant pathogens. Several cases of pneumococcal meningitis due to multidrug-resistant pneumococci failed to respond to conventional therapy with penicillin, chloramphenicol, or ceftriaxone [26]. It has been proposed that children with highly resistant pneumococcal meningitis not be treated with cefotaxime or ceftriaxone [27]. Bacteriologic and clinical failure was found in 38% of children with acute otitis media caused by *H. influenzae* who were treated with amoxicillin–clavulanic acid [28]. Both levofloxacin and ofloxacin were found to be associated with failures in the treatment of gonococcal urethritis [29, 30]. Levofloxacin was also associated with failure in 3 cases of pneumococcal respiratory tract infections [31] and also with pneumonia due to *M. catarrhalis* [32].

Recently, a case of fatal bacteremia and meningitis was reported despite treatment with levofloxacin [33]. For *Escherichia coli*, the most commonly encountered uropathogen, current resistance patterns indicate that nearly 40% of urinary tract isolates are resistant to ampicillin and resistance to TMP-SMX is approaching 20% (Bayer, data on file) [34]. Significantly, in vitro resistance to TMP-SMX has been strongly associated with bacteriologic and clinical failure in patients with pyelonephritis [35]. Furthermore, aside from clinical failures, infections caused by resistant strains have an increased likelihood of being treated with inappropriate initial therapy, which has been shown to be a predictor for a poor prognosis in severe CAP [36].

Treatment failures have an impact not just on the patient but also on the health care system as a whole, prolonging illness and leading to increased health care costs. A recent study in
the United States in premenopausal women with acute uncomplicated pyelonephritis demonstrated that *E. coli*, which caused >90% of infections, was more frequently resistant to TMP-SMX (18%) than to ciprofloxacin (0%), resulting in increased clinical failures (table 1). Because of the increased failures, TMP-SMX–treated patients required additional medical resources (table 2), driving up costs substantially, with the mean total cost per TMP-SMX–treated patient, at $687, which is 29% higher than the cost ($531) for the ciprofloxacin-treated patients [35].

There is clearly a need for the development and evaluation of new antimicrobials. Several new antimicrobial agents have been designed to combat these resistant pathogens. These agents include linezolid (an oxazolidinone), quinupristin-dalfopristin, ketolides, and the methoxyquinolones. Important considerations for using these novel agents include their proven clinical efficacy, decreased likelihood of developing resistance over time, ease of use, relative safety, and cost.

### FLUOROQUINOLONES

Until the development of the newer fluoroquinolones, this class of antimicrobial agents did not have reliable activity against gram-positive bacteria and was not considered suitable, for example, for the empiric treatment of pneumococcal pneumonia. It was not until the advent of the newer fluoroquinolones such as moxifloxacin and gatifloxacin that excellent activity against gram-positive pathogens was achieved. Levofoxacin has been approved for the treatment of penicillin-resistant *S. pneumoniae*. The fluoroquinolones exert their effect by binding to the enzymes DNA gyrase and topoisomerase IV, which are involved in DNA replication [37]. Development of resistance has been shown to arise by stepwise accumulation of mutations in the enzyme targets [38, 39] and also through active efflux [40, 41].

The most common adverse effects of the fluoroquinolones involve the gastrointestinal tract, skin, and central nervous system, with nausea and vomiting being the most common (event

### Table 1. Continued bacteriologic and clinical cure rates stratified by oral or iv administration of the first dose of antimicrobial in women with acute uncomplicated pyelonephritis.

<table>
<thead>
<tr>
<th>Response</th>
<th>Ciprofloxacin group, a n (%)</th>
<th>TMP-SMX group, b n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oral</td>
<td>iv</td>
</tr>
<tr>
<td>Bacteriologic cure through 4–11 d after therapy</td>
<td>75 (100)</td>
<td>37 (97)</td>
</tr>
<tr>
<td>Bacteriologic cure through 22–48 d after therapy</td>
<td>60 (83)</td>
<td>34 (87)</td>
</tr>
<tr>
<td>Clinical cure through 4–11 d after therapy</td>
<td>72 (96)</td>
<td>37 (98)</td>
</tr>
<tr>
<td>Clinical cure through 22–48 d after therapy</td>
<td>63 (89)</td>
<td>33 (94)</td>
</tr>
</tbody>
</table>

**NOTE.** Data include patients with eradication of the initially infecting strain and absence of recurrent infection or continued clinical cure, not requiring alternative antimicrobial therapy through the visits after therapy. See [35]. TMP-SMX, trimethoprim-sulfamethoxazole.

a Ciprofloxacin, 500 mg b.i.d. 7 d, ± an initial iv dose of ciprofloxacin, 400 mg.

b TMP-SMX, 160 and 180 mg, respectively, oral b.i.d. for 14 d, ± an initial iv dose of ceftriaxone, 1 g.

### Table 2. Additional medical resource use for women by treatment group.

<table>
<thead>
<tr>
<th>Resources</th>
<th>Ciprofloxacin group (n = 191)</th>
<th>TMP-SMX group (n = 187)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital stay, d</td>
<td>20.9</td>
<td>38.0</td>
</tr>
<tr>
<td>Medical visits or telephone consultations</td>
<td>23.6</td>
<td>30.5</td>
</tr>
<tr>
<td>Radiological procedures</td>
<td>13.1</td>
<td>9.1</td>
</tr>
<tr>
<td>Other therapeutic procedures</td>
<td>3.7</td>
<td>6.4</td>
</tr>
<tr>
<td>Laboratory tests</td>
<td>33.0</td>
<td>72.7</td>
</tr>
<tr>
<td>Cultures</td>
<td>18.8</td>
<td>28.9</td>
</tr>
<tr>
<td>Antimicrobial prescriptions</td>
<td>47.1</td>
<td>57.2</td>
</tr>
</tbody>
</table>

**NOTE.** TMP-SMX, trimethoprim-sulfamethoxazole. See [35]. Values are rates per 100 intent-to-treat subjects for additional resources associated with failures and adverse drug events (i.e., excluding resources required for initial management and follow-up visits after therapy for patients who did not previously fail to respond to treatment).
rates of 3.8 to 4.9 per 1000 patients), similar to those for azithromycin and cefixime [42]. Adverse events are usually mild and reversible. In many cases, the adverse effects due to fluoroquinolone are related to the structure of fluoroquinolone—that is, the halogen at the 8 position increases potential phototoxicity (e.g., sparflloxacin), whereas the 2,4-difluorophenyl substituent at the 1 position unique to temafloxacin and trovaflloxacin may have played a role in the adverse effects that are specific to these agents [42].

An ideal antimicrobial for treatment of ARTIs should have high bactericidal activity against the most likely gram-positive, gram-negative, and atypical pathogens, good tissue penetration throughout the dosing period, and proven clinical efficacy in pneumonia, bronchitis, and sinusitis. In addition, the drug should have a low propensity for selecting resistance, ease of use, and no serious side effects. Of the newer fluoroquinolones, moxifloxacin fulfills these criteria, largely as a result of modifications in structure at both the C-7 and C-8 positions.

PHARMACOKINETICS, IN VITRO ACTIVITY, CLINICAL EFFICACY, AND SAFETY OF MOXIFLOXACIN

Moxifloxacin is a 6-fluoro-8-methoxy quinolone with potent activity against gram-positive, gram-negative, atypical, and anaerobic bacteria. The methoxy group at the C-8 position enhances anaerobic activity, results in a lower potential for phototoxicity, and enables moxifloxacin to bind simultaneously and equally at both DNA gyrase and topoisomerase IV enzymes [43, 44]. This unique mechanism of action, targeting both DNA sites in S. pneumoniae, renders the development of resistance extremely unlikely, because for resistance to occur, 2 simultaneous mutations at the DNA that codes for binding at these enzymes would have to develop in a single pathogen.

After a 400-mg dose of oral or iv moxifloxacin, the concentration in serum is close to 5 mg/L [45]. The drug concentrates in the bronchial tree at levels well above the typical MICs for all of the relevant bacterial pathogens seen in ARTIs for 24 h after dosing; concentrations 5 and 50 times higher than in serum are found in alveolar macrophages and bronchial mucosa, respectively [46, 47]. Mean absorption time is 2.4 h, with peak concentrations in serum and respiratory tissue remaining far in excess of the MICs for most organisms for >24 h after dosing [48]. This makes moxifloxacin a highly effective drug for bacterial eradication, particularly for respiratory pathogens.

In vitro studies of moxifloxacin have demonstrated excellent activity against S. pneumoniae strains with MICs <0.25 mg/L regardless of whether strains are resistant to penicillin or macrolides [49, 50]. In addition, S. pneumoniae strains with reduced susceptibility to other fluoroquinolones were found to be 8–32 times more susceptible to moxifloxacin, including strains with mutations in both topoisomerase IV and DNA gyrase enzymes—that is, fluoroquinolone-resistant strains [17]. Similarly, MICs were unchanged (0.06 mg/L) for β-lactamase–positive and –negative strains of H. influenzae and M. catarrhalis. Good bacterial activity was also demonstrated against atypical pathogens such as Legionella species, C. pneumoniae, and M. pneumoniae [49]. Activity against anaerobic bacteria was found to be comparable to that of metronidazole [51].

In >26 clinical trials with a design enforced by the US Food and Drug Administration, moxifloxacin performed at least as well as the comparator agents. A comparison of the efficacy of fluoroquinolones versus currently accepted therapy for CAP demonstrated that, in vitro, moxifloxacin and trovaflloxacin were the most potent of the fluoroquinolones, with 50% MIC of 0.125 mg/L against S. pneumoniae, regardless of the penicillin susceptibility status of the S. pneumoniae strains [50]. An evaluation of published data showed that the clinical cure rate among common CAP therapies was highest with moxifloxacin, levofloxacin, and clarithromycin, reaching cure rates of ≥95% of patients at the end of treatment and maintaining these results at follow-up (table 3) [52, 53]. Bacterial eradication with moxifloxacin has been shown to be superior to that of clarithromycin or moxifloxacin versus chloramphenicol-resistant H. influenzae, K. pneumoniae, and S. aureus and comparable for S. pneumoniae, M. pneumoniae, and other common pathogens [54].

In AECB, a meta-analysis of bacteriologic eradication rates from 2 large multicenter trials showed that moxifloxacin had a higher overall bacteriologic eradication rate for the 4 most commonly isolated pathogens (95% for S. pneumoniae, H. influenzae, H. parainfluenzae, and M. catarrhalis) compared with clarithromycin and cefuroxime (87% and 83%, respectively) [55]. Similarly, an evaluation of 4 published comparative fluoroquinolone clinical studies and 4 comparative moxifloxacin phase 3, multicenter, double-blind, registration studies showed that moxifloxacin, 400 mg once daily, achieved clinical success rates of approximately ≥95%, whereas the clinical success rates

<table>
<thead>
<tr>
<th>Antibacterial agent</th>
<th>Daily dose</th>
<th>Clinically evaluable patients, n</th>
<th>Efficacy, %</th>
<th>End of treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>3 g</td>
<td>150</td>
<td>87.3</td>
<td>84.3</td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>1 g</td>
<td>188</td>
<td>95</td>
<td>99</td>
<td></td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>500 mg</td>
<td>234</td>
<td>94.9</td>
<td>96.1</td>
<td></td>
</tr>
<tr>
<td>Sparfoxacin</td>
<td>200 mg</td>
<td>136</td>
<td>91.9</td>
<td>88.9</td>
<td></td>
</tr>
<tr>
<td>Greefafoxacin</td>
<td>600 mg</td>
<td>237</td>
<td>87</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>400 mg</td>
<td>194</td>
<td>97</td>
<td>95</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. See also [52].
of ciprofloxacin, grepafloxacin, levofloxacin, and trovafloxacin ranged from 77% to 90% (figure 1) [55].

Furthermore, moxifloxacin demonstrates an advantage of a once-daily dosing duration and a short 5-day treatment duration over comparators in the treatment of AECB. Five-day treatment with moxifloxacin, 400 mg, was shown to be clinically equivalent to 7-day treatment with clarithromycin, 500 mg, (94.4% vs. 93.8% and 89.1% vs. 88.4% for moxifloxacin and clarithromycin at days 7 and 14, respectively) and bacteriologically superior to clarithromycin (91% vs. 68% and 77% vs. 62% for moxifloxacin and clarithromycin at days 7 and 14, respectively) [56]. The 5- and 10-day courses were found to be clinically and bacteriologically equivalent to 10 days of clarithromycin [57]. Moxifloxacin, 400 mg for 5 days, has also been shown to be as effective (93%) as co-amoxiclavulanic acid (91%) for 7 days [55].

In the treatment of acute bacterial rhinosinusitis, results from both North American and European studies indicate that moxifloxacin given once daily for 7–10 days is clinically equivalent to other fluoroquinolones (ciprofloxacin, levofloxacin, sparfoxacin, and trovafloxacin), with moxifloxacin cure rates and bacteriological eradication rates of ≥90% [58]. Controlled trials of once-daily moxifloxacin versus twice-daily cefuroxime, a commonly used treatment for acute bacterial rhinosinusitis, showed similar results (90% clinical cure with moxifloxacin vs. 89% for cefuroxime) with comparable tolerability [59, 60]. Compared with patients treated with trovafloxacin, patients

Table 4. Summary of adverse experience with moxifloxacin: postmarketing surveillance and clinical studies to February 2000.

<table>
<thead>
<tr>
<th>Result</th>
<th>PSS, Germany (n = 5805), n (%)</th>
<th>26 clinical studies (n = 6178), n (%)</th>
<th>Comparators* (n = 4809), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with AE</td>
<td>261 (5)</td>
<td>2800 (45)</td>
<td>2088 (43)</td>
</tr>
<tr>
<td>Patients with ADR</td>
<td>119 (2)</td>
<td>1619 (26)</td>
<td>1129 (23)</td>
</tr>
<tr>
<td>Patients with serious ADR</td>
<td>14 (&lt;1)</td>
<td>34 (&lt;1)</td>
<td>33 (&lt;1)</td>
</tr>
<tr>
<td>Premature discontinuations caused by ADR</td>
<td>68 (1)</td>
<td>186 (3)</td>
<td>157 (3)</td>
</tr>
<tr>
<td>Deaths</td>
<td>3 (&lt;1)</td>
<td>16 (&lt;1)</td>
<td>18 (&lt;1)</td>
</tr>
</tbody>
</table>

**NOTE.** ADR, adverse drug reaction; AE, adverse event; PSS, postmarketing surveillance study. See also [62].

* Comparators were cefuroxime axetil, trovafloxacin, clarithromycin, azithromycin, co-amoxiclavulanic acid, amoxicillin, cephalaxin, and ofloxacin.
treated with moxifloxacin experienced significantly better tolerability and lower incidence of overall side effects [61].

A recent review of 26 clinical studies comparing the safety of moxifloxacin, 400 mg for 5 days, in 6178 patients against comparator antibiotics in 4809 patients, plus a postmarketing surveillance study conducted with 5805 patients in Germany, indicates that the number of adverse events associated with moxifloxacin is consistent with comparator antibiotics (table 4) [62]. In the 26 clinical studies encompassing CAP, AECB, and acute sinusitis (and others), the type and frequency of the adverse drug reactions were comparable between moxifloxacin and comparators (table 5). In terms of hepatic safety, there were no adverse moxifloxacin reactions related to the liver other than 0.9% “abnormal liver function tests” for moxifloxacin, 400 mg, versus 1.1% for comparators.

The adverse drug reaction profile in moxifloxacin-treated patients with hepatic dysfunction was similar to that for all patients. There were no clinical events consistent with arrhythmia in patients treated with moxifloxacin who had significant QT prolongation and no deaths as an outcome of adverse cardiac moxifloxacin reactions. The frequency of significant changes in the corrected QT interval (according to European Medicines Evaluation Agency criteria) in a study of 2650 patients who underwent electrocardiograms were moxifloxacin 2.8% (mean corrected QT prolongation ± SD, 6 ± 26 ms) versus clarithromycin 3.7% (2 ± 23 ms) and all other comparators 2.2% (1 ± 23 ms) [62]. Dosage adjustment of moxifloxacin is not required in patients with renal function or elderly patients, nor between men and women. In addition, moxifloxacin does not interact with food, theophylline, morphine, calcium, anticoagulants such as warfarin, or histamine 2-receptor antagonists [63].

Finally, significant issues in today’s drug evaluations include health economic outcomes, such as hospitalization, infection-free interval, and death. A review of 8 controlled, double-blind studies (4 CAP and 4 AECB) that examined whether a newer agent such as moxifloxacin has an impact on mortality and economic outcomes found that the hospitalization and death rates for moxifloxacin-treated patients were significantly lower than those for comparator-treated patients (table 6) [64]. Although these comparators (CAP comparators were amoxicillin

| Table 5. Most frequent adverse drug reactions (incidence of >1%) of moxifloxacin and comparators: review of 26 clinical studies. |
|---|---|
| Adverse event | Moxifloxacin, 400 mg (n = 6178), n (%) | Comparatorsa (n = 4809), n (%) |
| Nausea | 477 (8) | 255 (5) |
| Diarrhea | 344 (6) | 221 (5) |
| Dizziness | 178 (3) | 120 (2) |
| Abdominal pain | 112 (2) | 74 (2) |
| Headache | 106 (2) | 102 (2) |
| Vomiting | 105 (2) | 80 (2) |
| Dyspepsia | 75 (1) | 48 (<1) |
| Dry mouth | 64 (1) | 19 (<1) |
| Taste perversion | 58 (<1) | 90 (2) |
| Liver function result abnormal | 54 (<1) | 51 (1) |

**NOTE.** See also [62].

a Comparators were cefuroxime, clarithromycin, amoxicillin, trovafloxacin, and co-amoxiclavulanic acid.

Table 6. Comparison of moxifloxacin and comparator-related deaths and hospitalizations in CAP and AECB: post hoc analysis of 8 studies.

<table>
<thead>
<tr>
<th>Result</th>
<th>Moxifloxacin</th>
<th>Comparatorsa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death as a result of CAP occurring within 30 d of end of treatment</td>
<td>701 4 (0.57)</td>
<td>705 12 (1.7)</td>
</tr>
<tr>
<td>Death as a result of AECB occurring within 30 d of end of treatment</td>
<td>1224 1 (0.08)</td>
<td>924 3 (0.32)</td>
</tr>
<tr>
<td>Hospitalizations as a result of CAP and AECB</td>
<td>1925 18 (0.94)</td>
<td>1629 30 (1.84)</td>
</tr>
</tbody>
</table>

**NOTE.** AECB, acute exacerbations of chronic bronchitis; CAP, community-acquired pneumonia. See also [64].

a CAP comparators were amoxicillin and amoxicillin; AECB comparators were clarithromycin, cefixime, and cefuroxime.
and clarithromycin; AECB comparators were clarithromycin, cefixime, and cefuroxime) are generally considered to be cost-effective therapies, perhaps the newer agents can elicit cure with significant added advantages, taking into consideration that when an agent prevents hospitalization, this can result not only in lower treatment costs but also in humanistic advantages, enabling individuals to continue normal daily activities without the significant disruption and distress that these conditions have on quality of life.

The pharmacodynamic profile of moxifloxacin favors once-daily, short (5 days in AECB, 10 days in sinusitis and CAP) courses of therapy, which makes the drug convenient to administer and encourages greater patient compliance. The high bactericidal activity of this drug makes it effective for strains with reduced susceptibility to β-lactams, macrolides, tetracyclines, and commonly used older fluoroquinolones; the safety profile is comparable to those of commonly used antimicrobials. However, as with all antimicrobial agents, issues regarding development of resistance should be considered, and appropriate use is essential if the drug class is to remain clinically viable.

References

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