hospitalized patients with moxifloxacin would inevitably lead to drug resistance in the near future—maybe not among respiratory pathogens, at least at first, but certainly among all gastrointestinal bacteria that are treated “for free” concurrently. This problem will get even bigger when, as unfortunately is the practice in the Netherlands, moxifloxacin is promoted for this indication in the general practice, too. Besides this, other adverse effects—for instance, Clostridium difficile–associated diarrhea—should also be considered when broad-spectrum antibiotics are used unnecessarily.

Because the authors did not provide oral step-down therapy in one of the study arms, the study arms are not comparable with regard to the duration of intravenous therapy and duration of hospitalization.

Finally, because the study was performed by the MOXIRAPID group, all authors received financial support from Bayer, the study as a whole was financially sponsored by Bayer, and statistical analysis was performed by Bayer, it would have been better to publish the article in the form of an advertisement instead of a peer-reviewed article in Clinical Infectious Diseases.

Acknowledgments


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Reply to Solnick and to Leenders

To the Editor—The criticism made by Leenders [1] concerning the missing microbiological processing data is justified. However, in the German Competence Network for Community-Acquired Pneumonia (CAPNETZ), my colleagues and I demonstrated that, despite thorough training, sputum specimens could be obtained in only 50% of all cases [2].

Barlett’s quality criteria for quality sputum specimens were only fulfilled in two-thirds of patients’ sputum samples. A pathogen could be found in only 50% of all specimens (i.e., 16% of all patients). This is not enough for scientific evaluation.

Solnick [3] and Leenders [1] remark that, in the ceftriaxon treatment arm, atypical pneumonia was not sufficiently assessed and that this may have influenced the outcome parameters for these patients. With PCR techniques, CAPNETZ revealed a prevalence of Mycobacterium pneumoniae infection of 3.7%; Legionella pneumonia and Chlamydia pneumoniae were found in 4.2% of cases, and Legionella infection, seems to have a high rate of spontaneous remission [4].

I agree with Solnick [3] that, because of the different methods used with regard to the sequential therapy, the study limbs cannot be compared in terms of length of hospital stay. The MOXIRAPID study was designed to observe clinical improvement over time; for this end parameter, the route of administration (parenteral or oral therapy) is not essential.

I support the Lenders’ [1] opinion concerning the administration of broad-spectrum antibiotics in the outpatient setting. However, the MOXIRAPID study included only hospitalized patients. Until recently, there has been no reason to believe that increasing rates of drug resistance would be expected with primary parenteral administration of sufficiently high doses of fluoroquinolones.

The MOXIRAPID study was a clinical trial in Germany sponsored by Bayer. Each study center that included patients in the study received financial compensation. This information had to be declared as a conflict of interest. The authors evaluated and interpreted the results according to scientific criteria. Publication was independent of any potential interests of the sponsor. As long as major clinical trials require support from the pharmaceutical industry, because public funding is not sufficient, such circumstances cannot be avoided.

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References

Response to Letters Regarding Optimizing Therapy for Community-Acquired Pneumonia with the Goal of Rapid Resolution of Illness

To the Editor—As was pointed out by the letters by Solnick [1] and Leenders [2], and as was discussed in our commentary [3], there are several limitations of the study by Welte et al. [4] that potentially reduce the significance of their findings in their comparison of 2 treatment regimens. However, the primary emphasis of our commentary was not to address the relative efficacy of either of the 2 regimens evaluated in this study, but rather to discuss the importance of including a systematic evaluation of the speed of resolution of illness as an end point for future randomized, clinical trials. Although the time to symptom resolution was assessed in the study by Welte and colleagues by the use of a patient diary, this process needs to be better evaluated. The standard test-of-cure evaluation in most previously published trials to have compared antimicrobial regimens has usually been 7–10 days after end of therapy (and, therefore, usually 14–21 days after the initiation of therapy). This end point is often not sensitive enough to evaluate the efficacy of different treatment arms, because many infections, even when treated with marginal therapy, are improved by the end of this time period.

The trend in the treatment of most infectious diseases, especially with the availability of more-potent antimicrobial agents, is for shorter-course therapy [5, 6]. There are several potential advantages to short-course therapy in general and with regard to community-acquired pneumonia in particular. These include the potential to reduce the selection pressure for resistance and adverse events that may emerge with prolonged antibiotic exposure. Presently, there is a relative dearth of well-performed studies to evaluate the appropriate duration of therapy for most infections. Studies that include time to resolution of disease and eradication of pathogens can be useful in helping one determine the appropriate duration of therapy; however, to properly interpret the results regarding the time to resolution of disease in randomized, clinical trials, the trials need to be better designed than are the studies that have already been published.

As indicated in our commentary [3], we propose that future studies of pneumonia should not only compare monotherapy to combination therapy with regard to clinical or microbiological cure, but they should stratify patients on the basis of varying severities of illness and comorbidities. A validated symptom score to assess resolution of illness should be evaluated. Ideally, studies should be prospective and double-blind, and an aggressive attempt to identify pathogens and to determine the speed of eradication of pathogens is necessary to correlate with the clinical manifestations.

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