A Study Evaluating the Efficacy, Safety, and Tolerability of Ertapenem versus Ceftriaxone for the Treatment of Community-Acquired Pneumonia in Adults

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In a double-blind, multicenter trial, 502 patients hospitalized with community-acquired pneumonia were randomized to receive therapy with either ertapenem or ceftriaxone (for each, 1 g given intravenously once daily). After a minimum of 3 days, therapy could be switched to oral amoxicillin-clavulanate. The median duration of intravenously administered therapy for the 383 clinically evaluable patients was 4 days for both treatment groups; 345 patients (90.1%) had their treatment switched to orally administered therapy. Of the clinically evaluable patients, 168 (92.3%) in the ertapenem group and 183 (91.0%) in the ceftriaxone group had a favorable clinical response. *Streptococcus pneumoniae* was the most commonly isolated pathogen, and high cure rates were observed both for penicillin-susceptible and -nonsusceptible infections in the ertapenem group (28 [87.5%] of 32 patients versus 17 [100%] of 17 patients, respectively). Both treatment regimens were generally well tolerated; the most common drug-related adverse events reported were diarrhea (2.9% versus 2.7%) and nausea (0.8% versus 2.0%) in the ertapenem and ceftriaxone groups, respectively. These results suggest that ertapenem and ceftriaxone therapy have similar efficacy and safety in hospitalized patients with community-acquired pneumonia.

Lower respiratory tract infections are a major cause of morbidity and mortality worldwide. Although the majority of patients with community-acquired pneumonia (CAP) are treated as outpatients, ~500,000 patients with CAP are hospitalized annually in the United States [1]. The mean mortality rate among hospitalized patients in the United States is ~14% [2]. Higher mortality rates have been reported among elderly persons and in developing countries [3, 4].

Ertapenem is a new parenteral antimicrobial agent with once-daily dosing that is highly active in vitro against respiratory pathogens typically associated with CAP, such as *Streptococcus pneumoniae* (including penicillin-nonsusceptible isolates), *Haemophilus influenzae*, and *Moraxella catarrhalis*. Like other β-lactams, this structurally unique carbapenem is not active against *Mycoplasma pneumoniae* or *Legionella* or *Chlamydia* species. Its long plasma half-life (~4 h) allows for once-daily dosing.

The primary objective of this study was to compare the clinical and microbiologic efficacy and the safety of ertapenem therapy with those of ceftriaxone therapy for the treatment of patients with CAP who require parenteral therapy. A secondary objective was to eval-
ulate the clinical and microbiologic responses in the subgroup of patients with pneumococcal infection, including infections with penicillin-resistant S. pneumoniae (PRSP) strains. The regimen used for comparison, 1 g of ceftriaxone given daily, is an accepted therapy for CAP and has been shown to be safe and effective in treating serious infections [5–7].

PATIENTS, MATERIALS, AND METHODS

Study design. A prospective, multinational, double-blind (with sponsor blinding), randomized study was developed to compare ertapenem with ceftriaxone therapy for patients with CAP that required parenteral therapy. The study, which was conducted from July 1998 through December 1999, included 62 investigator sites in North and South America, Europe, Asia, Australia, and South Africa. Written consent was obtained from all patients, and the institutional review board at each participating site approved the protocol.

Patient selection. Men and women aged ≥18 years who had CAP diagnosed and who required parenteral antibiotic therapy were randomized to 1 of the 2 study regimen groups in a 1:1 ratio. The diagnosis of CAP was made on the basis of the presence of signs and symptoms consistent with pneumonia (fever, chills, and/or hypothermia, plus ≥2 of the following symptoms: cough with sputum production, rales, auscultatory findings on pulmonary examination consistent with consolidation, dyspnea, tachypnea, hypoxemia, and pleuritic chest pain), abnormal findings on microscopic evaluation of sputum, chest radiographic findings (new or progressive infiltrate, consolidation, cavitation, or pleural effusion), and other supportive laboratory data (e.g., a peripheral WBC count of >10,000 cells/µL or with >15% immature neutrophils, or a blood culture positive for an organism consistent with a respiratory pathogen). The likelihood of enrolling patients who had atypical pneumonia was minimized for the following reasons: (1) patients with suspected legionnaires’ disease (e.g., a urine test positive for Legionella antigen) were excluded from the study, and (2) patients aged <40 years had to be able to produce purulent sputum.

Patients with any of the following conditions, treatment characteristics, or laboratory findings were excluded from the study: empyema, underlying structural lung abnormalities, lung malignancy, nosocomial pneumonia, requirement of mechanical ventilation, active tuberculosis, any rapidly progressive or terminal illness, immunocompromising disease or receipt of immunocompromising therapy, antibiotic treatment for ≥24 h during the 72 h before enrollment in the study (unless treatment failure was documented), aspartate aminotransferase or alanine aminotransferase (ALT) levels >6 times the upper limit of normal, bilirubin or alkaline phosphatase levels >3 times the upper limit of normal, an absolute neutrophil count of <1000 neutrophils/mm³, a platelet count of <75,000 platelets/mm³, hematocrit of <25%, or coagulation test results that were >1.5 times the upper limit of normal. Patients with laboratory values that exceeded any of these limits were allowed to enroll in the study, on an individual basis, if the abnormality was thought to be the result of acute infection. Patients with elevated creatinine clearance were excluded initially, but a subsequent study amendment allowed patients with severe renal insufficiency (creatinine clearance, <30 mL/min per 1.73 m²) to be given a reduced dosage of ertapenem (500 mg daily).

Antimicrobial susceptibility testing was required for all baseline pathogens isolated from sputum or blood cultures. Patients with baseline pathogens found to be resistant to 1 or both study drugs after they started receiving the study therapy continued enrollment in the study at the discretion of the investigator.

At study entry, randomization was stratified, for balance, into 4 groups, on the basis of disease severity, as defined by the pneumonia severity index (PSI; ≤3 or >3) and age (≤65 or >65 years). The PSI incorporates assessment of comorbid illness, acute physiological changes, and age; a PSI of 4 or 5 indicates severe illness [8].

Treatment regimens. Randomization resulted in patients having an equal chance of receiving either ertapenem (Merck & Co.; 1 g given intravenously) or ceftriaxone (Roche Pharmaceuticals; 1 g given intravenously) once per day for up to 14 days. Therapy that is effective against atypical respiratory pathogens was not provided. The intravenously administered study antibiotics were given over 30 min. Each day, patients received 1 infusion of a study drug and 1 infusion of placebo that matched the other study drug. To maintain blinding, a small amount of multivitamin concentrate was added to saline to produce placebo that matched the color of the ceftriaxone used for infusion. The study allowed patients with documented PRSP infection and a suboptimal clinical response to have the dose of ertapenem or ceftriaxone increased to 2 g per day at the discretion of the investigator. Investigators had the option to switch the patient’s therapy to orally administered amoxicillin-clavulanate (amoxicillin, 875 mg twice per day/clavulanate, 125 mg twice per day, or an equivalent dosage regimen) after ≥3 days of receipt of parenteral therapy, provided that the patient met protocol-specified criteria to indicate sufficient clinical improvement. The recommended total duration of antibiotic therapy was 10–14 days. Receipt of therapy with other antimicrobial agents that are potentially effective for management of pneumonia was not permitted during treatment or in the period before early follow-up, unless the study treatment failed.

Microbiologic procedures. At baseline, sputum specimens were obtained by expectoration (or by other methods of obtaining lower respiratory tract specimens) for Gram stain and culture. Blood cultures were also required for all patients. All
isolated bacteria were evaluated by the investigator and judged
to be pathogenic or nonpathogenic. For all pathogens, suscept-
bility to ertapenem, ceftriaxone, and amoxicillin–clavulanate
was evaluated at the site laboratory by use of the disk-diffusion
test, according to the guidelines of the National Committee for
Clinical Laboratory Standards [9]. For this purpose, paper disks
that contained 10 μg of ertapenem, 30 μg of ceftriaxone, or
20/10 μg of amoxicillin–clavulanate were provided to each site
by Merck Research Laboratories. In addition, 1-μg oxacillin
disks and penicillin E-test strips were provided for testing sus-
cceptibility of pneumococci to penicillin.

**Efficacy assessment.** Detailed clinical observations were
made at baseline and while patients were receiving intrave-
rously administered therapy. Investigators assessed the clinical
outcome when intravenously administered therapy was dis-
continued, at the early follow-up visit (7–14 days after cessation
of iv and optional oral antimicrobial therapy), and at late fol-
low-up (21–28 days after cessation of therapy). Test of cure
(TOC) was assessed at the early follow-up visit; relapse was
assessed at the late follow-up visit. For each patient, assessments
were based on signs and symptoms of pneumonia (each rated
individually), vital signs, oxygen saturation, chest radiograph
findings, and laboratory test results. The microbiologic response
for each baseline pathogen was based on culture results at the
TOC visit. If cultures were not repeated at the TOC visit, mi-
crobiologic outcomes were presumed on the basis of the clinical
response.

The evaluable patients for the analysis of efficacy was
determined prior to unblinding study therapy and was based
on prespecified criteria. These included minimum requirements
for confirmation of the diagnosis, prior and concomitant anti-
microbial therapy within prespecified limits, treatment duration
within specified limits (5–17 days to be considered clinical cure
and ≥48 h to be considered clinical failure), and a follow-up
assessment done ≥7 days after completion of all antimicrobial
therapy (including optional oral therapy).

The primary efficacy end point was the proportion of clin-
ically evaluable patients who had a favorable clinical response
assessment at TOC. In addition, a modified intent-to-treat
(MITT) analysis was done that included all patients who met
minimum requirements for diagnosis of pneumonia and who
had received ≥1 dose of ertapenem or ceftriaxone.

**Safety assessment.** Safety and local tolerability were eval-
uated in all patients who received ≥1 dose of intravenously
administered therapy. Adverse clinical and laboratory experi-
ences were evaluated during the entire antimicrobial therapy
period and for 14 days after completion of all study therapy
(intravenous and oral).

**Statistical analyses.** The study was designed to test for
equivalence (noninferiority) in the efficacy of ertapenem and
ceftriaxone in the clinically evaluable patients in the 2 treatment
groups. The study was not specifically powered to demonstrate
equivalence in subgroup analyses. The sample size (150 eval-
uable patients per group) was calculated by use of Blackwelder’s
formula [10] and the following values: α, 0.025; β, 0.20; and
the expected response rate, 90%. The criteria for equivalence
were (1) that the 2-sided 95% CI for the difference in response
rates between the 2 treatment groups contained 0, and (2) the
lower limit of the 95% CI was not less than −10 percentage
points. The 95% CIs were calculated by use of the normal
approximation to the binomial distribution, and the Cochran
approach [11] was used to account for stratification. A test of
treatment by stratum interaction was also performed by use of
the Breslow-Day test of homogeneity of ORs [12]. Patients with
PRSP infection were analyzed separately and were not included
in the primary evaluable patient population analyses. They were
included in the MITT analyses and in a specific analysis of
pneumococcal infection outcome.

**RESULTS**

Of the 502 patients enrolled in the study, 383 (76.3%) were
considered clinically evaluable; 182 were randomized to receive
ertapenem and 201 were randomized to receive ceftriaxone. A
total of 209 patients (41.6%) were microbiologically evaluable,
96 of whom were in the ertapenem group and 113 of whom
were in the ceftriaxone group. Figure 1 summarizes the number
of patients in each of the populations analyzed. The most com-
mon reasons that patients were considered clinically noneval-
uable were failure to receive sufficient study therapy or failure
to have an assessment at the TOC visit within the appropriate
time window. The most common reasons that patients were
considered microbiologically nonevaluable were that they were
not clinically evaluable or that they did not have a baseline
pathogen isolated.

![Figure 1](cid-2002-41fig1.jpg)

**Figure 1.** Profile of study enrollment, summarizing the number (%) of
patients in each of the evaluated populations. MITT, modified intent-to-
treat.
Baseline patient characteristics. The randomized and clinically evaluable populations in the 2 treatment groups were similar with respect to baseline characteristics (table 1). The microbiologically evaluable population and the MITT population were similar to the randomized population (data not shown). In each study population, patients in both treatment groups were comparable with respect to age, sex, race, secondary diagnoses, medications received, and clinical signs and symptoms. Approximately 60% of the clinically evaluable patients were male, and a similar percentage of the evaluable patients (men and women) were aged ≥65 years. Almost 20% of clinically evaluable patients were aged ≥75 years.

Baseline microbiologic findings. The 2 treatment groups were similar with respect to the distribution and susceptibility patterns of baseline pathogens. Of the bacteria isolated from all patients in both treatment groups for which susceptibility results were available, 287 (98.3%) of 292 isolates were susceptible to ertapenem and 270 (92.8%) of 291 were susceptible to ceftriaxone. The most frequently isolated pathogen resistant to 1 or both study drugs was methicillin-resistant *Staphylococcus aureus*, which was considered resistant to ertapenem and ceftriaxone, irrespective of reported in vitro susceptibility results. In addition, 3 and 4 isolates of *S. pneumoniae* were intermediate and resistant to ceftriaxone, respectively.

Of the clinically evaluable patients, 96 (52.7%) and 113 (56.2%) in the ertapenem and ceftriaxone groups, respectively, had ≥1 pathogen identified in sputum and/or blood samples. The most commonly isolated organisms were *S. pneumoniae, H. influenzae, M. catarrhalis*, and *S. aureus*. Twenty-nine patients (7.6%) had bacteremia at baseline: 10 in the ertapenem group and 19 in the ceftriaxone group. *S. pneumoniae* accounted for 24 (82.8%) of the blood isolates.

Dosage and duration of therapy. In no patient was the dose of ertapenem adjusted for renal failure, nor was the dose of either study drug increased to 2 g for treatment of PRSP infection. The median duration of intravenously administered therapy for clinically evaluable patients was 4 days (range, 2–17 days for ertapenem and 2–14 days for ceftriaxone); for total antimicrobial therapy, the median duration was 12 days (range, 3–21 days for patients in the ertapenem group and 3–17 days for patients in the ceftriaxone group). In clinically evaluable patients, 165 (90.7%) in the ertapenem group and 180 (89.6%) in the ceftriaxone group received oral antimicrobial therapy; overall, 334 (96.8%) received amoxicillin-clavulanate.

Efficacy results. For the TOC analysis, 92.4% (95% CI, 88.5%–96.2%) of clinically evaluable patients in the ertapenem group and 91.3% (95% CI, 87.3%–95.3%) of those in the ceftriaxone group were cured. The difference in response rates between the 2 groups, adjusting (weighting) for strata, was 1.0% (95% CI, −4.9% to 7.0%), which indicated that the rates for the 2 groups were equivalent. As shown in table 2, cure rates in the clinically evaluable population were >90% for each stratum in the ertapenem group and ranged from 86% to 91% for those in the ceftriaxone group. Slightly lower clinical success rates were observed in the MITT analysis (85.1% in the ertapenem group and 85.0% in the ceftriaxone group), which reflects the more conservative approach in the MITT outcome assessment, in which patients with inadequate information or indeterminate outcomes were considered to have had treatment failure. Also evident from table 2 are the high microbiologic

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Table 1. Baseline characteristics of 502 patients with community-acquired pneumonia enrolled in a study that compared ertapenem therapy with ceftriaxone therapy.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Randomized population, treatment group</th>
<th>Clinically evaluable population, treatment group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ertapenem <em>(n = 244)</em></td>
<td>Ceftriaxone <em>(n = 258)</em></td>
</tr>
<tr>
<td></td>
<td>Ertapenem <em>(n = 182)</em></td>
<td>Ceftriaxone <em>(n = 201)</em></td>
</tr>
<tr>
<td>Male sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>125 (51.2)</td>
<td>144 (55.8)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>63 (25.8)</td>
<td>61 (23.6)</td>
</tr>
<tr>
<td>Black</td>
<td>39 (15.6)</td>
<td>35 (13.6)</td>
</tr>
<tr>
<td>Other ethnic group</td>
<td>18 (7.4)</td>
<td>18 (7.0)</td>
</tr>
<tr>
<td>Age, mean years ± SD</td>
<td>55.9 ± 20.0</td>
<td>57.3 ± 19.7</td>
</tr>
<tr>
<td>Pneumonia severity index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>46 (18.9)</td>
<td>42 (16.3)</td>
</tr>
<tr>
<td>2</td>
<td>73 (29.9)</td>
<td>90 (34.9)</td>
</tr>
<tr>
<td>3</td>
<td>63 (25.8)</td>
<td>52 (20.2)</td>
</tr>
<tr>
<td>4</td>
<td>54 (22.1)</td>
<td>65 (25.2)</td>
</tr>
<tr>
<td>5</td>
<td>7 (2.9)</td>
<td>9 (3.5)</td>
</tr>
</tbody>
</table>

NOTE. Data are no. (%) of patients, unless otherwise indicated.
Table 2. Outcomes of clinically evaluable, microbiologically evaluable, and modified-intent-to-treat populations (MITT) at early follow-up (test of cure visit; 7–14 days after cessation of therapy) in a study that compared ertapenem therapy with ceftriaxone therapy.

<table>
<thead>
<tr>
<th>Patient group, characteristic</th>
<th>Ertapenem group</th>
<th>Ceftriaxone group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>No. (%) of patients cured</td>
</tr>
<tr>
<td>Clinically evaluable patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td>110</td>
<td>101 (91.8)</td>
</tr>
<tr>
<td>&gt;65</td>
<td>72</td>
<td>67 (93.1)</td>
</tr>
<tr>
<td>≥75</td>
<td>37</td>
<td>35 (94.6)</td>
</tr>
<tr>
<td>Pneumonia severity index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤3</td>
<td>138</td>
<td>128 (92.8)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>44</td>
<td>40 (90.9)</td>
</tr>
<tr>
<td>All</td>
<td>182</td>
<td>168 (92.3)</td>
</tr>
<tr>
<td>Microbiologically evaluable patients</td>
<td>96</td>
<td>89 (92.7)</td>
</tr>
<tr>
<td>Clinical MITT population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td>145</td>
<td>121 (83.4)</td>
</tr>
<tr>
<td>&gt;65</td>
<td>91</td>
<td>80 (87.9)</td>
</tr>
<tr>
<td>Pneumonia severity index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤3</td>
<td>177</td>
<td>153 (86.4)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>59</td>
<td>48 (81.4)</td>
</tr>
<tr>
<td>All</td>
<td>236</td>
<td>201 (85.2)</td>
</tr>
</tbody>
</table>

Note: Microbiologic cure rates were assessed at early follow-up and reflect eradication of all baseline pathogens. Cure rates in the MITT population were assessed as described in the Patients, Materials, and Methods section.

cure rates (i.e., eradication or presumed eradication of the baseline pathogen): 92.7% and 94.7% in the ertapenem and ceftriaxone groups, respectively.

Table 3 compares the per-pathogen clinical response rates between the 2 treatment groups, including patients with PRSP infection. Four patients with pneumococcal pneumonia (1 in the ertapenem group and 3 in the ceftriaxone group) were infected with a penicillin-resistant isolate (MIC, ≥2 μg/mL); all of these patients were cured at the TOC visit.

Clinical relapse rates, assessed at the 21–28-day visit, were low in both treatment groups: 3 (2.0%) of 148 patients in the ertapenem group and 1 (0.6%) of 155 patients in the ceftriaxone group had clinical relapse. No bacterial recurrences were reported in either treatment group, and no reported persistent pathogens acquired resistance to the study drug received.

Adverse events. Of the 502 patients randomized, 498 received ≥1 dose of parenteral therapy and were included in the analysis of adverse events. During parenteral therapy, clinical adverse events that were possibly, probably, or definitely drug related were reported for 27 patients (11.2%) in the ertapenem group and 43 (16.8%) in the ceftriaxone group, and drug-related laboratory adverse events were reported in 31 patients (13.4%) in the ertapenem group and 26 (10.7%) in the ceftriaxone group. The most common adverse events are listed in table 4. Of the patients with elevated liver enzyme levels, ALT levels increased to >5 times the upper limit of normal in 4 patients (2.1%) in the ertapenem group and in 5 (2.5%) in the ceftriaxone group. At the time of the follow-up examination, ALT levels had returned to normal or tended to return to baseline levels in all patients. One patient in the ertapenem group had a seizure, which the investigator reported as probably drug related. This seizure occurred in an 89-year-old woman who had a generalized tonic-clonic seizure that lasted ~1 min on study day 10, the final scheduled day of intravenously administered therapy. She recovered without receiving antiseizure medication. The findings of an electroencephalograph obtained on study day 53 were normal, and a neurologic examination performed during follow-up revealed no sequelae. No patient had study therapy discontinued because of a drug-related clinical or laboratory adverse experience. There were no drug-related deaths.

Local tolerability. Tolerability at the study drug intravenous infusion site was assessed daily while each patient was receiving study therapy. Of all patients who received ≥1 dose of study therapy, 37 (15.3%) of 242 in the ertapenem group and 44 (17.3%) of 255 in the ceftriaxone group experienced
Table 3. Clinical cure rates, by pathogen isolated at baseline, at early follow-up (test of cure visit) in a study that compared ertapenem therapy with ceftriaxone therapy.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Ertapenem group (n = 97)</th>
<th>Ceftriaxone group (n = 116)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>Response rate, %</td>
</tr>
<tr>
<td>Gram-positive bacteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptococcus pneumonia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>44/48</td>
<td>91.7</td>
</tr>
<tr>
<td>Penicillin-NS strains</td>
<td>11/11</td>
<td>100</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>8/8</td>
<td>100</td>
</tr>
<tr>
<td>Other</td>
<td>5/5</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>57/61</td>
<td>93.4</td>
</tr>
<tr>
<td>Gram-negative bacteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>17/21</td>
<td>81.0</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>10/10</td>
<td>100</td>
</tr>
<tr>
<td>Other</td>
<td>15/16</td>
<td>93.7</td>
</tr>
<tr>
<td>Total</td>
<td>42/47</td>
<td>89.4</td>
</tr>
</tbody>
</table>

**NOTE.** NS, nonsusceptible.

* No. of evaluable patients in each treatment group.

**Table 4. Most common drug-related clinical and laboratory adverse events reported during ertapenem and ceftriaxone therapy.**

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Ertapenem</th>
<th>Ceftriaxone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>7 (2.9%)</td>
<td>7 (2.7%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (0.8%)</td>
<td>5 (2.0%)</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (0.4%)</td>
<td>4 (1.6%)</td>
</tr>
<tr>
<td>Laboratorv</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased ALT level</td>
<td>18 (9.0%)</td>
<td>15 (7.2%)</td>
</tr>
<tr>
<td>Increased AST level</td>
<td>15 (7.4%)</td>
<td>13 (6.3%)</td>
</tr>
<tr>
<td>Increased alkaline phosphatase</td>
<td>3 (1.4%)</td>
<td>6 (2.8%)</td>
</tr>
<tr>
<td>Increased platelet count</td>
<td>4 (1.8%)</td>
<td>3 (1.3%)</td>
</tr>
</tbody>
</table>

**NOTE.** ALT, alanine aminotransferase; AST, aspartate aminotransferase.
which were recently revised. For hospitalized patients in a general ward, the recommended antimicrobial therapies are ceftaxime plus a macrolide, ceftriaxone plus a macrolide, or a fluoroquinolone alone [22]. However, in 1998, when the present study was designed and initiated, coverage for these organisms was considered optional in the IDSA guidelines [21], and therapy effective against M. pneumoniae, Chlamydia species, or Legionella species was not used. Nevertheless, because of the potentially serious nature of legionellosis, an attempt was made to exclude patients with this infection by testing urine samples for Legionella antigen. Treatment failure rates in the present study were similar to those in studies published elsewhere about CAP that included therapy with a macrolide or quinolone [19, 23]. This suggests that, in the present study, M. pneumoniae, Chlamydia species, and Legionella species were not important causes of treatment failure; however, this cannot be proved, because the frequency at which these organisms were responsible for disease was not systematically assessed.

The safety profile and tolerability of ertapenem were similar to those of ceftriaxone. The drug-related clinical adverse events reported for both agents were those commonly observed in association with cephalosporin therapy, and none of these events resulted in discontinuation of receipt of either drug. Only 1 serious drug-related adverse event, a seizure, occurred among patients treated with ertapenem. This generalized seizure was brief and without sequelae. The most common drug-related laboratory adverse event was elevation of the transaminase levels. The enzyme elevations were mild to moderate, were transient, and appeared to be of little clinical importance.

In summary, in adult patients with CAP who require parenteral therapy, 1 g of ertapenem given intravenously once per day for up to 14 days, with the option of switching to an orally administered agent after clinical improvement, was highly effective both clinically and microbiologically, regardless of the severity of the infection, and was as effective as therapy with ceftriaxone (1 g daily), which could also be switched to oral therapy. Ertapenem was generally well tolerated and had a safety profile comparable to that of ceftriaxone.

**STUDY GROUP MEMBERS**

Investigative members of the Protocol 018 Ertapenem Community-Acquired Pneumonia Study Group are as follows:

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