Linezolid versus Vancomycin in Treatment of Complicated Skin and Soft Tissue Infections

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Skin and soft tissue infections (SSTIs) are a common cause of morbidity in both the community and the hospital. An SSTI is classified as complicated if the infection has spread to the deeper soft tissues, if surgical intervention is necessary, or if the patient has a comorbid condition hindering treatment response (e.g., diabetes mellitus or human immunodeficiency virus). The purpose of this study was to compare linezolid to vancomycin in the treatment of suspected or proven methicillin-resistant gram-positive complicated SSTIs (CSSTIs) requiring hospitalization. This was a randomized, open-label, comparator-controlled, multicenter, multinational study that included patients with suspected or proven methicillin-resistant Staphylococcus aureus (MRSA) infections that involved substantial areas of skin or deeper soft tissues, such as cellulitis, abscesses, infected ulcers, or burns (<10% of total body surface area). Patients were randomized (1:1) to receive linezolid (600 mg) every 12 h either intravenously (i.v.) or orally or vancomycin (1 g) every 12 h i.v. In the intent-to-treat population, 92.2% and 88.5% of patients treated with linezolid and vancomycin, respectively, were clinically cured at the test-of-cure (TOC) visit (P = 0.057). Linezolid outcomes (124/140 patients or 88.6%) were superior to vancomycin outcomes (97/145 patients or 66.9%) at the TOC visit for patients with MRSA infections (P < 0.001). Drug-related adverse events were reported in similar numbers in both the linezolid and the vancomycin arms of the trial. The results of this study demonstrate that linezolid therapy is well tolerated, equivalent to vancomycin in treating CSSTIs, and superior to vancomycin in the treatment of CSSTIs due to MRSA.

Skin and soft tissue infections (SSTIs) are a common cause of morbidity in both the community and the hospital. Examples of SSTIs include cellulitis, abscesses, diabetic foot infections, and surgical site infections (32, 47). Superficial SSTIs are generally treated on an outpatient basis with oral antibiotics and topical care (32). However, complicated SSTIs (CSSTIs) may require hospitalization, intravenous (i.v.) antibiotics, and/or surgery (47). An SSTI is classified as complicated if the infection has spread to the deeper soft tissues, if surgical intervention is necessary, or if the patient has a comorbid condition hindering treatment response (e.g., diabetes mellitus or human immunodeficiency virus) (11, 31).

SSTIs may be caused by a wide range of pathogens, with Staphylococcus aureus recovered from 40% of SSTIs in the SENTRY Antimicrobial Surveillance Program (19). Other organisms recovered from ≥5% of infections included Pseudomonas aeruginosa (12%), Escherichia coli (10%), Enterococcus spp. (8%), Klebsiella spp. (6%), and Enterobacter spp. (6%) (19).

Methicillin-resistant S. aureus (MRSA) has become a predominant pathogen in many nosocomial infections, including CSSTIs (42). At the end of 2000, MRSA accounted for 29.5% of the S. aureus isolates in the SENTRY Antimicrobial Surveillance Program, a 6% increase from 1997 (6, 36). The prevalence of MRSA varies among countries but continues to increase, approaching 70% in Japan (33), 45% in the United Kingdom (England and Wales only), 40% in Italy and Greece (7), and 30% to 50% in the United States (18). Risk factors for MRSA include long hospital stay, invasive procedures, previous antibiotic use, diabetes, previous MRSA colonization, chronic wounds, and care in a long-term facility (14, 25, 27, 39).

Antistaphylococcal penicillins or cephalosporins are commonly used to treat SSTIs and are effective against methicillin-sensitive S. aureus (MSSA). Intravenous vancomycin has been the first-line therapy against MRSA because other antibiotics, particularly beta-lactams, are not active against these strains (1, 5).

Linezolid is a novel oxazolidinone agent that has demonstrated activity against antibiotic-susceptible and antibiotic-resistant gram-positive organisms (2, 28). The oral form of linezolid is 100% bioavailable (12, 38, 45), allowing for an early switch from i.v. to oral therapy. Linezolid has a unique mechanism of action whereby it selectively binds to the 50S ribosomal unit and prevents formation of the initiation complex (37). This action is thought to prevent cross-resistance with other antimicrobial agents (37). Previous clinical trials demonstrated that linezolid is well tolerated and is as effective as penicillinase-resistant penicillins or vancomycin in treating CSSTIs (40, 41). In these studies, there were trends favoring linezolid for MRSA patients and for overall eradication of S.
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**Materials and Methods**

This was a randomized, open-label, comparator-controlled, multicenter, multinational study conducted from October 2002 until March 2003. The goal of the study was to compare the clinical efficacies, safety, and tolerabilities of two regimens used to treat MRSA infections. Study sites obtained approval from local independent ethics committees, and each patient signed an informed consent before participating in the trial.

The study included patients with skin and skin structure infections of sufficient severity and with signs of systemic illness that required hospitalization. A surgical intervention was not necessary to enter this study, but surgical intervention was allowed. Entry criteria included suspected or proven MRSA infection that involved substantial areas of skin or deeper soft tissues, such as cellulitis, abscesses, infected ulcers, or burns (<10% of total body surface area). Required physical findings included (i) erythema with or without induration, (ii) fluctuation, (iii) heat/localized warmth, (iv) pain/tenderness, and (v) drainage/discharge. In addition, all patients were required to have at least one of the following symptoms: (i) fever, (ii) hypothermia, (iii) hypotension, (iv) a white blood cell count of <10,000/mm³, or (v) >15% immature neutrophils regardless of white blood cell count. Patients with gram-negative infections, osteomyelitis, endocarditis, meningitis, septic arthritis, necrotizing fasciitis, or gas gangrene were excluded. In addition, patients who were receiving another investigational medication concurrently or who had infected devices that were not removed, uncomplicated or superficial skin infections, or hypersensitivity to linezolid or vancomycin were excluded.

A medical history, vital signs, physical examination, wound description, and baseline laboratory values were obtained for each patient upon enrollment. The severity of illness was judged using the validated mortality probability model II (MPM II) scoring system (21). Investigators were encouraged to enroll patients with a presumed gram-positive infection and risks factors for MRSA. Patients were randomized (1:1) to receive linezolid (600 mg) every 12 h, either i.v. or orally, or vancomycin (1 g) every 12 h i.v. There were no planned vancomycin dose reductions or retreatments, and investigators were free to adjust dosages according to normal standards of care. Therapy could be initiated with oral linezolid, or patients could be switched to the oral formulation when able to tolerate diet. The protocol recommended that patients with documented MSSA infections receiving vancomycin were to be switched to oxacillin sodium, nafcillin, or flucloxacillin (1 to 2 g i.v. every 6 h or to dicloxacillin sodium (500 mg) orally every 6 h after initial vancomycin therapy. Concomitant use of astatine or other antibiotics for gram-negative organisms was permitted. The minimal treatment period was 4 days, and the treatment duration was intended to be 7 to 14 days but not longer than 21 days.

Clinical observations of the wound, the patient’s systemic response to infection, laboratory values, and culture follow-up, if possible, were followed and recorded during the first 4 days of therapy, on day 7, at the end of treatment (EOT), and at the test-of-cure (TOC) visit. The TOC visit was planned 7 days after the EOT. Observations were done daily while the patient was hospitalized and recorded at the EOT, at the TOC visit, and at long-term follow-up (day 35).

Clinical response to treatment was determined by resolution of the signs and symptoms of infection that were identified at baseline. Patients were judged as cured if complete resolution of all pretherapy clinical signs and symptoms of infection (e.g., body temperature and white blood cell count) was achieved, as judged by the investigator at the EOT and the TOC visit. Patients were considered improved at the EOT if two or more (but not all) of the pretherapy clinical signs and symptoms of CSSTI were resolved, and patients were considered failed if they exhibited persistence or progression of baseline clinical signs and symptoms of infection, development of new clinical findings consistent with active infection, or an inability to complete the study because of adverse events. Patients’ results were indeterminate if extenuating circumstances precluded classification to one of the above-described categories, usually because of missed appointments.

**Statistical analyses.** The primary endpoint of clinical cure for the intent-to-treat (ITT) population (see below) was used to estimate the required sample size based on a test of superiority, with the linezolid-treated patients expected to achieve higher cure rates than the vancomycin-treated patients. For linezolid-treated patients, a minimum of 85% treatment success rate was assumed with a success rate for vancomycin of between 75% and 77%. A significance level of 0.05 for a two-sided test, a power of 0.90, and 80% evaluability were assumed when calculating results for a sample size of 1,200 patients. A two-sided 95% confidence interval was used for the efficacy analyses. Demographics and baseline characteristics were compared between treatment groups by using the t test or Wilcoxon rank-sum test for quantitative variables and the chi-square or Fisher’s exact test for categorical variables as appropriate.

Four populations of patients were identified for analysis. These were (i) the ITT population, which included all randomized patients who received one or more doses of study medication; (ii) the modified intent-to-treat (MITT) population, which included all ITT patients who had a culture-confirmed gram-positive pathogen at baseline; (iii) the clinically evaluable (CE) population, which included all patients who received more than 4 days of therapy and returned for the TOC visit; and (iv) the microbiologically evaluable (ME) population, which included all CE patients who had one or more gram-positive pathogens at baseline that were not resistant to the study drug. Safety analyses were performed on the ITT population.

The primary efficacy outcome of this study was clinical response to treatment at the TOC visit in the ITT population. More than 4 days of treatment with study drug was required for an assessment of cured or improved, and at least 2 days of treatment with study drug was required for an assessment of failure. Microbiological outcomes were categorized as success (documented or presumed eradication of the pathogen present at baseline), failure (documented or presumed persistence of pathogen present at baseline), indeterminate (pathogen data indeterminate), or missing (pathogen data missing).

**Results**

Of 1,200 randomized patients, 1,180 patients comprised the ITT population; 592 received linezolid and 588 received vancomycin. Of the 20 patients who were randomized but who never received drug, 6 patients in the linezolid group and 10 patients in the vancomycin group did not have signs or symptoms of infection, 1 patient in each treatment group had osteomyelitis, 1 patient in the vancomycin group did not have erythema, and 1 patient had necrotizing fasciitis.

At baseline, no significant differences were seen in demographics and patient characteristics between treatment groups (Table 1). The most common types of infection among the ITT population were cellulitis (46.4%), major skin abscesses (25.8%), surgical site infections (10.8%), and infected ulcers (6.7%).

The overall mean treatment duration was longer for the linezolid group than for the vancomycin group (11.8 ± 4.9 days versus 10.9 ± 5.3 days, respectively; P < 0.004). However, the i.v. treatment duration was significantly shorter for ITT patients in the linezolid group than for those in the vancomycin group (4.0 ± 2.6 days versus 9.0 ± 5.3 days, respectively; P < 0.0001). Empirical coverage for gram-negative organisms was balanced between treatment groups: 218/592 (37%) of linezolid-treated patients and 225/582 (39%) of vancomycin-treated patients.

**Clinical efficacy.** In the ITT population, 92.2% and 88.5% of patients treated with linezolid and vancomycin, respectively, were clinically cured at the TOC visit (P = 0.057) (Table 2). A sensitivity analysis was performed, with patients with indeterminate outcomes at the TOC visit coded as failures. Response
rates in the ITT population were 439/583 (75.3%) of linezolid-treated patients and 402/573 (70.2%) of vancomycin-treated patients ($P = 0.0496$). Significantly more patients with major skin abscesses treated with linezolid were cured than were patients treated with vancomycin (Table 3), and 115/190 (60.5%) of the ME patients had MRSA cultured at baseline.

Of the 592 patients in the linezolid group, 308 (52.0%) were started on oral therapy. In the ITT population, 93.5% and 91.2% ($P = 0.337$) of patients who received i.v. linezolid followed by oral linezolid or oral linezolid alone, respectively, were clinically cured. Cure rates were similar in the MITT, CE, and ME populations whether patients were started on oral or i.v. linezolid.

**Microbiological efficacy.** MRSA (42%) and MSSA (29%) were the most common pathogens isolated at baseline (Table 1). The mean baseline severity scores were 4.07 for MRSA patients and 2.73 for MSSA patients ($P = 0.002$). Microbiological outcomes in both the MITT and the ME MRSA patient groups favored linezolid over vancomycin at the TOC visit. Patients with MSSA who switched from vancomycin to a beta-lactam and who completed sufficient antibiotic therapy (ME population) for evaluation did not have outcomes different than those of patients who were maintained on vancomycin (Table 5).

**Safety and tolerability.** Approximately half of the patients in each treatment group experienced one or more adverse events (all causality) during the study, most often classified as mild to moderate. Drug-related adverse events were reported in similar numbers in both the linezolid and the vancomycin arms of the trial (Table 6). Drug-related adverse events in linezolid-treated patients were noted most often in the digestive system and by lab tests documenting thrombocytopenia. Rash, anaphylaxis, drug-related allergic reaction, and phlebitis were reported significantly more often by patients in the vancomycin treatment group.

4. The mean baseline severity scores were 4.07 for MRSA patients and 2.73 for MSSA patients ($P = 0.002$). Microbiological outcomes in both the MITT and the ME MRSA patient groups favored linezolid over vancomycin at the TOC visit. Patients with MSSA who switched from vancomycin to a beta-lactam and who completed sufficient antibiotic therapy (ME population) for evaluation did not have outcomes different than those of patients who were maintained on vancomycin (Table 5).

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**Table 2. Clinical outcomes at TOC visit**

<table>
<thead>
<tr>
<th>Population</th>
<th>% of patients (no. cured/total) after treatment with:</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Linezolid</td>
<td>Vancomycin</td>
<td></td>
</tr>
<tr>
<td>ITT</td>
<td>92.2 (439/476)</td>
<td>88.5 (402/454)</td>
<td>−0.11, 7.47</td>
</tr>
<tr>
<td>MITT</td>
<td>92.9 (314/338)</td>
<td>88.0 (287/326)</td>
<td>−0.40, 9.32</td>
</tr>
<tr>
<td>CE</td>
<td>94.4 (436/462)</td>
<td>90.4 (394/436)</td>
<td>0.53, 7.48</td>
</tr>
<tr>
<td>ME</td>
<td>94.5 (312/330)</td>
<td>89.7 (278/310)</td>
<td>0.69, 9.05</td>
</tr>
</tbody>
</table>

*Results do not include indeterminate outcomes. TOC visits occurred 7 days after the end of treatment. CI, confidence interval.*

*Patients could be switched to nafcillin, oxacillin, dicloxacillin, or flucloxacillin based on culture results.*

**Table 3. Clinical success at TOC visit of CE and ME patients by baseline diagnosis**

<table>
<thead>
<tr>
<th>Organism and pathogen</th>
<th>% of patients (no. cured/total) after treatment with:</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linezolid</td>
<td>Vancomycin</td>
<td>Linezolid</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>Major skin abscess</td>
<td>CE patients</td>
<td>98.3 (116/118)</td>
<td>91.1 (92/101)</td>
</tr>
<tr>
<td>ME patients</td>
<td>98.0 (97/99)</td>
<td>90.1 (82/91)</td>
<td>1.14, 14.6</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>CE patients</td>
<td>91.5 (205/224)</td>
<td>91.5 (184/201)</td>
</tr>
<tr>
<td>ME patients</td>
<td>91.6 (120/131)</td>
<td>91.7 (99/108)</td>
<td>−7.12, 6.99</td>
</tr>
<tr>
<td>Infected surgical incision</td>
<td>CE patients</td>
<td>98.0 (50/51)</td>
<td>88.2 (45/51)</td>
</tr>
<tr>
<td>ME patients</td>
<td>97.7 (43/44)</td>
<td>88.1 (37/42)</td>
<td>−1.11, 20.37</td>
</tr>
</tbody>
</table>

*Results do not include indeterminate outcomes. TOC visits occurred 7 days after the end of treatment. CI, confidence interval.*

*Patients could be switched to nafcillin, oxacillin, dicloxacillin, or flucloxacillin based on culture results.*

**Table 4. Microbiological outcomes at TOC visit by baseline pathogen in ME and MITT patient populations treated with linezolid or comparator drugs**

<table>
<thead>
<tr>
<th>Organism and pathogen</th>
<th>% of patients cured (no. cured/total) after treatment with:</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linezolid</td>
<td>Vancomycin</td>
<td>Linezolid</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>MRSA</td>
<td>ME</td>
<td>88.6 (124/140)</td>
<td>66.9 (97/145)</td>
</tr>
<tr>
<td>MITT</td>
<td>71.0 (125/176)</td>
<td>55.1 (102/185)</td>
<td>6.08, 25.70</td>
</tr>
<tr>
<td>MSSA</td>
<td>ME</td>
<td>84.9 (90/106)</td>
<td>75.3 (70/93)</td>
</tr>
<tr>
<td>MITT</td>
<td>73.0 (92/126)</td>
<td>66.4 (75/113)</td>
<td>−5.02, 18.30</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>ME</td>
<td>86.7 (13/15)</td>
<td>94.4 (17/18)</td>
</tr>
<tr>
<td>MITT</td>
<td>68.4 (13/19)</td>
<td>65.4 (17/26)</td>
<td>−24.73, 30.81</td>
</tr>
</tbody>
</table>

*TOC visits occurred 7 days after the end of treatment. CI, confidence interval.*

*Patients could be switched to nafcillin, oxacillin, dicloxacillin, or flucloxacillin based on culture results.*
TABLE 5. Microbiological outcomes at TOC visit of ME and MITT patients with MSSA at baseline treated with linezolid or comparator drugs

<table>
<thead>
<tr>
<th>Patient population</th>
<th>% of patients cured (no. cured/total) after:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Linezolid (N = 592)</td>
</tr>
<tr>
<td>ME</td>
<td>84.9 (90/106)</td>
</tr>
<tr>
<td>MITT</td>
<td>73 (92/126)</td>
</tr>
</tbody>
</table>

* a Patients could be switched to nafcillin, oxacillin, dicloxacillin, or flucloxacillin.

There was no significant difference between groups in frequency of adverse events leading to discontinuation (5.1% of linezolid patients and 5.8% of vancomycin patients; P = 0.588). A significantly greater percentage of vancomycin-treated patients reported adverse events in the skin system leading to discontinuation (P = 0.012). Rash was the only drug-related adverse event reported by >1% of patients (eight patients; P = 0.004). Rash was reported only in vancomycin-treated patients, and anaphylaxis, drug-induced allergic reaction, and fever were reported more often in this treatment group. Diarrhea was the most common reason for discontinuation for patients in the linezolid group, with one case of *Clostridium difficile* diarrhea each documented in the linezolid and vancomycin arms of the study. Thrombocytopenia was also reported as leading to discontinuation for patients in the linezolid group.

Drug-related serious adverse events were reported rarely in this study, by two linezolid-treated patients and eight vancomycin-treated patients. There was no significant difference in the percentages of patients reporting drug-related serious adverse events leading to treatment discontinuation (P = 0.300).

There were nine deaths in the linezolid group and seven deaths in the vancomycin group (P = 0.605). In each case, the cause of death was judged by the investigator to be unrelated to the study drug.

**DISCUSSION**

An STI generally develops after skin integrity is interrupted. The injury allows organisms commonly found on the skin to cross this protective barrier and cause infection (9). In addition to antimicrobial efficacy, many factors, including the host, the environment, or bacteria, can influence the outcome of CSSTIs. For example, host factors that negatively impact patient outcome include comorbid conditions, a blood urea nitrogen level of >30 mg/dl, a sodium level of <130 meq/ml, and a hematocrit of <30%. Environmental factors that reduce cure rates include a lesion area of ≥150 cm² and a surgical wound infection (48).

The type of infecting organism also plays a role, and MRSA has become a predominant pathogen in nosocomial infections (42). In 1999, a National Nosocomial Infection Surveillance System report documented that 54.5% of *S. aureus* isolates from nosocomial infections in intensive care unit patients were methicillin resistant, which was a 43% increase from 1998 (17). Risk factors for MRSA are often divided into patient- and treatment-related groups (39). Patient-related risk factors include known colonization, immunosuppression, diabetes, open chronic wounds, and increased illness severity. Treatment-related factors include previous antibiotic use, intravascular catheterization, and prolonged hospitalization. MRSA infections are associated with an increased incidence of bacteremia, septic shock, amputation, and mortality (8, 16, 24, 35). Additionally, infections due to MRSA can significantly prolong hospitalization, which can more than double treatment costs (4, 16).

Given the rising prevalence of MRSA, the associated costs, and the devastating consequences, this organism must be considered when treating patients with CSSTIs. Until recently, therapy for MRSA strains with multidrug resistance has been limited to vancomycin. New drugs with activity against MRSA strains with multidrug resistance have been considered when treating patients with CSSTIs. Until recently, therapy for MRSA strains with multidrug resistance has been limited to vancomycin. New drugs with activity against MRSA have been developed, and linezolid is one of these agents (10).

This study is the largest comparator-controlled clinical trial of linezolid reported to date for the treatment of CSSTIs with MRSA as a leading pathogen. The study was designed as a clinical outcome study to compare vancomycin and linezolid used for patients with CSSTIs. Conduct attempted to mimic the real-world use of vancomycin and linezolid. Recommended doses were used in both arms, but no pharmacokinetic monitoring was mandated.

The results indicate that the two drugs are equivalent for the ITT population, with linezolid superior to the comparative regimen in the per-protocol analysis and to vancomycin in the MRSA subset. The difference between linezolid and vancomycin results was most dramatic in patients with abscesses and surgical-site infections caused by MRSA. The superior results in the MRSA patient group compared to the trend for better outcome noted in the MSSA group may be explained by the more-severe infections in the MRSA group, thus allowing easier differentiation of clinical responses. In addition, the MSSA group was smaller, making statistical significance more difficult to achieve. The better outcomes among MRSA-infected patients also could be related to the enhanced skin and tissue penetration of linezolid (12, 20, 26, 34) or to the inadequate...
dosing of vancomycin. The consensus on evidence-based guidelines for dosing vancomycin is poor (43). The dose of 1 g every 12 h for patients with normal renal function used in this study is the recommended dose and is commonly used for treating patients with CSSTIs (46). In addition, investigators were allowed to monitor and adjust vancomycin levels according to practices at their institutions. Linezolid-treated patients also had quicker resolution of their symptom scores at day 4 than vancomycin-treated patients had. However, this did not equate to a reduction in the total number of days the patients received antibiotics. However, the longer total treatment duration for the linezolid arm might be explained by the convenience of an oral drug compared to that of i.v. vancomycin. Studies of shorter treatment lengths would be useful to evaluate optimal treatment duration and to minimize drug-related adverse events, such as thrombocytopenia, that are associated with linezolid.

Linezolid and vancomycin were both well tolerated. While more adverse events occurred overall with linezolid, the numbers of patients who had the drugs stopped prematurely due to adverse reactions were similar. Thrombocytopenia, considered to be an adverse event by investigators, was more common in patients treated with linezolid (3.5%). Previous studies have shown that linezolid can cause mild, reversible, time-dependent myelosuppression, particularly when patients are treated for longer than 14 days (3, 13). Patients with underlying hematologic abnormalities or lower baseline values may be at increased risk of thrombocytopenia during treatment with linezolid, as with many antibiotics, and should be monitored, especially when treatment exceeds 14 days.

Our study design has a few limitations. The study was open label because conduct of a double-blind trial was not feasible due to differences in dosing intervals and availability of bioavailable oral formulations for vancomycin. Three aspects of the open-label design could have influenced the study results, namely, randomization to treatment, patient demographics, and clinical endpoints. Randomization was performed according to the predefined study protocol, and a demographic analysis revealed comparable populations in both arms for all characteristics examined, including, most importantly, the baseline MMP severity score. Clinical resolution of a complicated skin infection is not a subtle finding; hence, bias due to investigator assessment is also unlikely. We conclude that the magnitude of any bias, from the sources considered, is unlikely to account for the results observed in this study, especially given the size of the study and the multiple investigators involved. In addition, the lack of culture material in patients with cellulitis is a problem for microbiological efficacy but not for clinical efficacy, which was the primary endpoint. Cellulitis patients were equally distributed between the two arms and should not have affected the overall outcome.

The 100% oral bioavailability of linezolid also allowed some investigators to avoid the i.v. route for linezolid. Comparing the patients treated only with oral linezolid to the patients treated with i.v. vancomycin revealed no difference in outcomes despite the different routes of administration. Patients with MRSA infections who are treated with linezolid have shorter i.v. treatment times and an increased chance of being discharged from the hospital in 1 week (15, 33). Other advantages of oral over i.v. therapy include no need for i.v. access, no risk of catheter-related infection, and decreased pharmacy and nursing time to administer the drug while the patient is hospitalized (22, 23, 30).

The emergence of community-acquired MRSA SSTIs poses a new dilemma for practicing physicians, and epidemiologic studies are needed to determine the prevalence of MRSA SSTIs in communities (29). However, selection of patients at high risk for hospital-acquired MRSA infection is possible based on clinical risk factors (39). It seems prudent to prescribe an agent effective against MRSA to patients with risk factors for hospital-acquired MRSA or to patients who have presumed staphylococcal infections where the prevalence of MRSA is known to be >20% in the hospital or if the infection is severe. The results of this study demonstrate that linezolid therapy is safe, well tolerated, and superior to vancomycin in the treatment of CSSTIs due to MRSA.

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