MAJOR ARTICLE

Randomized, Double-Blind Comparison of Once-Weekly Dalbavancin versus Twice-Daily Linezolid Therapy for the Treatment of Complicated Skin and Skin Structure Infections

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Background. Dalbavancin, a novel lipoglycopeptide with a pharmacokinetic profile that allows weekly dosing, is active against gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA). The efficacy of dalbavancin for treatment of skin and skin structure infections (SSSIs) was demonstrated in a phase 2 study.

Methods. In a phase 3 noninferiority study, patients with complicated SSSIs, including infections known or suspected to involve MRSA, were randomized (ratio, 2:1) in a double-blind manner to receive dalbavancin (1000 mg given intravenously on day 1 and 500 mg given intravenously on day 8) or linezolid (600 mg given intravenously or intravenously/orally every 12 h for 14 days). Efficacy was assessed by determining clinical and microbiological responses at the end of therapy and at the test-of-cure visit. Relapses were identified by additional follow-up ~1 month later.

Results. MRSA was identified in 51% of patients from whom a pathogen was isolated at baseline. Dalbavancin and linezolid demonstrated comparable clinical efficacy in the clinically evaluable population at the test-of-cure visit (88.9% and 91.2% success, respectively). The rate of clinical success at the end of therapy was >90% in both arms. Less than 1.0% of patients in either treatment arm experienced relapse after the test-of-cure visit. Both treatments yielded successful microbiological response in excess of 85% among microbiologically evaluable patients at end of therapy and at the test-of-cure visit for all pathogens combined, for all *S. aureus* strains, and for MRSA. Gastrointestinal symptoms were among the most common adverse events in both arms. A higher proportion of patients in the linezolid arm reported adverse events that were judged by the investigator to be probably/possibly related to treatment (dalbavancin arm, 25.4% of subjects; linezolid arm, 32.2% of subjects).

Conclusions. Two doses of dalbavancin (1000 mg given on day 1 followed by 500 mg given on day 8) were as well tolerated and as effective as linezolid given twice daily for 14 days for the treatment of patients with complicated SSSI, including those infected with MRSA.

Dalbavancin is a novel, semisynthetic lipoglycopeptide antibacterial with a pharmacokinetic profile that allows weekly dosing. It has potent in vitro activity against gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA), and it is superior to most of the other antibiotics used to treat gram-positive bacterial infections, including vancomycin [1, 2]. In addition, dalbavancin has demonstrated superior in vivo activity against infection due to MRSA and other bacteria in animal infection models [3–5]. Its spectrum of activity suggests that dalbavancin has the potential to be useful for treatment of skin and skin structure infections (SSSIs). Gram-positive bacteria—in particular, *S. aureus* and *Streptococcus pyogenes*—are among the most common pathogens implicated in SSSI, with

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S. aureus accounting for more than one-half of the isolates [6], and the prevalence of MRSA as a pathogen in institutional and community settings [7].

The half-life of dalbavancin in humans (~8.5 days) allows weekly administration of the drug, with therapeutic concentrations in plasma maintained for the entire 7-day period between doses. In a phase 2 investigation of dalbavancin treatment for SSSI, a 2-dose regimen (a 1000-mg dose given on day 1 followed by a 500-mg dose given on day 8) appeared to be well tolerated and to be more effective for the treatment of SSSI due to gram-positive bacteria, compared with either a single-dose dalbavancin regimen (1100 mg given on day 1) or the investigator-chosen standard of care [8]. The goal of the present study was to demonstrate the safety and efficacy of dalbavancin for the treatment of patients with complicated SSSI, compared with linezolid, an antibacterial used for treatment of such infections.

PATIENTS, MATERIALS, AND METHODS

Study population. Participants consisted of adults with suspected or confirmed SSSI due to gram-positive pathogens that warranted initial parenteral therapy. Complicated SSSI was defined as infection that involved deeper soft tissue or that required significant surgical intervention (e.g., major abscesses, major burns, traumatic or surgical wound infections, and deep skin/skin-structure infection, such as extensive/ulcerating cellulitis) or as an SSSI known or suspected to be caused by MRSA. Patients were also required to have at least 2 local signs and/or symptoms of complicated SSSI (i.e., drainage/discharge, erythema, fluctuance, heat/localized warmth, pain/tenderness to palpation, or swelling/induration) and at least 1 sign of systemic infection or of another complicating factor, such that the patient required parenteral therapy. Patients known or suspected to have osteomyelitis or septic arthritis, those with infections expected to require >2 surgical interventions during the study, and those with concomitant conditions requiring antimicrobial therapy that would interfere with the evaluability of the condition under study were excluded from participation.

Study design and treatments. This randomized, double-blind, study enrolled patients at 65 centers in 7 countries (United States, Latvia, Lithuania, Canada, the United Kingdom, Estonia, and Germany) during the period of January 2003 through May 2004. Before the study was initiated, the health care centers obtained approval for participation from an institutional review board or independent ethics committee. All patients provided informed consent before undergoing any study procedures.

An unblinded third party who was otherwise uninvolved in the study (e.g., a study pharmacist) called an interactive voice-activated randomization system to obtain treatment assignments. Patients were randomized to treatment arms in a 2:1 ratio to receive dalbavancin or linezolid. Patients in the dalbavancin arm received a 1000-mg dose on day 1, followed by a 500-mg dose on day 8, with a possible switch to oral placebo if criteria for a switch from intravenous to oral therapy were met (i.e., defervescence or clinical improvement at the SSSI site after $\geqslant$24 h of parenteral therapy). Patients randomized to the linezolid arm received 600 mg of linezolid intravenously every 12 h, with a possible switch to orally administered linezolid (600 mg every 12 h) after at least 24 h of intravenous therapy. For both treatment arms, the total course of therapy (intravenous and oral) was 14 days. Each dalbavancin dose was defined as 7 days of therapy.

For blinding purposes, after the initial dalbavancin dose was administered, patients in the dalbavancin arm received placebo infusions of 5% dextrose for infusion or normal saline every 12 h until the treatment was switched to oral placebo. All patients (regardless of treatment assignment) received an intravenous infusion of study medication on day 8. Patients in the dalbavancin arm received 500 mg of intravenous dalbavancin (plus oral placebo if they had already switched to oral therapy). Patients in the linezolid arm either continued to receive intravenous linezolid or received an intravenous placebo infusion on day 8, plus the oral linezolid regimen, if they had already switched to oral therapy.

Empirical use of aztreonam and/or metronidazole was permitted for suspected mixed infections due to gram-negative pathogens. These treatments were discontinued if the etiology was determined to be strictly gram-positive pathogens. Use of any other antibacterial was prohibited.

Clinical and microbiological evaluations. Patients were assessed at baseline and on the day of the switch from intravenous to oral therapy, in addition to the following study visits: day 4, day 8, the end-of-therapy (EOT) visit (within 3 days after completion of treatment with the study medication), and the test-of-cure (TOC) visit (14 ± 2 days after completion of treatment with the study medication). Signs and symptoms of SSSIs were recorded at each visit. The investigator assessed patients as having an outcome of clinical success, clinical failure, or indeterminate at the EOT and TOC visits on the basis of presentation of the SSSI. Samples for SSSI cultures were obtained at baseline, and cultures were repeated at each study visit if clinically warranted or if the patient was determined to have experienced treatment failure. If appropriate, blood samples were obtained for culture at baseline, and cultures were repeated until the results were negative if they had been positive initially. Adverse events, concomitant medications, and vital signs were recorded at each visit. Blood samples were obtained for evaluation of hematology, and clinical chemistry parameters were determined at baseline, day 8, the EOT visit, and the TOC visit.

Table 1. Study population and reasons for exclusion in a study of once-weekly dalbavancin versus twice-daily linezolid therapy for the treatment of complicated skin and skin structure infections (SSSIs).

Variable	No. (%) of patients	
	Dalbavancin arm	Linezolid arm
Intent-to-treat population		
All	571 (100)	283 (100)
Excluded patients		
Received prohibited antibiotic[a]	55 (10)	28 (10)
Clinical response of indeterminate at TOC visit	38 (7)	20 (7)
Received <3 days of study medication, including placebo[b]	24 (4)	2 (1)
Other[c]	20 (4)	7 (2)
Patients who were clinically evaluable at the TOC visit	434 (76)	226 (80)
Microbiological intent-to-treat population	358 (63)	192 (68)
Patients who were microbiologically evaluable at the TOC visit	277 (77)[d]	152 (79)[d]

NOTE. TOC, test of cure.

[a] Received >24 h of another systemic antibacterial therapy with documented activity against the causative organism within 7 days prior to receipt of the first dose of study medication through the TOC visit or topical antibacterials for SSSI during the study, unless antibiotic was given for clinical failure.

[b] To determine clinical evaluability in a blinded manner, all patients were required to receive ⩾72 h of study medication (active or active/placebo), irrespective of treatment assignment. Patients who received <72 h of treatment were assigned an indeterminate clinical response.

[c] Includes TOC visits outside the protocol-defined window, violations of inclusion/exclusion criteria that affected efficacy, and unanticipated surgical intervention for SSSI (clinical successes only).

[d] Denominator for percentage calculation is the no. of patients in the microbiological intent-to-treat population.

In addition, patients who were determined to have had clinical success at the TOC visit were contacted ~1 month after the 14-day treatment period (day 39 ± 3 days) for completion of a late follow-up questionnaire. By phone interview, site personnel completed a standardized questionnaire of the patient's responses to inquiries regarding visits to a health care provider for the SSSI after the TOC visit, the status of SSSI signs and/or symptoms, the presence of fever, the occurrence of serious adverse events, and receipt of antibacterials for an SSSI after the TOC visit.

Statistical analysis. Efficacy was determined by evaluation of clinical and microbiological responses, both separately and combined, at the EOT and TOC visits. The primary end point was clinical success at the TOC visit. A successful clinical response was one in which signs and symptoms of SSSI had improved such that no further antibacterial therapy was warranted. A response of failure was assigned to patients for whom the SSSI had not improved or had worsened or who required additional antibacterials for the SSSI. Patients who received <72 h of study medication or who did not present for evaluation were considered to have indeterminate results. Relapse was defined as receipt of antibacterials for the SSSI after the TOC visit. The presence or absence of baseline gram-positive pathogens at the EOT and TOC visits was used for programmatic determination of microbiological response for each patient and pathogen. Microbiological response was presumed on the basis of clinical response if no culture results were available. Successful microbiological response at the patient level included eradication or presumed eradication of all baseline gram-positive pathogens. Overall response combined clinical and microbiological response for a comprehensive assessment of efficacy.

Four populations were prospectively identified for evaluation of efficacy: the intent-to-treat population, the clinically evaluable population, the microbiological intent-to-treat population, and microbiologically evaluable population. The intent-to-treat population consisted of all treated patients. Clinically evaluable patients received at least 72 h of treatment with the blinded study medication, did not have an indeterminate clinical response, and fulfilled all other protocol requirements relating to concurrent use of antibacterials, surgical intervention of the SSSI, and efficacy-related inclusion/exclusion criteria. The microbiological intent-to-treat population was the subset of the intent-to-treat population with a baseline gram-positive pathogen. Microbiologically evaluable patients were patients who were clinically evaluable and for whom there was a baseline gram-positive pathogen. The primary analysis was a comparison of the clinical success rates between treatment arms among clinically evaluable patients at the TOC visit [9]. A 1-sided 97.5% CI was calculated for the true difference in efficacy be-

Table 2. Selected demographic and baseline characteristics of the overall study population.

Characteristic	Dalbavancin arm (n = 571)	Linezolid arm (n = 283)
Demographic characteristic		
Male sex	353 (62)	172 (61)
Age, years		
Mean ± SD	47 ± 16	46 ± 17
Range	18–93	18–92
Ethnicity		
White	390 (68)	194 (69)
Hispanic/Latino	109 (19)	45 (16)
Black	59 (10)	32 (11)
Other	13 (2)	12 (4)
SSSI history		
Cause of infection		
Spontaneous	286 (50)	133 (47)
Trauma	141 (25)	77 (27)
Postsurgery infection	57 (10)	31 (11)
Bite	54 (9)	18 (6)
Other	33 (6)	24 (8)
Type of infection		
Major abscess	190 (33)	86 (30)
Cellulitis	157 (27)	84 (30)
Other deep soft-tissue infection	96 (17)	46 (16)
Traumatic wound infection	63 (11)	33 (12)
Surgical wound infection	47 (8)	27 (10)
Infected major burn[a]	18 (3)	7 (2)
Medical history		
Baseline hospitalization	357 (63)	182 (64)
Diabetes mellitus	139 (24)	60 (21)
Vascular disease	61 (11)	18 (6)
Use of prosthetic devices	30 (5)	10 (4)
Cancer	3 (1)	2 (1)

NOTE. Data are no. (%) of patients, unless otherwise indicated.

[a] Burn on ≤20% of body surface.

tween dalbavancin and linezolid. Noninferiority was concluded if the lower limit of the 1-sided 97.5% CI did not exceed −12.5%. Safety was evaluated for the intent-to-treat population by collection and analysis of data on adverse events, clinical laboratory test results, and vital signs.

RESULTS

Study population. Eight hundred fifty-four patients with complicated SSSI received treatment under this protocol. Centers in North America enrolled and treated 87% of the patients. Of the 854 treated patients, 700 (82%) were clinically evaluable at the EOT visit, and 660 (77%) were clinically evaluable at the TOC visit. The primary reasons for nonevaluability are listed in table 1. The proportions of patients excluded for each reason were similar between treatment arms, except for patients who received <72 h of treatment, for which the proportion was higher in the dalbavancin arm.

The treatment arms were well matched with respect to demographic and baseline characteristics (table 2). The sole relevant difference between groups was a significantly higher incidence of vascular disease in the dalbavancin arm. Cause, type, and presentation of SSSI were also similar between treatment arms. Approximately one-half of the SSSIs were spontaneous in origin; 26% resulted from trauma. Major abscesses (32%) and cellulitis (28%) were the predominant infection types. Signs and/or symptoms of SSSI reported at baseline for >95% of patients included erythema, heat/localized warmth, pain/tenderness to palpation, and swelling/induration.

Baseline microbiological findings. Baseline cultures yielded at least 1 gram-positive pathogen for 550 patients (64%; the microbiological intent-to-treat population). Of these, 90% presented with a single gram-positive pathogen. *S. aureus* was predominant (89% of all patients). Of the *S. aureus* isolates, 278 (57%) of 492 were MRSA. Overall, 51% of patients presented with SSSI that involved MRSA. No pathogen species other than *S. aureus* accounted for >6% of SSSIs in either arm (table 3).

Clinical efficacy. Among patients who were clinically evaluable at the TOC visit, 88.9% in the dalbavancin arm and 91.2% in the linezolid arm achieved clinical success. The lower limit of the 95% CI (−7.28%) was within the limit for demonstration of noninferiority (−12.5%) that was prospectively defined for the primary end point. Figure 1 compares clinical success rates and other end points at the EOT and TOC visits in the 2 treatment arms.

Clinical failures occurred predominantly by the EOT (≥70%

Table 3. Distribution of gram-positive pathogens isolated from baseline skin and skin structure infection and/or blood cultures.

Gram-positive pathogen	Dalbavancin arm (n = 358)	Linezolid arm (n = 192)
Total no. of gram-positive pathogen isolates	391	215
Staphylococcus aureus		
All[a]	318 (89)	174 (91)
MRSA	181 (51)	97 (51)
No. (%) of *S. aureus* isolates that were MRSA	181 (57)	97 (56)
Streptococcus pyogenes	19 (5)	12 (6)
Streptococcus agalactiae	16 (4)	10 (5)
Viridans *Streptococcus* species	15 (4)	6 (3)
Group G *Streptococcus* species	10 (3)	6 (3)
Group C *Streptococcus* species	5 (1)	3 (2)

NOTE. Data are no. (%) of patients in the microbiological intent-to-treat population of each treatment arm, unless otherwise indicated. MRSA, methicillin-resistant *S. aureus*.

[a] Includes strains identified as MRSA.

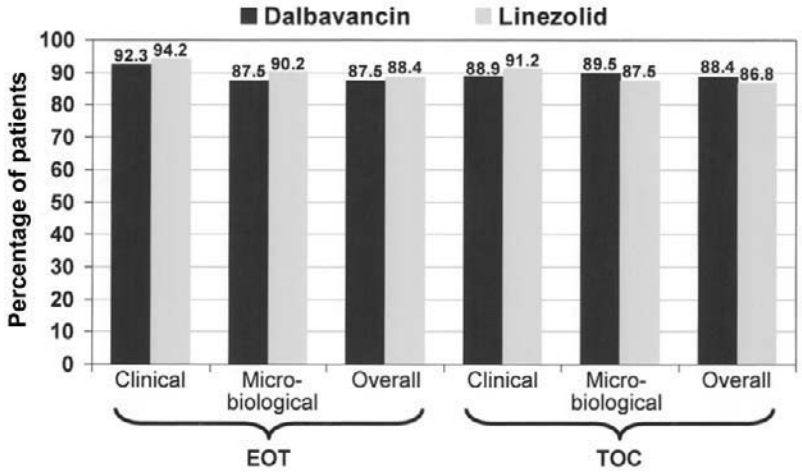

Figure 1. Summary of response end points in the evaluable populations illustrating the similarity between the dalbavancin and linezolid arms in the percentages of patients with clinical, microbiological, and overall (combined clinical/microbiological) success at end-of-therapy (EOT) and test-of-cure (TOC) visits.

of patients in each treatment arm). The clinical response of treatment failure for these patients was carried forward to the TOC visit. Efficacy was independent of infection type (e.g., major abscess and cellulitis).

Microbiological efficacy. Microbiological success at the patient level was similar between treatment arms among microbiologically evaluable patients at the EOT and TOC visits (figure 1). Microbiological response reflected the results for clinical response. Documented persistence of baseline pathogens occurred at the EOT visit for 8% and 7% of patients in the dalbavancin and linezolid arms, respectively, and for ⩽2% of patients in either treatment arm at the TOC visit. Recurrence of initial pathogen(s) at the TOC visit was documented for a small percentage of patients (1% for the dalbavancin arm and 4% for the linezolid arm).

On a pathogen basis, dalbavancin and linezolid both eradicated at least 85% of baseline pathogens at both the EOT and TOC visits. MRSA eradication rates at the TOC visit (eradicated or presumed eradicated) were 91% and 89% for the dalbavancin and linezolid arms, respectively. Emergence of new pathogens at the TOC visit (i.e., superinfection) occurred rarely (<1% of patients in either arm).

Overall response. Overall success rates were similar between treatment arms at the EOT and TOC visits (figure 1).

Durability of response. The late follow-up assessment applied only to patients with a clinical response of success at the

Table 4. Evaluation of responses to a late follow-up questionnaire.

Variable	No. (%) of clinically evaluable patients	
	Dalbavancin arm (n = 434)	Linezolid arm (n = 226)
Patients eligible for late follow-up assessment[a]	316	163
Response		
Success		
All	298 (94)	151 (93)
No visit to health care provider for SSSI after the TOC visit	282 (89)	135 (83)
Contacted health care provider after TOC visit regarding SSSI but did not receive additional antibiotics	16 (5)	16 (10)
Failure[b]	2 (0.6)	1 (0.6)
Unavailable for interview	16 (5)	11 (7)

NOTE. SSSI, skin and skin structure infection; TOC, test of cure.

[a] Clinically evaluable patients with successful clinical response at the TOC visit.

[b] Patient received additional antibiotics for treatment of SSSI after the TOC visit.

Table 5. Adverse events with probable or possible relationship to treatment.

Event	Percentage of patients	
	Dalbavancin arm (n = 571)	Linezolid arm (n = 283)
Any event	25.4	32.2
Nausea	3.2	5.3
Diarrhea	2.5	5.7
Elevated blood lactate dehydrogenase level	1.9	1.8
Headache	1.9	1.8
Elevated γ-glutamyltransferase level	1.9	1.4
Vomiting	1.9	1.1
Rash	1.8	1.8
Abnormal liver function test results	1.6	1.1
Elevated alanine aminotransferase level	1.2	1.8
Fungal vaginosis	0.9	1.8
Loose stools	0.4	2.1
Thrombocytopenia	0.2	2.5

NOTE. Table lists adverse events with probable or possible relationship with treatment that were experienced by ⩾2% of patients in the study.

TOC visit. Among the 94% of eligible evaluable patients interviewed, the vast majority in each treatment arm had not contacted a health care provider regarding their SSSI after the TOC visit (table 4). Reports of persistent or new signs/symptoms of SSSI were infrequent. Only 0.6% of contacted patients in each treatment arm were considered to have experienced a relapse on the basis of receipt of additional antibacterial therapy for SSSI after the TOC visit.

Safety. Patients in the dalbavancin arm received a mean of 1.9 active doses during the study. The majority of patients in the dalbavancin arm (87%) received both active doses (i.e., the doses given on day 1 and day 8) and were thus considered to have been exposed to 14 days of treatment. In the linezolid arm, patients received a mean of 26.2 doses of active medication (intravenous plus oral medication). Of linezolid recipients, 85% received intravenous or intravenous and oral treatment for ⩾14

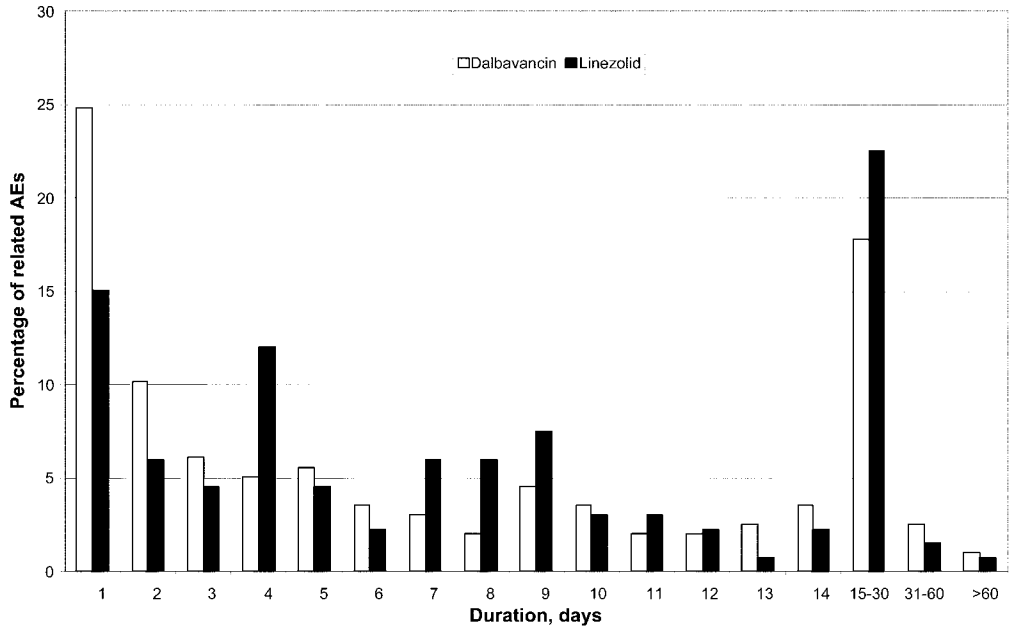

Figure 2. Duration of adverse events related to dalbavancin and linezolid therapy in the intent-to-treat population

days. Adverse events, which were generally mild or moderate in intensity, were reported by 56% of patients in the dalbavancin arm and by 61% in the linezolid arm. Adverse events that were considered probably or possibly related to treatment were more frequent in the linezolid arm (32.2%) than in the dalbavancin arm (25.4%) (table 5). Overall, the type and severity of adverse events were comparable between the treatment arms. An analysis of duration of adverse events by treatment arm for which start and stop dates were available demonstrated that the median duration of adverse events was 1 day shorter for dalbavancin-treated patients than for comparator-treated patients; the mean duration of adverse events was similar between treatment groups. Figure 2 shows a comparison of the duration of adverse events for dalbavancin-treated patients versus comparator-treated patients. The incidence of infusion site reactions was low in both treatment arms (2.8% in the dalbavancin arm and 3.9% in the linezolid arm). No cases of red man syndrome were reported during the study.

A small percentage of patients in each arm (3.9% for the dalbavancin arm and 3.2% for the linezolid arm) discontinued treatment because of adverse events. Serious adverse events were reported by 8% of patients overall (7.5% in the dalbavancin arm and 8.5% in the linezolid arm). All but 3 serious adverse events (1 in the dalbavancin arm and 2 in the linezolid arm) were considered to be unrelated or unlikely related to study medication. All 3 treatment-related serious adverse events pertained to laboratory abnormalities (in the dalbavancin arm, the adverse event was mild leukopenia, which resolved spontaneously; in the linezolid arms, the adverse events were moderate thrombocytopenia, which resolved spontaneously, and severe pancytopenia, which resolved with treatment). Four deaths occurred during the study (2 in the dalbavancin arm and 2 in the linezolid arm). All adverse events associated with death were considered by the investigator to be unrelated or unlikely to be related to treatment.

Abnormalities in hematological findings and/or clinical chemistry parameters with potential clinical relevance occurred infrequently in both treatment arms. Additional examination of specific abnormalities in the alanine aminotransferase level, aspartate aminotransferase level, and combined alanine aminotransferase and total bilirubin elevations; transitions in hepatobiliary parameters; and changes in vital signs during the study did not reveal any areas of clinical concern.

DISCUSSION

The objectives of this study were to determine the efficacy and the safety of dalbavancin, compared with linezolid, for the treatment of adults with complicated SSSI. The high degree of sustained clinical success reveals that dalbavancin has excellent clinical efficacy. The data are robust, as indicated by the concordance in success rates for other end points. Figure 1 illustrates the similarity in response between dalbavancin treatment and linezolid treatment for clinical, microbiological, and overall response at both the EOT visit and the TOC visit, thus conferring clinical relevance to the statistical conclusion of noninferiority for the primary end point. The high rates of clinical success were comparable to published clinical cure rates for linezolid, oxacillin/dicloxacillin, and flucloxacillin and higher than published rates for daptomycin, ertapenem, piperacillin-tazobactam, and quinupristin/dalfopristin [10–15]. Durability of clinical success was supported by post–TOC visit patient reports of low rates of antibacterial use and lack of signs or symptoms of SSSI.

Our study enrolled a population representative of a broad range of complicated SSSIs. The treatment arms were very well matched with respect to demographic characteristics and location, type, and cause of infection. High rates of pathogen recovery were achieved at baseline. As expected, *S. aureus* was the predominant gram-positive pathogen. The 51% incidence of MRSA was higher than would be predicted by centralized epidemiological data from the Centers for Disease Control and Prevention National Nosocomial Infections Surveillance system for patients originating from the community (26%) [7].

Recent reports in the medical literature describe an increasing incidence of community-acquired MRSA infection [16], including outbreaks in settings where MRSA represented >50% of *S. aureus* isolates [17, 18]. Until recently, community-based SSSIs that involve MRSA typically occurred in patients with predisposing risk factors, such as recent hospitalization, contact with a recently hospitalized individual, or previous antimicrobial therapy. However, SSSI due to MRSA is becoming increasingly common in patients without such risk factors, and the organisms have new characteristics, leading to their designation as community-acquired MRSA isolates [16, 19, 20]. Environments and situations in which there is close physical contact (e.g., sports teams and military recruit training centers) are the most likely setting for outbreaks of community-acquired MRSA infection; however, spread of MRSA can also occur in the absence of physical contact [17, 21]. MRSA infection in ambulatory outpatients who develop SSSI is a distinct possibility and should be considered during treatment selection.

Dalbavancin demonstrated excellent efficacy against MRSA. The 91% eradication rate exceeds published values for a number of antibacterials (quinupristin/dalfopristin, ertapenem, levofloxacin, ticarcillin/clavulanate, and amoxicillin/clavulanate) [14, 15, 22]. Because it can be administered on an outpatient basis, dalbavancin may be a reasonable option for empirical treatment of patients with SSSI that is suspected of involving MRSA.

Dalbavancin was well tolerated and has a safety profile similar to that of linezolid. Gastrointestinal events—particularly those events considered to be related to treatment—appeared to be

more prevalent with linezolid therapy. The excellent tolerability of dalbavancin infusions observed in our study is in contrast to that of quinupristin/dalfopristin, for which adverse venous events are common [15]. This low incidence of infusion-related reactions occurred in a structured environment in which patients in the dalbavancin arm received more infusions and perhaps retained indwelling catheters longer than would be otherwise required outside of the context of a clinical study. In an actual clinical setting, patients would have received only two 30-min infusions of dalbavancin instead of the higher number of doses they received in the trial because of the double-blind study design.

Because of the double-blind study design, which was essential for an unbiased determination of efficacy and safety, the impact of dalbavancin's weekly dosing schedule on patient compliance, hospitalization, or health care costs cannot be ascertained from our study. It has been demonstrated that treatment with the intravenous and the 100% bioavailable oral formulations of linezolid results in a decreased duration of hospitalization and decreased health care costs for patients with complicated SSSI known or suspected to involve MRSA [23, 24]. The presence of MRSA in SSSI has been independently correlated with increased cost [25]. The potential advantages of dalbavancin in patient acceptance and health outcomes are being examined in a separate study.

In summary, dalbavancin is well tolerated and highly effective for the treatment of patients with complicated SSSI, including infections involving MRSA. Dalbavancin could provide an alternative to vancomycin and linezolid for treatment of SSSIs due to gram-positive pathogens.

DALBAVANCIN COMPLICATED SKIN AND SKIN STRUCTURE INFECTION STUDY GROUP MEMBERS

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