MAJOR ARTICLE

Single-Dose Oritavancin Versus 7–10 Days of Vancomycin in the Treatment of Gram-Positive Acute Bacterial Skin and Skin Structure Infections: The SOLO II Noninferiority Study

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Background. Oritavancin is a lipoglycopeptide antibiotic with rapid bactericidal activity against gram-positive bacteria. Its concentration-dependent activity and long half-life allow for single-dose treatment.

Methods. In a randomized, double-blind trial, adults with acute bacterial skin and skin structure infections (ABSSSIs) received either a single intravenous 1200-mg dose of oritavancin or 7–10 days of twice-daily vancomycin. Three efficacy endpoints were tested for noninferiority: (1) primary composite endpoint at 48–72 hours (cessation of spreading or reduction in lesion size, absence of fever, and no rescue antibiotic); (2) investigator-assessed clinical cure 7–14 days after end of treatment; and (3) ≥20% reduction in lesion area at 48–72 hours.

Results. A total of 503 and 502 patients comprised the modified intent-to-treat population for oritavancin and vancomycin, respectively. All 3 efficacy endpoints met the 10% noninferiority margin: the primary composite endpoint (80.1% vs 82.9%; 95% confidence interval [CI], −7.5 to 2.0), investigator-assessed clinical cure (82.7% vs 80.5%; 95% CI, −2.6 to 7.0), and proportion of patients attaining ≥20% reduction in lesion area (85.9% vs 85.3%; 95% CI, −3.7 to 5.0) for oritavancin vs vancomycin, respectively. Efficacy outcomes by pathogen, including methicillin-resistant *Staphylococcus aureus* and the frequency of adverse events, were similar between treatment groups.

Conclusions. A single 1200-mg dose of oritavancin was noninferior to 7–10 days of vancomycin in treating ABSSSIs caused by gram-positive pathogens, and was well tolerated. Oritavancin provides a single-dose alternative to multidose therapies for the treatment of ABSSSIs.

Clinical Trials Registration. NCT01252732.

Keywords. oritavancin; lipoglycopeptide; vancomycin; methicillin-resistant *Staphylococcus aureus* (MRSA); acute bacterial skin and skin structure infection (ABSSSI).

Acute bacterial skin and skin structure infections (ABSSSIs) are among the most common infections seen in clinical practice. These infections may require systemic antibiotic therapy, surgical management, and hospitalization and, if untreated, may become severe or life-threatening [1, 2]. The clinical complications of delayed or inappropriate treatment of ABSSSIs can be serious, including those resulting from local spread or secondary bacteremia with potential for distant metastatic foci of infection [3]. The economic burden of ABSSSI remains substantial and is driven by high costs of hospitalization [4, 5] and treatment with intravenous agents that require once- or twice-daily dosing for a total treatment duration often exceeding 7–10 days [4, 6, 7, 8–14]. Treatment for ABSSSI often requires coverage against methicillin-resistant *Staphylococcus*

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aureus (MRSA), which continues to be the predominant causative pathogen in many countries [15–17]. Treatment in the outpatient setting may not overcome the limitations of multiple administrations, incomplete medication adherence [18], and complexity of serum drug monitoring [19].

Oritavancin is a novel semisynthetic lipoglycopeptide antibiotic with potent activity against gram-positive pathogens, including MRSA [20–22]. The pharmacokinetic/pharmacodynamic (PK/PD) profile of oritavancin includes concentration-dependent bacterial killing [23] and an extended plasma elimination half-life [24, 25]. Oritavancin does not require dose adjustment for age or renal function or in patients with moderate hepatic impairment [24]. Dose adjustment in patients undergoing dialysis is also unlikely to be required as oritavancin was not removed by dialysis in an in vitro study [26]. Because the PK/PD profile of oritavancin allows for single-dose treatment [27, 28], the phase 3 study presented here A Multicenter, Double-Blind, Randomized Study to Evaluate the Efficacy and Safety of Single-Dose IV Oritavancin versus IV Vancomycin for the Treatment of Patients with ABSSSI (SOLO II) was designed to evaluate the efficacy and safety of a single dose of oritavancin compared with a regimen of twice-daily vancomycin for 7–10 days in adults with ABSSSI.

METHODS

Study Design and Treatment

SOLO II was a phase 3, global, multicenter, randomized, double-blind, comparative efficacy and safety study evaluating single-dose intravenous oritavancin vs intravenous vancomycin for 7–10 days in adults with ABSSSIs comprising wound infection, cellulitis, and major cutaneous abscess. The study design was consistent with the SOLO I study and current regulatory guidances [29–32]. The protocol was approved by institutional review boards/ethics committees, and all patients provided written informed consent. The study was conducted from January 2011 through June 2013. Study participants were randomized 1:1 to receive either a single 1200-mg intravenous dose of oritavancin infused over 3 hours, followed by intravenous placebo (every 12 hours) or intravenous vancomycin (1 g or 15 mg/kg, every 12 hours) for 7–10 days. Individual site personnel were permitted to make dosing adjustments to vancomycin according to standard practice. Aztreonam and metronidazole were permitted for gram-negative and anaerobic coverage, respectively.

Randomization was stratified by geographic region, site, and presence of diabetes mellitus. Enrollment of patients with major cutaneous abscesses was capped at 30%.

Clinical evaluations were performed at the following time points: 48–72 hours after the initiation of the study drug infusion (early clinical evaluation [ECE]); days 7–10 or the day the patient stopped study drug (end of therapy [EOT]); day 10 evaluation; 7–14 days after the EOT visit (posttherapy evaluation [PTE]); and an extended safety follow-up period of 60 days. Safety data were reviewed by an external independent data safety monitoring committee after 670 patients were treated in the study. The definitions of the analysis populations are provided in Figure 1.

Patient Eligibility

Eligible patients were to be at least 18 years of age with diagnosis of ABSSSI suspected or proven to be due to a gram-positive pathogen and which in the judgment of the investigator would require at least 7 days of intravenous therapy. Each lesion required surrounding erythema, edema, and/or induration of at least 75 cm^2. Patients also had to present with signs and symptoms of systemic inflammation. Details surrounding the eligibility criteria are presented in the Supplementary Appendix.

Efficacy Assessments

The primary efficacy endpoint was a composite outcome at ECE that comprised (1) cessation of spreading or reduction in the size of the baseline lesion, (2) absence of fever, and (3) no rescue antibiotic medication, as defined by the US Food and Drug Administration (FDA) [30].

The key secondary endpoint was investigator-assessed clinical cure at PTE, as defined by the European Medicines Agency [31].

An additional main secondary efficacy outcome was lesion area decrease ≥20% from baseline at ECE, as suggested by the Foundation for the National Institutes of Health [32].

The outcomes were analyzed in the modified intent-to-treat (mITT) population as well as in the clinically evaluable, microbiological intent-to-treat, and microbiologically evaluable populations (Figure 1). Efficacy endpoints are explained further in the Supplementary Appendix.

Safety Assessments

Safety assessments (safety population) included vital signs, electrocardiography, clinical chemistry and hematology parameters, and reporting of adverse events (AEs) and serious adverse events (SAEs). Treatment-emergent adverse events (TEAEs) were defined as AEs with onset or worsening severity at or after the first dose of study drug through the safety follow-up visit (day 60).

Statistical Methods

A sample size of 960 patients (480 per treatment group) provided at least 90% power to test noninferiority of oritavancin against vancomycin with respect to the primary efficacy outcome rate using a 10% noninferiority margin at the 1-sided α level of .025, when the primary efficacy outcome rate is assumed to be 75% in both treatment groups. This sample size also provided at least 90% power to test noninferiority for the

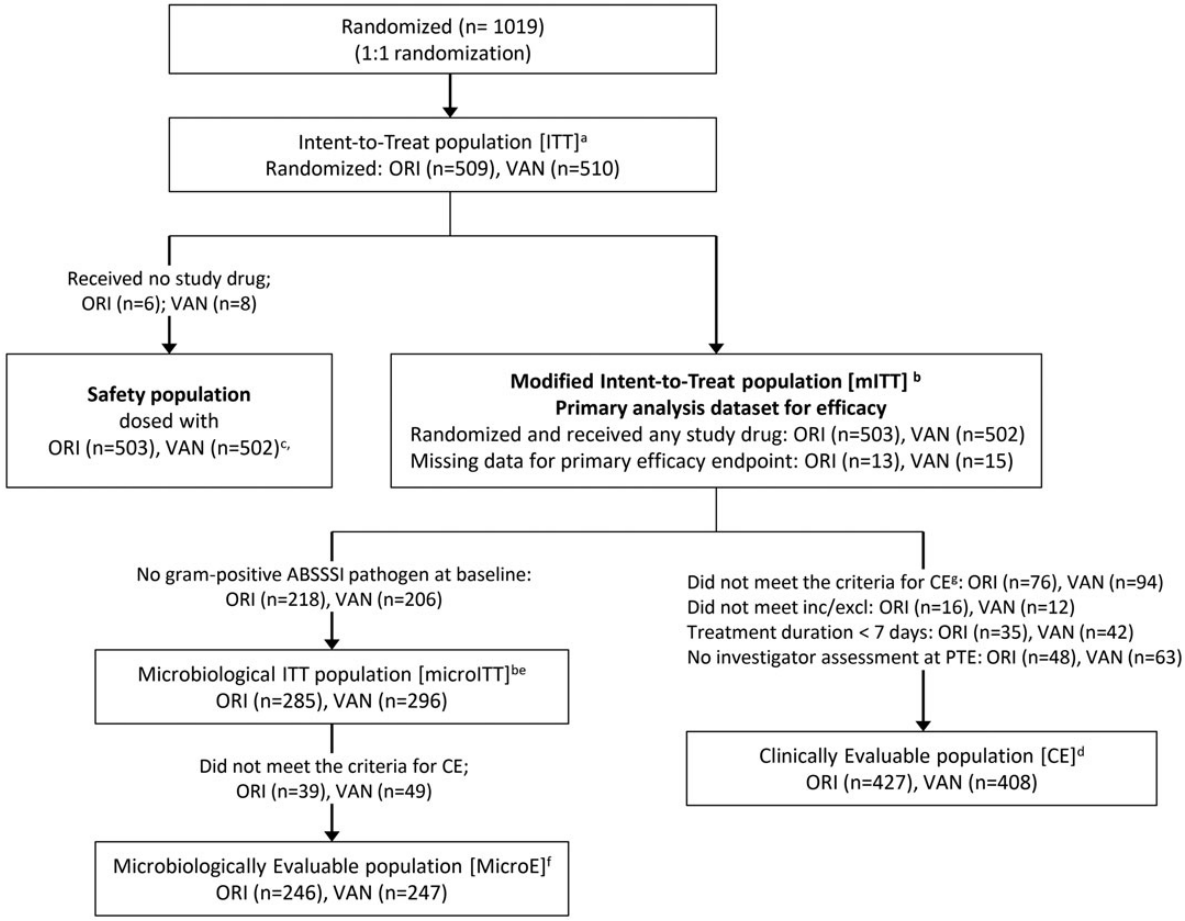

Figure 1. Disposition and Analysis Sets of Patients in the SOLO II Trial. [a] The intent-to-treat (ITT) population included all patients randomized into the study. [b] The modified intent-to-treat (mITT) was the primary population for all the efficacy analyses and included all randomized patients who received any study drug. Missing data for secondary endpoint: Investigator assessed clinical cure at post-therapy evaluation (PTE): Oritavancin (n = 50), Vancomycin (n = 60), VAN (n = 60). [c] The safety population was the primary population for all the safety analyses, and consisted of all patients who were dosed with study drug, irrespective of randomization. Treatment classification was based on the actual treatment received. [d] The clinically evaluable (CE) population consisted of all mITT patients who met the inclusion/exclusion criteria, received the full-course of randomized study treatment (for a minimum of 7 days), and had investigator assessment for clinical cure at PTE. The CE population was used to confirm the efficacy analyses. [e] The microbiologically ITT (MicroITT) population consisted of all mITT patients with baseline gram-positive pathogen(s) known to cause ABSSSI and they were used for the secondary efficacy analyses. [f] The microbiologically evaluable (MicroE) population was used to confirm the secondary efficacy analyses and consisted of all patients who were in both the MicroITT and CE populations. [g] Patients may appear in more than one category. Abbreviations: ABSSSI, acute bacterial skin and skin structure infection; ORI: oritavancin; VAN: vancomycin.

investigator-assessed clinical cure at PTE, using a 10% noninferiority at the 1-sided α level of .025, assuming the clinical cure event rate of 65% in both oritavancin and vancomycin.

For the primary efficacy assessment at ECE, the investigator-assessed clinical cure at PTE, and lesion area decrease by ≥20% from baseline to ECE, a 2-sided 95% confidence interval (CI) for the difference in rates between the 2 treatment groups (oritavancin rate minus vancomycin rate) was derived, using a 2-group large-sample normal approximation test of proportions. If the lower bound of the 2-sided 95% CI was greater than −10%, noninferiority of oritavancin was claimed at the 1-sided α level of .025. A hierarchical ordering of statistical testing was assumed such that the primary efficacy endpoint at ECE was tested first, followed by the investigator-assessed clinical cure at PTE and then lesion area decrease by ≥20% from baseline to ECE.

The 10% noninferiority margin for the primary efficacy endpoint and the endpoint of lesion area decrease ≥20% from baseline was based on guidance provided by the FDA [33]. Missing assessments were considered as failures for the primary and secondary efficacy outcomes. For additional endpoints, 95% CIs are provided for descriptive purposes only.

For safety assessments, descriptive analyses were performed in the safety population for all safety parameters by treatment group. Microbiologic methods are outlined in the Supplementary Data.

RESULTS

Patient Demographics and Baseline Medical Characteristics

Figure 1 depicts the patient disposition and analysis populations in the study. For the mITT population, there were no differences observed between patients enrolled in the oritavancin and vancomycin treatment arms in terms of demographics, type of ABSSSI, and relevant medical history (Table 1). The mean age of patients was 45.0 and 44.4 years, respectively, with 7.8% at least 65 years of age. Patients were predominantly white and male. Infection types were balanced in the oritavancin and vancomycin groups, with approximately 30.9% cellulitis, 32.5% abscess, and 36.5% wound infection. The median infection area at baseline was 287.8 cm^2 for the oritavancin group and 308.8 cm^2 for the vancomycin group. Demographics and baseline characteristics were similar in the clinically evaluable population (Supplementary Table 7).

A baseline pathogen was isolated from approximately 70% of patients in both treatment groups; 97% of these patients had a gram-positive pathogen known to cause ABSSSIs. *Staphylococcus aureus* was the most common pathogen and MRSA was recovered in 201 patients. For *S. aureus* (n = 509), the oritavancin minimum inhibitory concentration (MIC) range was ≤0.008–0.25 μg/mL and minimum inhibitory concentration required to inhibit the growth of 90% of organisms (MIC_{90}) was 0.12 μg/mL; for vancomycin, the MIC range was ≤0.25–1 μg/mL and vancomycin MIC_{90} was 1 μg/mL. There were no associations between MICs and outcomes at ECE or PTE for any baseline pathogen. No treatment-emergent MIC increases were noted for either vancomycin or oritavancin.

Clinical Outcomes

The single 1200-mg intravenous dose of oritavancin demonstrated similar efficacy to 7–10 days of intravenous vancomycin at the ECE and PTE time points. Oritavancin was noninferior to vancomycin for the primary composite endpoint at ECE (80.1% for oritavancin vs 82.9% for vancomycin), the investigator-assessed clinical cure endpoint at PTE (82.7% vs 80.5%, respectively), and the ≥20% reduction in lesion size endpoint at ECE (85.9% vs 85.3%, respectively), as the lower limit of the 95% CI for each endpoint was greater than −10% (Figure 2). Furthermore, high concordance rates were observed between success at the early endpoint and investigator-assessed clinical cure at PTE (Supplementary Table 9).

The early clinical response rates for oritavancin and vancomycin were similar when analyzed by body mass index (BMI), age, MRSA, sex, and race (Supplementary Figure 1 and Supplementary Table 8). In patients with a major cutaneous abscess, oritavancin had a lower response rate at ECE (primary endpoint) than vancomycin (oritavancin, 136/168 [81.0%]; vancomycin, 143/159 [89.9%]); however, a similar proportion of patients in each

Table 1. Demographics and Baseline Characteristics (Modified Intent-to-Treat Population)

Characteristic	Oritavancin (n = 503)	Vancomycin (n = 502)
Age, y		
Mean (SD)	45.0 (13.40)	44.4 (14.29)
Median (min, max)	45.0 (18, 85)	44.0 (18, 92)
≥65 y	39 (7.8)	39 (7.8)
Sex		
Male	338 (67.2)	343 (68.3)
Race		
White	356 (70.8)	356 (70.9)
Black	14 (2.8)	17 (3.4)
Asian	122 (24.3)	122 (24.3)
Other	11 (2.2)	7 (1.4)
Body weight, kg		
Mean (SD)	76.2 (20.57)	78.0 (23.24)
Median (min, max)	73.1 (41, 171)	73.7 (36, 189)
Body mass index, kg/m^2		
Mean (SD)	26.8 (6.74)	26.8 (7.07)
Median (min, max)	25.0 (16, 58)	25.0 (16, 65)
<25 kg/m^2	244 (48.5)	245 (48.8)
25–29.9 kg/m^2	136 (27.0)	144 (28.7)
≥30 kg/m^2	123 (24.5)	113 (22.5)
Infection type		
Wound infection	191 (38.0)	176 (35.1)
Confirmed MRSA	39/191 (20.4)	45/176 (25.6)
Cellulitis	144 (28.6)	167 (33.3)
Confirmed MRSA	12/144 (8.3)	18/167 (10.8)
Abscess	168 (33.4)	159 (31.7)
Confirmed MRSA	49/168 (29.2)	38/159 (23.9)
Diabetes mellitus (yes)	46 (9.1)	45 (9.0)
Temperature ≥38.0°C, proportion	118/502 (23.5)	106/501 (21.2)
WBC >12 000 cells/μL	112/453 (24.7)	125/449 (27.8)
Lesion area, cm^2		
Median (min, max)	287.8 (19, 4250)	308.8 (57, 2184)
≥75 cm^2	498/502 (99.2)	498/502 (99.2)
Patients received permitted medications		
Aztreonam	46 (9.1)	45 (9.0)
Metronidazole	32 (6.4)	22 (4.4)
Positive infection site culture, proportion	351/503 (69.8)	352/502 (70.1)
Any gram-positive pathogen	340/351 (96.9)	344/352 (97.7)
Staphylococcus aureus	250/340 (73.5)	258/344 (75.0)
MRSA[a]	100	101
Positive blood culture at baseline	10 (2.0)	10 (2.0)
S. aureus	2	1

Data are presented as No. (%) unless otherwise specified. Percentages may not add up to 100% due to rounding.

Abbreviations: max, maximum; min, minimum; MRSA, methicillin-resistant *Staphylococcus aureus*; SD, standard deviation; WBC, white blood cell.

[a] Includes both infection site culture and blood culture.

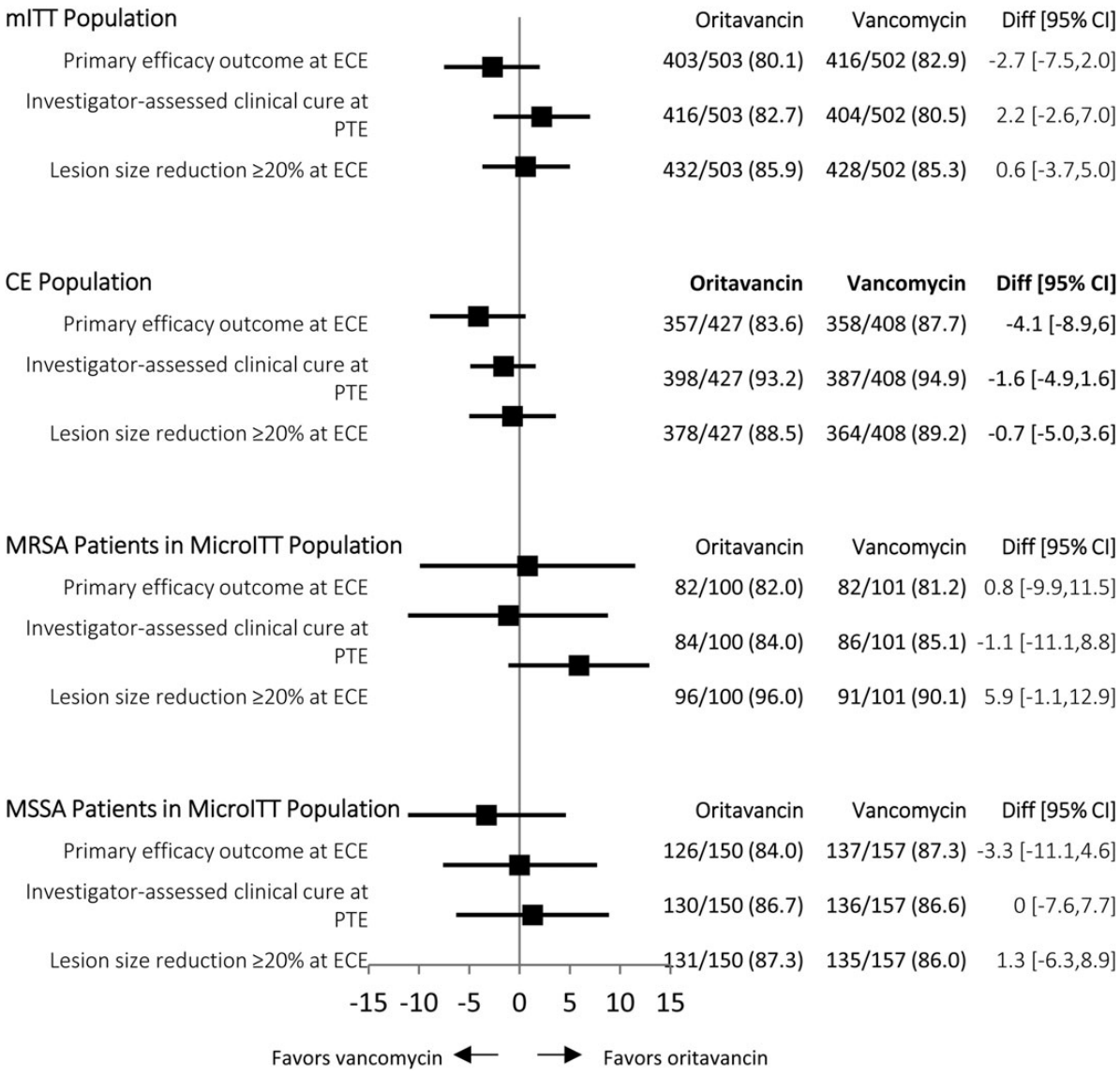

Figure 2. Results of the primary and secondary efficacy endpoints by analysis population and subgroup. Abbreviations: CE, clinically evaluable; CI, confidence interval; ECE, early clinical evaluation; mITT, modified intent-to-treat; MicroITT, microbiological intent-to-treat; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; PTE, posttherapy evaluation.

treatment group achieved ≥20% reduction in lesion size at ECE. Moreover, this difference was not observed at the PTE time point (Supplementary Figure 2). Approximately 24% of patients had a BMI >30 kg/m^2, and there were no differences in efficacy outcomes between the oritavancin and vancomycin treatment groups at ECE (whether early clinical response or ≥20% reduction in lesion size) or at PTE (investigator-assessed clinical cure) in this subgroup. Differences in response rates observed between treatment groups in the diabetic subgroup were noted (Supplementary Figures 1 and 2); however, the subgroup analyses were based on a relatively small number of patients and should be interpreted with caution. Furthermore, these results are not consistent with results observed in the SOLO I study, which had a greater number of patients with diabetes and demonstrated similar response rates between treatments in this subgroup [29].

The number of patients who were classified as failing treatment and the reasons for failure at both ECE and PTE were balanced across the 2 treatment groups (Supplementary Tables 2 and 3). Overall, 9.9% (50/503) of patients in the oritavancin group and 12.0% (60/502) of patients in the vancomycin group were deemed failures for the investigator-assessed clinical cure endpoint due to missing data. The majority of these 110 patients (99.1%) were considered to have failed treatment because they did not attend the PTE visit. Results in the mITT population were

Table 2. Primary Efficacy Outcome at Early Clinical Response by Baseline Pathogen[a] (Microbiological Intent-to-Treat Population)

Baseline Pathogen	Oritavancin (n = 285), no./No. (%)	Vancomycin (n = 296), no./No. (%)	Difference (95% CI)
No. of patients with at least 1 pathogen	234/285 (82.1)	252/296 (85.1)	−3.0 (−9.0 to 3.0)
Staphylococcus aureus	208/250 (83.2)	219/258 (84.9)	−1.7 (−8.1 to 4.7)
MRSA	82/100 (82.0)	82/101 (81.2)	0.8 (−9.9 to 11.5)
MSSA	126/150 (84.0)	137/157 (87.3)	−3.3 (−11.1 to 4.6)
Streptococcus species	36/48 (75.0)	50/57 (87.7)	−12.7 (−27.6 to 2.2)
S. anginosus group[b]	14/18 (77.8)	24/27 (88.9)	−11.1 (−33.7 to 11.5)
S. pyogenes	16/23 (69.6)	18/22 (81.8)	−12.3 (−37.0 to 12.5)
S. dysgalactiae	5/6 (83.3)	3/3 (100.0)	
S. agalactiae	1/1 (100.0)	4/4 (100.0)	
Enterococcus faecalis	5/6 (83.3)	6/7 (85.7)	

Patients with multiple pathogens are counted once in the rows for each pathogen. Only pathogens that appeared in both treatment arms are listed.

Abbreviations: CI, confidence interval; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.

[a] Includes only gram-positive pathogens known to cause acute bacterial skin and skin structure infections, whether isolated from infection site culture or blood culture.

[b] Includes *Streptococcus anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*.

consistent with those in the clinically evaluable population (Figure 2 and Supplementary Table 4). Results from sensitivity analyses were similar across treatment groups irrespective of the method used for handling missing data (Supplementary Table 5).

Similar efficacy was demonstrated across the 2 treatment groups in the MRSA and methicillin-susceptible *S. aureus* (MSSA) subpopulations for the primary and secondary endpoints (Figure 2). Within the MRSA subpopulation of the microbiological ITT population, similar efficacy was seen across treatment groups at both early and late endpoints (Figure 2), and consistent results were observed with the microbiologically evaluable population (Supplementary Table 6).

Results for the primary endpoint by baseline pathogen are presented in Table 2. Oritavancin showed similar efficacy against these pathogens compared with vancomycin. The mean total daily vancomycin dose in the safety population was 2.1 g (standard deviation [SD], 0.63 g), and the mean duration of vancomycin therapy was 8.4 days (SD, 2.12 days). The mean vancomycin concentration from the 465 patients with a measured trough (prior to fourth dose) was 14.20 μg/mL (SD, 12.37 μg/mL), and the median level was 10.5 μg/mL.

Safety and Tolerability

The incidence of TEAEs, regardless of relationship to study drug, was similar between the oritavancin and vancomycin groups (Table 3); TEAEs were primarily mild in severity. The most frequently reported AEs in the oritavancin and the vancomycin groups were nausea (8.9% vs 12.0%. respectively), headache (7.0% vs 5.6%), vomiting (4.4% vs 5.6%), cellulitis (3.4% vs 3.0%), increased alanine aminotransferase (3.2% vs 2.0%), and infusion site phlebitis (3.2% vs 1.0%) (Table 3). The proportion of patients experiencing a TEAE that led to discontinuation of the study drug was similar between the treatment groups: 3.6% for oritavancin (discontinued placebo dosing) and 2.6% for vancomycin. In the oritavancin treatment group, TEAEs that led to discontinuation in >1 patient were cellulitis (2 patients vs 2 patients), infection (2 patients vs 0 patients), and osteomyelitis (2 patients vs 0 patients) for oritavancin and vancomycin, respectively. Five patients in the oritavancin group and none in the vancomycin group had osteomyelitis reported as an AE during the study; all events occurred within 1–9 days after study drug initiation, suggesting that it may have been preexisting at the time of study entry.

The frequency and distribution of SAEs was similar in both groups (oritavancin, 4.4%; vancomycin, 4.6%) (Table 3). Two patients died during the study: 1 patient treated with oritavancin died due to electromechanical dissociation, and 1 patient treated with vancomycin died from an acute myocardial infarction. Both deaths were assessed by the investigator to be unrelated to study drug.

The incidence of laboratory abnormalities was balanced between the treatment groups and no clinically meaningful differences were observed in either treatment group. Transient, asymptomatic elevations in liver enzymes were noted in both treatment groups; however, none were reported as serious, and none of the patients discontinued study drug due to these elevations. Furthermore, no patients' hepatic profile met Hy's law criteria [33, 34] (a serum alanine or aspartate aminotransferase level that is >3 times the upper limit of normal range and a serum total bilirubin level that is >2 times the upper limit of the normal range in the absence of initial findings of cholestasis, with no other explanation for the combination of elevated aminotransferase and total bilirubin levels), and no findings were indicative of drug-induced liver injury. No difference in vital signs or electrocardiographic findings was identified between the treatment groups.

Table 3. Patients With Adverse Events (Safety Population)

Category	Oritavancin (n = 503), No. (%)	Vancomycin (n = 502), No. (%)
At least 1 TEAE	256 (50.9)	252 (50.2)
Study drug-related TEAE[a]	109 (21.7)	128 (25.5)
TEAE leading to study drug discontinuation	18 (3.6)	13 (2.6)
SAE[b]	22 (4.4)	23 (4.6)
AE leading to fatal outcome	1 (0.2)	1 (0.2)
Most commonly reported TEAEs (>2%)		
Nausea	45 (8.9)	60 (12.0)
Headache	35 (7.0)	28 (5.6)
Vomiting	22 (4.4)	28 (5.6)
Cellulitis	17 (3.4)	15 (3.0)
Alanine aminotransferase increased	16 (3.2)	10 (2.0)
Infusion site phlebitis	16 (3.2)	5 (1.0)
Pyrexia	15 (3.0)	11 (2.2)
Infusion site extravasation	15 (3.0)	10 (2.0)
Tachycardia	15 (3.0)	7 (1.4)
Constipation	14 (2.8)	17 (3.4)
Abscess limb	14 (2.8)	8 (1.6)
Pruritus	13 (2.6)	29 (5.8)
Diarrhea	13 (2.6)	15 (3.0)
Aspartate aminotransferase increased	11 (2.2)	11 (2.2)
Dizziness	11 (2.2)	11 (2.2)

Abbreviations: AE, adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

[a] Relationship to study drug was determined by the investigator.

[b] For SAEs, all events are incorporated including treatment-emergent events.

DISCUSSION

In the SOLO II study, a single 1200-mg dose of oritavancin was noninferior to 7–10 days of twice-daily vancomycin in adults with ABSSSIs for both the primary efficacy endpoint (early clinical response at ECE) and key secondary efficacy endpoint (investigator-assessed clinical cure at PTE). Efficacy demonstrated at ECE with oritavancin (lesion size reduction) was concordant with investigator-assessed clinical cure at PTE (Supplementary Table 9). Efficacy in patients who received oritavancin was similar to that observed in the overall population and for subgroups defined by demographic characteristics, geographic region, ABSSSI type, renal function, and baseline pathogen, including MSSA and MRSA. Failure rates for oritavancin and vancomycin were balanced, and reasons for failure were similar across the treatment groups. Failures at ECE were driven primarily by presence of fever and missing temperature measurements (Supplementary Table 2). At PTE, failures were primarily due to missing data, with the majority of instances corresponding to patients not returning for their follow-up visit. Sensitivity analyses with missing data (mITT population), either excluded or treated as success at both ECE and PTE, in addition to analyses in the clinically evaluable population, confirmed that the results for oritavancin and vancomycin were similar.

The frequency, distribution, and severity of TEAEs were generally comparable for single-dose oritavancin and 7–10 days of vancomycin in SOLO II. Discontinuations due to TEAEs were uncommon, and no deaths were assessed by the investigator to be related to study drug in either treatment group. In SOLO II, a single dose of oritavancin with its extended plasma elimination half-life [24] was not associated with any untoward safety effects as assessed throughout the study including the day 60 follow-up.

Efficacy and safety conclusions from the SOLO II study were generally consistent with those of the SOLO I study, which was of identical design [29]. Importantly there were differences between the 2 studies. More patients were enrolled into the SOLO II study overall, with a greater number of patients recruited in Eastern Europe (2.9% in SOLO I and 18.2% in SOLO II) and fewer patients recruited from North America and India (56% and 23%, respectively). In addition, the efficacy outcome for the primary endpoint at ECE in SOLO II appeared somewhat lower for oritavancin than for vancomycin in patients with streptococci, diabetes, and subcutaneous abscesses at baseline. The same phenomenon was not observed in SOLO I [29]. The subgroup analyses were based on a relatively small number of patients in the individual studies and should be interpreted with caution. Whereas in SOLO II there were 5 cases of osteomyelitis reported in patients who received oritavancin and none in the vancomycin group, in SOLO I there were 2 cases of osteomyelitis reported, 1 patient in each treatment group.

The severity of the baseline infection was underscored both by the requirement for at least 7 days of intravenous therapy, as judged by the investigator, and by the median lesion area at baseline, including surrounding erythema, edema, and induration of approximately 300 cm^2, substantially larger than the 75 cm^2 as defined in the inclusion criteria. The fact that approximately 20% of the patients in SOLO II had systemic inflammatory response syndrome at baseline, approximately 10% of the patients had diabetes mellitus, and all patients had at least 1 sign of systemic inflammation at baseline further attests to the complicated nature of the infections.

Currently available therapeutic options for the treatment of ABSSSIs require multidose and multiday regimens, with some requiring dosage adjustments for renal insufficiency and some requiring monitoring of plasma drug concentration and individualization of dose. Repeat administrations may require patients to be hospitalized for the course of their antibiotic treatment over multiple days, increasing the risk of complications associated with hospitalization. Treatment noncompliance

can also be an issue with oral antibiotic regimens, increasing the potential for pathogen resistance [16]. A single-dose treatment for ABSSSIs that achieves early and sustained clinical response could potentially reduce complications associated with multiple intravenous administrations in patients with ABSSSIs and improve treatment compliance.

The extended (60 days) follow-up of the 503 patients treated with oritavancin in the SOLO II study failed to identify prolonged or delayed adverse events. Safety and efficacy results from SOLO II bolster those from the SOLO I study and provide impetus to quantitate health economic outcomes in patients with ABSSSIs. Other potential uses for oritavancin in the treatment of serious gram-positive infections remain to be defined.

In conclusion, oritavancin offers a single-dose alternative to multidose therapies for ABSSSIs, representing a new option and adding flexibility to the treatment of these serious infections.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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