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A Randomized, Evaluator-Blind, Phase 2 Study Comparing the Safety and Efficacy of Omadacycline to Those of Linezolid for Treatment of Complicated Skin and Skin Structure Infections

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A randomized, investigator-blind, multicenter phase 2 trial involving patients with complicated skin and skin structure infections (cSSSI) compared the safety and efficacy of omadacycline, a broad-spectrum agent with activity against methicillin-resistant *Staphylococcus aureus* (MRSA), to those of linezolid (with or without aztreonam). Patients were randomized 1:1 to omadacycline (100 mg intravenously [i.v.] once a day [QD] with an option to transition to 200 mg orally QD) or linezolid (600 mg i.v. twice daily [BID] with an option to transition to 600 mg orally BID) at 11 U.S. sites. Patients suspected or documented to have infections caused by Gram-negative bacteria were given aztreonam (2 g i.v. every 12 h [q12h]) if randomized to linezolid or matching placebo infusions if randomized to omadacycline. Adverse events were reported in 46 (41.4%) omadacycline-treated and 55 (50.9%) linezolid-treated patients. Adverse events related to treatment were assessed by investigators in 24 (21.6%) omadacycline-treated and 33 (30.6%) linezolid-treated patients. The gastrointestinal tract was most commonly involved, with adverse events reported in 21 (18.9%) patients exposed to omadacycline and 20 (18.5%) exposed to linezolid. Rates of successful clinical response in the intent-to-treat (ITT) and clinical evaluable (CE) populations favored omadacycline (ITT, 88.3% versus 75.9%; 95% confidence interval [CI], 1.9 to 22.9; CE, 98.0% versus 93.2%; 95% CI, −1.7 to 11.3). For microbiologically evaluable (ME) patients with *S. aureus* infections, the clinical success rates were 97.2% (70/72) in omadacycline-treated and 92.7% (51/55) in linezolid-treated patients. This phase 2 experience supports conclusions that omadacycline is well tolerated in cSSSI patients and that this aminomethylcycline has potential to be an effective treatment for serious skin infections.

Omadacycline belongs to a new class of compounds, the aminomethylcyclines, which are semisynthetic derivatives of minocycline (1, 6). Omadacycline retains many of the characteristics that have made tetracyclines successful drugs. In addition, it has proven activity against tetracycline-resistant pathogens, including those that are the leading causes of serious skin and soft tissue infections. In both *in vitro* testing and animal models of infection, omadacycline demonstrates consistent activity against methicillin-susceptible and -resistant staphylococci (coagulase positive and negative) as well as streptococci and enterococci (8). Beyond this activity against Gram-positive bacteria, omadacycline has activity against many clinically important *Enterobacteriaceae* and a wide range of anaerobes (5). Omadacycline also has pharmacologic properties that allow it to be administered either by intravenous (i.v.) infusion or orally (p.o.), using once-daily dosing.

Based on this unique profile, omadacycline has progressed into the later stages of clinical development (2, 7). This report describes the initial phase 2 trial, in which omadacycline was compared to linezolid (Zyvox) (with or without aztreonam) as treatment of patients with serious infections of the skin and soft tissues.

MATERIALS AND METHODS

This randomized, controlled, evaluator-blinded phase 2 study compared omadacycline and linezolid for the treatment of complicated skin and skin structure infections (cSSSI). Patients were enrolled between July 2007 and January 2008 at 11 sites in the United States. Randomized study arm assignment was accomplished by generating a randomization schedule linking subject numbers to treatment assignment before the study started and then giving each subject who qualified for enrollment a subject number prior to dosing. The primary objective of this study was to compare the safety and tolerability of omadacycline to those of linezolid in patients with cSSSI. A comparison of efficacies in the two treatment groups was a key secondary objective.

Study population. To be eligible for study, patients ≥18 years of age needed to have one of four general categories of cSSSI: wound infection, major abscess, infected ulcers in the lower extremity, or cellulitis. Patients with infections that were able to be controlled by surgical intervention (e.g., amputation, incision, and drainage) alone were not eligible for enrollment. Major abscesses were defined as any abscess which involved subcutaneous or deeper tissues that either had spontaneously ruptured and were draining or required surgical incision and drainage. Patients with diabetes mellitus or documented vascular insufficiency with infected ulcers of the lower extremity were eligible if the lesion was acutely infected and the ulcer was not present for more than 3 months. Patients with cellulitis alone were eligible if they had diabetes mellitus or vascular insufficiency or if they received immunosuppressive therapy within a period of 3 months prior to developing cellulitis. Patients were eligible if they had received <48 h of antibiotic therapy prior to enrollment or if they had received ≥48 h of therapy and a resistant pathogen was identified.

Patients with erysipelas, cellulitis (but were otherwise healthy), decubitus ulcers, infections considered life-threatening, infections potentially involving bone, or infections that were able to resolve with surgical intervention alone were not eligible.

Study design. Following randomization (1:1), all patients initially received intravenous therapy with either omadacycline (100 mg) every 24 h

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or linezolid (600 mg) every 12 h. The dosing rationale for omadacycline was based on achieving patient exposures that were estimated to exceed the area under the curve (AUC)/MIC ratios identified as potentially effective in animal models of soft tissue infection. Based on this analysis, it was estimated that infections caused by pathogens with an MIC of ≤2 μg/ml would be effectively treated. Measurement of omadacycline serum concentrations was done to assess estimated exposure on this regimen and to provide further information to be used in selection of doses for subsequent clinical trials.

To maintain blinding, patients randomized to omadacycline were given placebo (250 ml of 5% dextrose water) to match the 12-h dosing regimen used in the linezolid treatment arm. For patients with infections suspected or documented to involve Gram-negative bacteria, the investigator had the option of adding to the study regimen. In these cases, patients assigned to linezolid also received 2 g aztreonam (in 50 ml) every 12 h. Because omadacycline has activity against many of the Gram-negative bacteria that commonly cause these infections, patients assigned to omadacycline with infections suspected or documented to involve Gram-negative bacteria were given placebo (50 ml of 5% dextrose water) every 12 h to maintain the blind. All infusions were administered over 30 min. All infusion bags were covered, and the blinded clinical evaluator was not present during the infusions.

Transition to oral therapy was based on a clinician's judgment of the appropriateness of hospital discharge and continuation of oral therapy. This clinician remained blinded to the patient's study drug assignment and was considered a "blinded evaluator" of the patients' progress and outcome. Patients randomized to omadacycline took 200 mg of omadacycline (dosed as two 100-mg tablets) daily. Patients randomized to linezolid took one 600-mg tablet of linezolid twice daily. Given the differences in the appearance of the tablets and the number of tablets, patients may have been aware of study drug assignment if they were transitioned to oral therapy. Patients were instructed not to share any information that was related to the number or frequency of oral tablets taken with their blinded evaluator.

Assessment of patients. Patients had four structured evaluations: baseline, end of i.v. treatment (EOIV), end of treatment (EOT), and 10 to 17 days after the last dose of the treatment (test of cure evaluation [TOC]). Clinical response to treatment at the TOC was considered successful if the blinded evaluator assessed that a patient's infection was sufficiently resolved such that no additional antibiotics were needed. Any patient whose primary site of infection was surgically removed was considered a clinical failure. All patients with abscesses had their infections incised and drained prior to or within the first 24 h of treatment. Each patient's lesion size was recorded at enrollment, at the end of i.v. therapy, and at the TOC assessment by measuring the maximal linear dimension of continuous involvement of the infection. Monitoring for adverse events and concomitant medications was performed continuously throughout the study.

Analysis populations. The primary analysis population was the safety population that included all patients who received at least one dose of study medication. The four analysis populations used in assessing efficacy were the (i) intent-to-treat (ITT), (ii) modified intent-to-treat (MITT), (iii) clinically evaluable (CE), and (iv) microbiologically evaluable (ME) populations.

Statistical analyses. The primary hypothesis tested was that the safety and tolerability of omadacycline were comparable to those of linezolid in the treatment of adults with cSSSI. This hypothesis was evaluated by analysis of adverse events and other safety measurements using descriptive statistics.

The secondary hypothesis tested was that the rate of successful clinical response at the TOC among omadacycline-treated cSSSI patients was not inferior to that of linezolid-treated patients. Two-sided 95% confidence intervals (CIs) were calculated for the differences in success rates between treatment arms. Consistent with other phase 2 trials involving patients with cSSSI and not based on analysis aimed at preserving a defined proportion of the antibiotic treatment effect, the hypothesis that omadacycline was noninferior to linezolid was considered supported if the lower limit of the 95% confidence interval (omadacycline results minus linezolid results) was greater than −20%.

TABLE 1 Summary of analysis populations

Population[a]	No. (%) of randomized patients in each group receiving:	
	Omadacycline	Linezolid
Randomized patients	118 (100)	116 (100)
Safety	111 (94.1)	108 (93.1)
Intent to treat	111 (94.1)	108 (93.1)
Modified intent to treat	84 (71.2)	78 (67.2)
Clinically evaluable	100 (84.7)	88 (69.0)[b]
Microbiologically evaluable	77 (65.3)	63 (54.3)

[a] Safety, patients dosed with the study drug; intent to treat, all enrolled subjects receiving ≥1 dose of study medication; modified intent to treat, ITT with baseline pathogen; clinically evaluable, all subjects in the ITT population who had a protocol-defined qualifying infection, received the study drug for ≥5 days, had all protocol-defined clinical evaluations, and had not received non-study antibiotics; microbiologically evaluable, CE with baseline pathogen.
[b] The primary factor contributing to the lower evaluability rate in the linezolid treatment group was subjects who completed treatment but were then lost to follow-up and were not seen for the test of cure visit.

RESULTS

Patient disposition and characteristics. The distribution of subjects in the 5 analysis populations is shown in Table 1. The percentages of patients meeting MITT criteria were slightly higher for omadacycline than for linezolid (75.7% versus 72.2%, respectively). These differences were more evident in CE and ME analysis populations. On review, the primary factor contributing to the lower evaluability rate in the linezolid treatment group was subjects who completed treatment but were then lost to follow-up and were not seen for the test of cure visit.

Baseline characteristics. The baseline characteristics of ITT patients are shown in Table 2. Two-thirds (66.2%) of ITT subjects were diagnosed as having major abscesses. The mean maximal dimension of these abscesses was 12.0 cm (12.6 cm in omadacycline-treated and 11.3 cm in linezolid-treated patients). Because lesions were measured only in a single dimension, the total area of involvement was not able to be calculated. Patients with major abscesses were distributed equally across treatment arms (65.8% of omadacycline-treated and 66.7% of linezolid-treated patients). The second most common diagnosis was wound infection, and the majority of these (29/38; 76.3%) were infections associated with traumatic injuries. The mean maximal linear dimension of the infections among ITT patients was 13.6 cm, and over two-thirds of patients had moderate to severe erythema, induration, and pain at baseline.

Safety and tolerability. The mean (standard deviation [SD]) duration of study drug exposure in the safety analysis population was 10.0 (3.91) days in omadacycline patients and 9.6 (4.36) days in linezolid patients. In each treatment group, the mean duration of i.v. exposure was 4.3 days.

There were 3 serious adverse events reported, 1 in an omadacycline-treated patient and 2 in linezolid-treated patients. The omadacycline-treated patient was a 72-year-old female hospitalized for worsening confusion a week after completing treatment; the event was considered unrelated to the study drug and related to an underlying condition. The study drug was stopped due to an

TABLE 2 Baseline patient characteristics

Characteristic	No. (%)[a] of patients with each characteristic receiving:	
	Omadacycline ($n = 111$)	Linezolid ($n = 108$)
Male sex	66 (59)	57 (53)
Race		
Caucasian	97 (87)	99 (92)
Black	8 (7)	6 (5)
Other	6 (5)	3 (3)
Age (yr)		
18–44	51 (46)	50 (46)
45–64	50 (45)	48 (44)
≥65	10 (9)	10 (9)
Infection diagnosis		
Major abscess	73 (66)	72 (67)
Wound infection	21 (19)	17 (16)
Lower extremity ulcer	9 (8)	9 (8)
Cellulitis	8 (7)	10 (9)
Mean maximal linear dimension of infection (SD) (cm)	14.2 (13.5)	12.0 (11.5)
Mean no. of days of study therapy (SD)	10.0 (3.9)	9.6 (4.4)
Mean no. of days of intravenous therapy (SD)	4.3 (2.4)	4.3 (3.4)
Signs and symptoms assessed as moderate or severe[b]		
Erythema	90 (81)	83 (77)
Edema/induration	85 (77)	72 (67)
Fluctuance	30 (27)	26 (24)
Necrotic tissue	11 (10)	5 (5)
Purulence	36 (32)	33 (31)
Tenderness/pain	102 (92)	96 (89)
No. with each pathogen identified as the cause of infection in the ME population[c]		
S. aureus	72	55
MRSA	44	32
Gram-positive bacterium other than *S. aureus*	3	7
Gram-negative bacterium	2	1

[a] Values are numbers (percentages) unless otherwise indicated.
[b] Data missing on 2 linezolid-treated patients.
[c] The total number of patients in the ME population who were treated with omadacycline is 77, and the total number treated with linezolid is 63.

TABLE 3 Treatment-emergent adverse events by preferred term that were reported in 5 or more patients in either treatment group in the safety population

Adverse event[a]	No. (%) of patients with each adverse event who were given:	
	Omadacycline ($n = 111$)	Comparator ($n = 108$) [no. of subjects given linezolid plus aztreonam]
Nausea	13 (11.7)	8 (7.4) [3]
Vomiting	5 (4.5)	4 (3.7) [1]
Diarrhea	3 (2.7)	6 (5.6) [5]
Constipation	5 (4.5)	2 (1.9) [2]
Fatigue	5 (4.5)	2 (1.9) [1]
Alanine aminotransferase increase	3 (2.7)	7 (6.5) [6]
Aspartate aminotransferase increase	3 (2.7)	5 (4.6) [5]
Dizziness	4 (3.6)	5 (4.6) [2]
Headache	7 (6.3)	9 (8.3) [5]
Rash/rash erythematous	5 (4.5)	2 (1.9) [1]

[a] Coded using the Medical Dictionary for Regulatory Affairs, version 12.0.

adverse event in one omadacycline-treated patient and in two linezolid-treated patients. In the omadacycline-treated patient, treatment was stopped on study day 3 when a preenrollment X-ray, initially read as unremarkable, was interpreted as suggesting necrotizing anaerobic infection. Although the patient was clinically stable, the investigator considered that finding to warrant withdrawing the patient from the study. This event was considered unrelated to the study drug. The two linezolid-treated patients discontinued study drug therapy due to events (heart burn, pruritic rash) that were considered to be possibly related to the study drug.

Among the 111 omadacycline-exposed patients, 46 (41.4%) experienced one or more treatment-emergent adverse events and 24 (21.6%) had treatment-related adverse events. This compared to 55 (50.9%) patients with treatment-emergent adverse events and 33 (30.6%) with treatment-related adverse events among the 108 linezolid-exposed patients. The initial onset of treatment-related adverse events occurred during intravenous dosing in 16 (66.7%) of the 24 omadacycline-treated patients and 19 (63.3%) of 33 linezolid-treated patients. Two adverse events were assessed as marked (severe) intensity and included decreased weight in an omadacycline patient and osteomyelitis in a linezolid patient. Events of moderate intensity were reported in 6 (13%) omadacycline and 9 (16%) linezolid patients. All other events were assessed as mild.

For both drugs, the most frequently involved organ system was the gastrointestinal tract, with events reported in 21 (18.9%) omadacycline-treated patients and 18 (16.7%) linezolid-treated patients.

Ten specific treatment-emergent adverse events occurred in 5 or more patients in either treatment group (Table 3). There were no clinically meaningful differences between the two treatment groups, given the size of the total study population. Among the omadacycline-treated patients with these events, only 5 had events that were assessed as moderate intensity (3 nausea, 1 diarrhea, and 1 rash).

Two adverse events associated with laboratory abnormalities occurred in ≥2 patients in either treatment group, specifically, elevation of serum transaminases (3 omadacycline-treated and 7 linezolid-treated patients) and elevation of creatine phosphokinase (3 omadacycline-treated patients and 1 linezolid-treated patient). None of these events resulted in discontinuation of the study drug or required therapeutic intervention. In the three patients with elevation of creatine phosphokinase, one had an elevation (1,244 U/liter) recorded at day 5 of therapy (end of i.v. treatment) which returned to normal levels by the end of therapy and one had an elevation reported at the EOT visit (1,474 U/liter) which returned to normal levels by the TOC evaluation. The third patient had an elevated level recorded (918 U/liter) 2 days after

TABLE 4 Rates of successful clinical response at test of cure by analysis population

Population	Rate of clinical response (% [no. successful/total no.]) in patients given:		% difference (95% CI)
	Omadacycline	Linezolid	
Intent to treat	88.3 (98/111)	75.9 (82/108)	12.4 (1.9–22.9)
Modified intent to treat	89.3 (75/84)	75.6 (59/78)	13.6 (1.4–25.9)
Clinically evaluable	98.0 (98/100)	93.2 (82/88)	4.8 (−1.7–11.3)
Subjects with no prior antibiotics[a]	96.3 (53/55)	95.2 (40/42)	
Microbiologically evaluable	97.4 (75/77)	93.7 (59/63)	3.8 (−4.0–11.5)
S. aureus	97.2 (70/72)	92.7 (51/55)	
MRSA	97.7 (43/44)	93.8 (30/32)	
Gram-positive bacterium other than *S. aureus*	100 (3/3)	100 (7/7)	
Gram-negative bacterium	100 (2/2)	100 (1/1)	

[a] No prior antibiotic exposure 72 h before enrollment.

completing therapy that was associated with a traumatic fall. This patient's level was recorded to be at a near-normal level (182 U/liter; 170 U/liter = upper limits of normal) 40 days later. Statistical analyses were performed comparing the hematology and chemistry results for two treatment groups for changes from baseline to the end of i.v. therapy, to EOT, or to TOC. Platelet counts were the only parameter that showed a statistically significant difference, with a mean increase from baseline to EOT of 30.7 $\times$ 10^9/liter among omadacycline-treated patients and a mean decrease of 11.5 $\times$ 10^9/liter in linezolid-treated patients ($P < 0.001$).

There were no significant differences in vital signs across treatment groups. Mild increases in heart rate had been observed in healthy volunteers in phase 1 studies of omadacycline and have been shown to be unrelated to a change (increase or decrease) in duration of ventricular repolarization (QT or QT intervals on an electrocardiogram [ECG]). In contrast to those observations made in healthy volunteers, an effect on heart rate was not apparent in this clinical population. Compared to baseline, changes in mean heart rate (beats per minute [bpm]) were −0.9 ± 14.1 bpm and −1.7 ± 13.5 bpm at the end of i.v. therapy and 1.1 ± 12.2 bpm and −0.6 ± 13.34 bpm at the EOT in omadacycline-treated and linezolid-treated patients, respectively. Heart rates in the omadacycline-treated group ranged from 45 to 114 bpm predose, 44 to 113 bpm at the end of i.v. therapy, and 50 to 122 bpm at EOT. These results were comparable to those in the linezolid-treated group, in which heart rates ranged from 52 to 114 bpm predose, 50 to 107 bpm at the end of i.v. therapy, and 47 to 111 bpm at EOT. There were three adverse events of tachycardia (in 3 omadacycline-treated patients; assessed as mild in intensity, asymptomatic, and unrelated to the study drug), two episodes of bradycardia (2 linezolid-treated patients), and one episode of palpitations (1 omadacycline patient). Among the episodes of tachycardia in omadacycline-treated patients, one event occurred 12 days posttreatment and was associated with a new infection. The other 2 events were reported to start during the i.v. treatment period (day 4 and day 3), with increases in heart rate from baseline (before the first infusion) of 9 bpm (maximum rate, 101 bpm; baseline, 92 bpm) and 34 bpm (maximum rate, 115 bpm; baseline, 81 bpm), respectively.

Responses assessing efficacy. Clinical responses at TOC for the ITT, MITT, CE, and ME analysis populations are shown in Table 4. In all four populations, the successful clinical response rates were higher in omadacycline-treated patients than in linezolid-treated patients. The observed differences ranged from 3.8% to 13.6%, and the lower limits of the 95% confidence interval ranged from −4.0% to +1.9%, thus meeting the prespecified criteria for concluding that omadacycline was noninferior to linezolid for the treatment of cSSSI. Per protocol, ITT or MITT patients who did not have evaluations performed at TOC were considered treatment failures. Eleven of the 13 ITT omadacycline-treated patients (84.6%) and 7 of the 9 MITT omadacycline-treated patients (77.8%) categorized as clinical failures were not evaluated at TOC. Twenty of the 26 ITT linezolid-treated patients (76.9%) and 15 of the 19 MITT linezolid-treated patients (78.9%) categorized as clinical failures were not evaluated at TOC.

Analyses of clinical responses by category of cSSSI showed that favorable outcomes with omadacycline occurred consistently across infection types. For subjects with major abscesses, the differences in successful clinical responses were 11.3% (95% CI, −2.6 to 25.2), favoring omadacycline treatment (89.7% versus 78.3%), in the MITT population and 3.6% (95% CI, −3.7 to 10.9), favoring omadacycline treatment (98.5% versus 94.8%), in the CE population. For the next most frequent infection type, wound infections associated with trauma, the differences in successful clinical response were 16.7% (95% CI, −21.5 to 54.8), favoring omadacycline treatment (100% versus 83.3%), in the MITT population and 10.0% (95% CI, −13.6 to 33.6), favoring omadacycline treatment (100% versus 90%), in the CE population.

In the ME population, major abscess was the most common infection type in both treatment groups (53/77 for omadacycline and 49/63 for linezolid). *Staphylococcus aureus* was the most common pathogen isolated from abscesses (50/53 for omadacycline and 43/49 for linezolid). Of these abscessed patients with *S. aureus* infections, 32 omadacycline-treated and 27 linezolid-treated patients were infected with methicillin-resistant *Staphylococcus aureus* (MRSA). Among ME patients in whom *S. aureus* was identified as the primary pathogen causing infection, the clinical success rates were 97.2% (70/72) in omadacycline-treated and 92.7% (51/55) in linezolid-treated patients (Table 4). Similar success rates were observed among patients with MRSA infections (Table 4). For the 3 omadacycline-treated and 7 linezolid-treated ME patients who had infection assessed to be caused primarily by a Gram-positive bacterium that was not *S. aureus*, no omadacycline-treated or linezolid-treated patient was assessed to be a clin-

ical failure. For the 2 omadacycline-treated ME patients and 1 linezolid-treated ME patient who had infections caused by Gram-negative bacteria, none were assessed as clinical failures.

Since the design and completion of this study, regulatory review of new antibiotics for the treatment of serious skin infections has emphasized the clinical response during the first 72 h after starting therapy (3), including the cessation of an increase in maximal lesion dimension and the absence of fever (temperature $<$ 38.0°C). In a retrospective analysis of the ITT patients for whom data were available to assess these responses, 96.8% (30/31) of omadacycline-treated patients and 94.4% (34/36) of linezolid-treated patients met these two criteria. Among the omadacycline patients, the maximal lesion dimension decreased an average of 31.8% relative to pretreatment, compared to a 6.7% reduction in the linezolid-treated patients. Because of the trial design, this assessment was limited to patients being transitioned from intravenous to oral therapy during the first 72 h of therapy. An additional concern raised about the impact of prior antibiotics on clinical outcome was also addressed in a retrospective evaluation of the CE population that excluded subjects that had received systemic or topical antibiotic treatment within the 3 days prior to enrollment. In this analysis, similar clinical response rates were evident across treatment arms for patients who had not received prior antibiotic treatment (Table 4). These response rates were similar to response rates measured for all subjects in the CE population (Table 4).

DISCUSSION

The results of this randomized, double-blinded during i.v. treatment, evaluator-blinded during oral treatment, phase 2 trial support the continued development of omadacycline as a broad-spectrum aminomethylcycline with potent activity against the leading causes of serious skin infections. The safety and tolerability profile of omadacycline appeared comparable to that of linezolid and was consistent with that of tetracyclines, which are the most closely physicochemically related drugs to omadacycline. Among the 111 omadacycline-treated patients in this trial, there were no drug-related serious adverse events. The singular event that resulted in discontinuation of omadacycline therapy was unrelated to the drug (misassessment of the severity of infection at enrollment). The most common adverse events reported among omadacycline-exposed patients were related to the gastrointestinal system. Although these events contributed to over three-fourths of the adverse events reported with omadacycline treatment, none of these events was described as severe and nearly all were reported as mild. Taken together with the analyses of laboratory values and vital sign measurements, these results support the conclusion that daily doses of 100 mg i.v. or 200 mg p.o. are well tolerated by most patients and are suitable for further evaluation in larger numbers of patients in phase 3 trials.

Assessment of the potential for omadacycline to be effective in treating patients with serious infections was another important goal of this study. In each of the efficacy analysis populations (ITT, MITT, CE, and ME), successful clinical response rates were higher in omadacycline-treated patients than in linezolid-treated patients and differences in these rates met criteria for concluding that omadacycline was not inferior to linezolid treatment.

Consistency of outcomes across subgroups of patients with serious infections of the skin and soft tissue is an important consideration in assessing a new agent. Eighty-three percent (183/219) of patients enrolled in this phase 2 trial had either major abscesses or wound infections due to trauma. Prior to treatment, the majority of these patients reported moderate to severe pain and were observed to have moderate to severe induration and erythema. Successful clinical responses in the CE population were observed in 90% or more of patients in both types of infection. Although the experience with other serious skin infection types (cellulitis, postoperative wound infections, and infected lower extremity ulcers) was less extensive, successful response rates were comparable in these patients as well. MRSA is now the leading cause of serious infections of the skin in the United States, and in our study, 76 out of 140 patients in the ME population were infected with this pathogen (4). Among the 44 patients in the ME population who were infected with MRSA and treated with omadacycline, 43 were assessed to have a successful clinical response.

In summary, the results of this phase 2 trial with omadacycline indicate that this new agent was well tolerated and effective in treating patients with serious infections involving the skin and soft tissues. Omadacycline, which is available in both intravenous and oral formulations, is suitable for once-daily dosing, and has activity against MRSA, is a promising investigational drug for the treatment of patients with serious infections.

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