REVIEW ARTICLE

Real-World Use of Oritavancin for the Treatment of Osteomyelitis

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Abstract

Osteomyelitis is a difficult-to-treat disease that can require both surgical debridement and a prolonged course of antimicrobial therapy. Current standard of care for the antimicrobial treatment of osteomyelitis is fraught with multiple challenges and limitations. Patients typically require the insertion of an indwelling catheter for single or multiple daily intravenous antibiotic infusions for up to 6 weeks. Currently, there are treatment guidelines for only vertebral osteomyelitis, indicating the complexity of the condition. Oritavancin is a long-acting, second-generation lipoglycopeptide, administered intravenously once per week, which has potential to be a useful alternative in the treatment of osteomyelitis. This article reviews occurrence and outcomes of off-label oritavancin use for treatment of osteomyelitis as described in case reports. Analysis included 23 patients treated for osteomyelitis with single- or multiple-dose oritavancin. Overall, clinical cure or improvement was achieved in 87% of patients, and adverse events were mild and reported in only two patients. Clinical efficacy was demonstrated in 81.8% of methicillin-resistant *Staphylococcus aureus* (MRSA), 71.4% of methicillin-sensitive *S. aureus* (MSSA), 50% of vancomycin-resistant *Enterococcus* (VRE), and in the single case of *Streptococcus pyogenes*. Oritavancin has shown efficacy against Gram-positive pathogens in osteomyelitis, and offers a possible outpatient treatment option for osteomyelitis patients. Future studies are needed to determine dosing frequency in osteomyelitis patients.

Key Points

Review of case studies of off-label use of oritavancin for osteomyelitis has shown clinical success against Gram-positive pathogens in osteomyelitis, and it should be considered an effective treatment option.

Oritavancin could offer a more patient-friendly treatment option as it can be administered intravenously (IV) once a week compared to daily IV treatment for multiple consecutive days or oral tablets, thus reducing impact on daily activities, and potentially reducing the length of hospitalization or avoiding it.

Future studies are needed to explore outpatient use of oritavancin for osteomyelitis treatment, the possible pharmacoeconomic benefits and patient impact.

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1 Introduction

Osteomyelitis is an infectious, inflammatory disease of the bone that remains difficult to treat, typically requiring a prolonged course of intravenous (IV) antibiotics [1]. The incidence of osteomyelitis has been reported to be as high as 21.8 cases per 100,000 person-years, and was higher for men than for women and increased with age ($p < 0.001$) [2]. Over a 40-year period, annual osteomyelitis incidence rates have increased from 11.4 cases to 24.4 per 100,000 person-years ($p < 0.001$) [2]. Osteomyelitis occurs when microorganisms invade previously healthy bone, leading to an inflammatory response and concomitant destruction of the bone, which are the hallmarks of osteomyelitis [3–5]. Antibiotics poorly penetrate dead bone and infected fluids; surgical treatment with debridement of the necrotic bone accompanied by the identification of the infectious etiology, via surgical sampling or needle aspiration, allows for the optimization of antibiotic therapy [5, 6]. There are two major classification schemes for osteomyelitis [6, 7]: The Lew and Waldvogel [6] system classifies osteomyelitis by duration of disease—either acute or chronic, as well as infection mechanism—hematogenous or contiguous infection. Histopathology of osteomyelitis rather than duration of illness is used to categorize whether osteomyelitis is chronic or acute [8]. Acute osteomyelitis is defined as

infection occurring before the development of sequestra, which usually occurs within 2 weeks of initial disease onset [9]. Chronic osteomyelitis is defined as longstanding infection that evolves over months or even years, characterized by the persistence of microorganisms, low-grade inflammation, and the presence of dead bone and fistulous tracts [4, 6]. Clinical signs persisting for longer than 10 days are associated with the development of necrotic bone and chronic osteomyelitis. Chronic osteomyelitis may also present as a recurrent or intermittent disease, with periods of dormancy of variable duration [10, 11]. Additionally, osteomyelitis classification is divided into one of two categories (defined by physiologic mechanism): contiguous dissemination (trauma, surgery, or prosthetic hardware), or via hematogenous seeding. Contiguous osteomyelitis is further subdivided into whether or not there is vascular insufficiency [3, 6]. The gold standard for diagnosing osteomyelitis is bone biopsy and tissue culture; however, these invasive procedures often prove prohibitive—indeed chronic osteomyelitis remains challenging to diagnose, and clinicians use a combination of clinical symptoms, laboratory, radiographic, and microbiological findings to do so.

The Cierny-Mader scheme classifies osteomyelitis by anatomic stages and patient health status, in order to provide patient management guidance. Stages 1–4 describe anatomic location and progression, and host health status categories by local and systemic factors that affect immune surveillance, metabolism, and bone vascularity [7, 10].

While other causative pathogens have been identified in osteomyelitis, *Staphylococcus aureus*, in particular methicillin-resistant *S. aureus* (MRSA), is among the most common. MRSA has advantageous features for bone infection; an array of virulence factors (including the production and release of cytotoxins), enhanced pathogenesis, and biofilm formation, while concomitantly impairing host/immune response [7]. Co-morbidities impairing peripheral blood flow, including diabetes mellitus, may make osteomyelitis in these patients even more difficult to treat [5, 6].

Osteomyelitis treatment usually includes the use of prolonged, high-dose, IV antibiotics [1, 12–16]. However, this tactic must be balanced against antimicrobial stewardship to avoid resistance, as well as the risks associated with IV catheters, and costs accompanying agents themselves [12, 17]. There is a paucity of randomized, clinical trials to suggest the use of a single antibiotic or combination of agents for osteomyelitis in adults, and the optimal route and duration of antibiotics with osteomyelitis remains ill-defined due to limited prospective clinical trials. Most experts in the USA recommend 4–6 weeks of IV antibiotic therapy for osteomyelitis [1, 12–15]. Once the patient is stable for discharge, treatment can be continued, either administered via outpatient parenteral antibiotic therapy (OPAT) with substantial vascular access, such as a peripherally inserted central catheter (PICC), or transition to a suitable oral alternative [18].

Vancomycin is usually the core of IV therapy, particularly for MRSA infections. However, vancomycin use is challenging because of the weight-based dosing, dosing frequency, the necessity of single and multiple daily doses, the need for therapeutic drug-level monitoring and for vascular access, and toxicities associated with its use [16, 19, 20]. Other antibiotic therapies available have adverse events that can develop with prolonged use, or limit their usage in certain populations. Development of neutropenia and thrombocytopenia is associated with extended use (> 14 days) of ceftaroline or linezolid, respectively [21, 22], and linezolid treatment for > 28 days can cause lactic acidosis and optic neuritis [23]. Additionally, linezolid patients concurrently taking selected serotonin reuptake inhibitors can develop serotonin toxicity, and concurrent monoamine oxidase inhibitor use has been associated with hypoglycemia [24–26]. Daptomycin can cause elevated creatinine phosphokinase (CPK), myopathies, or eosinophilic pneumonia [22]. Delafloxacin is an effective agent that requires a loading dose—it also has a better safety profile than other fluoroquinolones; however, the fluoroquinolone warning issued by the US Food and Drug Administration (FDA) is still applicable [27].

In addition, many antibiotics, including vancomycin, often have difficulty penetrating biofilm formations and most fail to penetrate bone. When long-term treatment courses are necessary, availability of antibiotics with longer dosing intervals, fewer toxicities, and minimal to no requirement for monitoring therapeutic drug levels, would be preferred.

Oritavancin is a long-acting, semi-synthetic, second-generation lipoglycopeptide approved by the FDA for the treatment of acute bacterial skin and skin structure infections (ABSSSIs) [28–30]. The pharmacokinetic/pharmacodynamic (PK/PD) data showed that administration of a large, single 1200 mg dose of oritavancin was safe, well tolerated, and optimizes concentration-dependent killing against several Gram-positive organisms, resulting in more effective and pronounced bactericidality as compared with the smaller, originally traditional doses and dosing schemes of oritavancin [31, 32]. The large volume of distribution of oritavancin and penetration into bone are favorable for exploring its use in osteomyelitis [31–33]. Oritavancin demonstrates potent in vitro activity against most Gram-positive organisms, most notably *Staphylococcus*, *Streptococcus*, and *Enterococcus* species [32, 34–36]. The in vitro bactericidal activity of oritavancin against stationary-phase *S. aureus* cells, and sterilization of biofilms, is a particularly appealing feature when treating osteomyelitis with or without the addition of prosthetic devices and hardware [37]. Specifically, against enterococci, oritavancin is only approved for vancomycin-susceptible *Enterococcus faecalis* [30]. However, oritavancin also has activity against other *Enterococcus*

species, including vanA-producing vancomycin-resistant *Enterococcus faecium* (VRE) [36, 38].

Oritavancin has favorable PK/PD, achieves wide distribution and penetration, and has potent in vitro activity against common osteomyelitis-causing pathogens. Additionally, a PICC is not necessary. These features make oritavancin a potentially useful option for the treatment osteomyelitis, although the physiological complexity, severity, and recurrence of these infections will likely require more than a single dose. The use of oritavancin in the off-label treatment of osteomyelitis is currently restricted to a series of case reports, which show that multiple doses of oritavancin are safe and effective in the treatment of osteomyelitis caused by VRE, MSSA, and MRSA [39–46]. We present the reported outcomes of multiple-dose oritavancin therapy in patients with osteomyelitis.

2 Methods

This was a comprehensive literature review of microbiologically positive patients who received oritavancin for the treatment of acute or chronic osteomyelitis. Searches of PubMed and Google Scholar for papers, case reports, or other available data were conducted using the following search terms: "osteomyelitis" and "oritavancin"; "osteomyelitis" AND "oritavancin" AND "off-label"; osteomyelitis AND oritavancin AND off-label AND multiple dose. This search identified 17 resources in PubMed and in Google Scholar 73 additional (not duplicate) resources. These were reviewed and reduced to only resources that included cases of osteomyelitis and treatment with single or multiple doses of oritavancin. Reports were included if patients had a microbiologically confirmed osteomyelitis infection and were treated with oritavancin. A total of 38 cases were retrieved for analysis; 20 from seven published papers and 18 from the Clinical and Historic Registry and Orbactiv Medical Evaluation (CHROME) registry. From the 38 cases, 23 had microbiologically confirmed osteomyelitis infections and were included in the final review.

Both "clinical cure" and "clinical success" were used interchangeably throughout the analyzed literature and had the same definition: resolution of clinical signs and symptoms of infections, wound closure, resolution of fever, normalization of white blood cell count, no additional infection-related hospital admission, surgical debridement or amputation, no need for additional antibiotic therapy for the indication for which oritavancin was initially administered. Clinical "cure" or "success" are identified within the tables; however, we consider them under the same definition as clinical cure. Clinical improvement was defined as recovery from infection with need for additional Gram-positive therapy after completion of oritavancin treatment. Clinical failure was defined as inadequate resolution or progressive worsening of infection, and need for continued or alternative Gram-positive therapy at completion of oritavancin therapy, or loss at follow-up.

3 Results

Seven papers and cases from the CHROME registry were used for our analysis, which included 23 patients with microbiologically confirmed infections who received oritavancin for the treatment of osteomyelitis. These chart reviews and case studies reported administration of oritavancin, but not why it was selected by the clinician. However, clinical status of the patient, anatomic location of the infection, patient availability for follow-up, safety of other available treatments, and relevant co-morbidities would have been considered. Patients who received only one or two doses of oritavancin were still included because they were deemed to either exhibit clinical improvement or were a clinical success (Tables 1, 2, 3, 4, 5). The median age was 50 years (range 26–98 years), and 54% (13/23) were female. The most common co-morbidities were diabetes mellitus and hypertension. Osteomyelitis was confirmed in patients by either nuclear bone scans or by MRI. A total of 14 patients (56%) had documentation of antimicrobial treatment prior to administration of oritavancin, and one patient received concurrent doxycycline. All patients received at least one 1200 mg dose of oritavancin, and the majority (22) of patients received one 1200 mg dose followed by at least two further 1200 mg doses over a varied timeline (Tables 1, 2, 3, 4, 5).

The most common pathogen was MRSA, which was isolated in 48% ($n = 11$) of patients. Overall, clinical cure was achieved in 65% of patients ($n = 15/23$); however, clinical improvement was also demonstrated among patients—when combined, the overall rates of clinical success increased to 87% ($n = 20/23$).

Three clinical failures were documented. One osteomyelitis patient with confirmed *MRSA*, *E. faecalis*, and *E. coli,* who had received trimethoprim/sulfamethoxazole (TMP/SMX) therapy prior to one 1200 mg dose of oritavancin, was considered a treatment failure, and was then switched to ciprofloxacin and doxycycline. The second patient had a confirmed osteomyelitis MRSA infection, and oritavancin was given at two doses of 1200 mg every 9 days, which was switched to doxycycline after failure. The third patient was an active intravenous drug user (IVDU), and over a period of 71 days experienced multiple treatment failures. Initially administered vancomycin and cefazolin, once osteomyelitis infection was confirmed as MSSA this was reduced to just cefazolin; on day 8 of treatment, one 1200 mg dose of oritavancin was given

Table 1 Patients receiving oritavancin to treat culture-positive osteomyelitis—results per pathogen, methicillin-resistant *Staphylococcus aureus*

Reference	Sex/age (years)	Site of infection	Antimicrobials prior to oritavancin	Oritavancin dosing regimen	Concomitant antimicrobials	Outcome	Time of follow-up	Adverse events
Chastain et al. [44]	M/65	Right great toe	None	1200 mg × 2; on days 1 and 13	Doxycycline × 3 months	Clinical cure	6 months	None reported
	M/31	Left distal metatarsal	Clindamycin × 1 week	1200 mg × 3 on days 1, 52, and 90	None	Clinical cure	6 months	None reported
	M/47	Right distal first metatarsal	Clindamycin × 1 week, then doxycycline × 3 months	1200 mg × 2; on days 1 and 72	None	Clinical cure	6 months	None reported
	F/89	Left lateral malleolus	None	1200 mg × 4; on days 1, 36, 73, and 147	None	Clinical cure	6 months	None reported
	M/62	Right calcaneus	None	1200 mg × 6; on days 1, 14, 28, 70, 84, and 113	None	Clinical cure	6 months	None reported
Ruggero et al. [41]	M/46	Native, vertebral osteomyelitis	Aztreonam, vancomycin, metronidazole, doxycycline, TMP/SMX	1200 mg every 2 weeks × 4 doses, then 1200 mg 1 month later	TMP/SMX	Clinical improvement	5 months, and 1 year	None reported
CHROME Registry [46]	F/47	Not specified	TMP/SMX	1200 mg × 1	None	Failure	N/A	None reported
	F/70	Not specified	None	1200 mg × 10 doses every 7–8 days	None	Clinical improvement	N/A	None reported
	F/46	Skull	Vancomycin	1200 mg × 6 doses every 7–14 days	None	Clinical cure	N/A	None reported
	M/58	Left foot	Minocycline, vancomycin	1200 mg × 1, then in 14 days, AE occurred with second dose	Linezolid	Clinical improvement	N/A	Infusion discontinued; moderate, not serious infusion-related reaction; sent to ED for observation
	F/47	Not specified	None	1200 mg × 2 doses every 9 days	TMP/SMX	Failure	N/A	None reported

M male, *F* female, *TMP/SMX* trimethoprim/sulfamethoxazole, *AE* adverse event, *ED* emergency department, *N/A* information not available

Table 2 Patients receiving oritavancin to treat culture-positive osteomyelitis—results per pathogen, methicillin-sensitive *Staphylococcus aureus*

Reference	Sex/age (years)	Site of infection	Antimicrobials prior to oritavancin	Oritavancin dosing regimen	Concomitant antimicrobials	Outcome	Time of follow-up	Adverse events
Schulz et al. [40]	F/76	Not specified	None	1200 mg twice a week×2 doses	Transitioned to doxycycline×10 days	Clinical improvement	2 weeks	Anemia and leukopenia in 1 patient
Stewart et al. [42]	F/26	Sacral joint	Cefazolin; pip/tazo	1200 mg×1 dose	None	Failure	6 weeks	None reported
Delaportas et al. [39]	F/49	Right tibia	None	1200 mg weekly×6 doses	None	Clinical success	1, 4, 8, 12, 24, and 40 weeks	None reported
CHROME registry [46]	M/60	Not specified	Amox/clav, vancomycin, cefazolin/cephalexin	1200 mg×1	None	Clinical cure	N/A	None reported
	F/98	Not specified	Ceftriaxone, levofloxacin	1200 mg×1 (did not finish)	Ciprofloxacin	Clinical cure	N/A	None
	M/46	Not specified	Amoxicillin	1200 mg×6 doses every 6–8 days	None	Clinical cure	N/A	None
	F/36	Not specified	Amp/sul, ceftriaxone, TMP/SMX, vancomycin, cefazolin, cephalexin	1200 mg×3 doses every 14 days	None	Clinical cure	N/A	None

F female, *M* male, *TMP/SMX* trimethoprim/sulfamethoxazole, *amox/clav* amoxicillin/clavulanic acid, *amp/sul* ampicillin/sulbactam, *pip/tazo* piperacillin/tazobactam, *N/A* information not available

Table 3 Patients receiving oritavancin to treat culture-positive osteomyelitis—results per pathogen, vancomycin-resistant *Enterococcus* (daptomycin non-susceptible)

Reference	Sex/age (years)	Site of infection	Antimicrobials prior to oritavancin	Oritavancin dosing regimen	Concomitant antimicrobials	Outcome	Time of follow-up	Adverse events
Foster et al. [45]	M/57	Hip	Daptomycin, ciprofloxacin	1200 mg once weekly×6 weeks	Ciprofloxacin	Clinical success	9.5 months, and 14.5 months	None
Dahesh et al. [43]	M/57	Vertebral	Tigecycline, quinupristin-dalfopristin	1200 mg weekly×2 doses, then 800 mg weekly×8 doses	Ampicillin	Clinical improvement	N/A	None
CHROME registry [46]	F/50	Not specified	None	1200 mg×1	None	Clinical cure	N/A	None
	F/50	Not specified	None	1200 mg×1	None	Clinical improvement	N/A	None

M male, *F* female, *N/A* information not available

and the patient was discharged on oral clindamycin. This patient then returned on day 50 of treatment, reporting non-adherence to clindamycin, and cephalexin was given for 1 month. At day 71 the patient presented with recurrent and worsening infection and eventually was discharged on TMP/SMX and rifampin for 3 months. Two months later the patient returned and a small aortic valve vegetation was identified alongside osteomyelitis; cefazolin was

Table 4 Patients receiving oritavancin to treat culture-positive osteomyelitis—results per pathogen, group A *Streptococcus pyogenes*

Reference	Sex/age (years)	Site of infection	Antimicrobials prior to oritavancin	Oritavancin dosing regimen	Concomitant antimicrobials	Outcome	Time of follow-up	Adverse events
CHROME registry (46)	M/70	Not specified	Cephalexin; dalbavancin	1200 mg × 2 doses every 6 days	None	Clinical cure	N/A	None

N/A information not available

initiated followed by chronic suppressive therapy with cephalexin. All treatment failure cases received a regimen of only one or two doses of oritavancin, which is inconsistent with osteomyelitis treatment guidelines, which suggest 4–6 weeks of antimicrobial treatment [47].

All patients were included in the safety analysis. Oritavancin was well tolerated with adverse events (AEs) reported in only two cases (8.7%). One patient developed a moderate, infusion-related reaction during the second dose of oritavancin; the infusion was stopped and the patient was sent to the emergency department (ED) for observation and switched to linezolid. The second patient, who received only two oritavancin doses, was found to have anemia and leukopenia, and was transitioned to doxycycline for an additional 10 days. Clinical improvement was demonstrated in both patients prior to terminating oritavancin therapy due to AEs.

4 Discussion

Osteomyelitis remains a difficult to treat infection with significant treatment challenges, commonly requiring both surgical debridement and concomitant antibiotic therapy with agents active against the bone-infecting pathogen. MRSA is responsible for the majority of cases of osteomyelitis, which can persist and/or recur in up to 40% of patients [48]. While vancomycin remains the most frequently selected antibiotic for the treatment of osteomyelitis [16], vancomycin use is associated with increased rates of failure and recurrence, likely due to its poor penetration into bone and biofilm formations, as well as the occurrence of vancomycin-intermediate *S. aureus* (VISA), heterogenous VISA (hVISA), and *S. aureus* isolates with increasing minimum inhibitory concentrations (MICs) [49, 50]. Antimicrobial selection needs to consider whether the agent achieves adequate bone penetration, with bioavailable bone concentrations exceeding the pathogen MIC. Anatomical location of infected bone, as well as vascularity, which may be compromised, affects achievable bone concentrations. Oritavancin has been shown to rapidly penetrate osseous tissues in rabbit tibia models and drug levels are maintained for greater than 168 h. The active ratio of oritavancin in bone is still unknown; in this animal model, bone penetration, defined as the tissue to serum

AUC_{0-168} ratio into bone matrix and bone marrow, was 1.7 and 3.1, respectively, which is higher than that of linezolid, vancomycin, teicoplanin, and dalbavancin [33]. One caveat to note is that the concentrations of oritavancin obtained in the rabbit study by Lehoux (and those of the cited comparators) represent total drug concentrations, and the active fraction of each drug in bone remains to be described [33]. Therefore, the PK/PD relationship of oritavancin in bone and other tissues should be interpreted with caution. These data provided the stimulus for using single and multiple oritavancin dosing in patients with osteomyelitis. Clinical outcomes of oritavancin treatment for osteomyelitis caused by MRSA, MSSA, VRE, and *S. pyogenes* from the analyzed case reports and data are collated in Tables 1, 2, 3, 4. Oritavancin has been shown to be efficacious in a wide range of Gram-positive bone infections, with a 1200 mg dose (occasionally, a continued 800 mg dose) administered once a week for 4–8 weeks, with few adverse events. In this review, we chronicled the efficacy, safety, and clinical outcomes of 23 pathogen culture-positive patients with osteomyelitis who were treated with oritavancin in published case reports and also from the CHROME registry. Bone biopsy and tissue culture are the gold standard of osteomyelitis diagnosis; however, the use of these methods can be challenging due to their invasive nature. Thus, in the reviewed case reports, real-world diagnostic methods were made using bone scans or MRI. Real-world evidence regarding oritavancin shows high rates of clinical success with both single or multiple doses to treat osteomyelitis, and is well tolerated with minimal adverse events, without need for therapeutic drug monitoring (Table 5). In ABSSSIs, recent studies have demonstrated the potential opportunity for oritavancin to facilitate early discharge for patients, as the IV infusions are once per week, and it has also been administered in the ED to avoid hospitalization of patients for IV treatment [51]. While certainly promising, these findings are limited by the number of case reports and the unique circumstances of each case, as well as the potential influence of prior or concomitant antimicrobial therapy to successful outcomes; thus, future analysis is needed. Additionally, these data may be useful in identifying the optimal dosing frequency, which remains to be established, and we suggest each regimen should be adapted for the management of individual patients.

Table 5 Summary of the real-world experience using oritavancin for microbiologically positive osteomyelitis

Study	Patient background	Pathogens	Oritavancin dose and duration	Outcome	Adverse effects
Schulz et al. [32]	4 patients; median age 59 years (31–76); 25% male	MSSA	3 patients: 1200 mg × 1 dose, then 800 mg weekly ≥ 2 doses 1 patient: 1200 mg × 2/week	Success × 2 Improvement × 2	Anemia and leukopenia in 1 patient
Chastain et al. [36]	12 patients, median age 65 years (47–79), 67% male, 67% DM	MRSA	3 patients = 1200 mg × 1 dose 9 patients = 1200 mg × ≥ 2 doses	100% Success	None
Foster et al. [37]	57 y/o M with osteomyelitis secondary to prosthetic hip replacement	Daptomycin non-susceptible VRE	1200 mg once weekly × 6 weeks	Success	None
Delaportas et al. [31]	49 y/o F with right tibial osteomyelitis secondary to retained intramedullary nail	MSSA	1200 mg once weekly × 6 weeks	Success	None
Ruggero et al. [33]	46 y/o M with native vertebral osteomyelitis	MRSA	1200 mg every 2 weeks × 4 doses, then 1200 mg 1 month later	Improvement	None
Dahesh et al. [35]	59 y/o M with hardware-associated vertebral osteomyelitis	Vancomycin-resistant and daptomycin NS E. faecium	1200 mg weekly × 2 doses, then 800 mg weekly × 8 doses	Improvement	None
Stewart et al. [34]	26 y/o F with sacral joint osteomyelitis; IVDU	MSSA	1200 mg × 1 dose	Failure	None
CHROME Registry [38]	18 patients; mean age 58.4 years, 38.9% male, 77.8% prior antibiotics, 50% failure prior antibiotics	MRSA, MSSA, coagulase-negative Staphylococcus, E. faecalis, E. faecium, S. pyogenes	10 patients = 1200 mg × 1 dose 8 patients = 1200 mg × ≥ 2 doses	Clinical success: Single dose: 90% Multi-dose: 87.5%	Moderate, not serious infusion-related reaction (in multidose patient)

M male, F female, y years, MSSA methicillin-sensitive Staphylococcus aureus, MRSA methicillin-resistant Staphylococcus aureus, VRE vancomycin-resistant Enterococcus, NS non-susceptible, DM diabetes mellitus, IVDU intravenous drug user

5 Conclusion

We reported on 23 microbiologically positive patients who received oritavancin, either in single or multiple doses, for the treatment of osteomyelitis. Few adverse events were noted, and they were generally mild and reversible. Oritavancin treatment for osteomyelitis was generally safe, effective, and well tolerated, and was able to facilitate outpatient therapy. The clinical success in these patients suggests that use of oritavancin, given at 1200 mg or 800 mg in multiple doses, can be beneficial for the treatment of osteomyelitis. The long half-life of oritavancin lends itself to a convenient treatment for patients, as a once-per-week IV infusion, and may reduce the need for central line placement, which could have a positive impact on a patient's quality of life. Future studies to evaluate the potential pharmacoeconomic benefits of oritavancin for osteomyelitis treatment, as well as the impact of infrequent IV infusions in the OPAT setting on patients' lives and productivity, should be explored. Clinicians should consider the use of oritavancin in the treatment of those patients with osteomyelitis as a safe and efficacious option.

Compliance with Ethical Standards

Conflict of Interest P.J.S. serves as a consultant for Iterum Pharmaceuticals LTD, Shionogi & Co., LTD, and Spero Therapeutics. JR receives speaker fees from Melinta Therapeutics. GST serves as consultant to Melinta Therapeutcs, Shionogi Inc, Summit plc, KBP Biosciences and Aim Max Therapeutics.

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