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Short Communication

# Outpatient treatment of osteomyelitis with telavancin

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ABSTRACT

Telavancin is a lipoglycopeptide antibiotic with bactericidal activity against Gram-positive pathogens including *Staphylococcus aureus*, the most frequent cause of osteomyelitis. Treatment is often challenging due to needs for surgical intervention along with prolonged administration of intravenous antimicrobials, frequently in an outpatient setting. This was a retrospective analysis of the efficacy and safety of telavancin for treatment of osteomyelitis provided as outpatient parenteral antimicrobial therapy (OPAT) in physician office infusion centres. Medical records of 60 patients receiving telavancin for osteomyelitis in 22 physician office infusion centres from 2010 to 2011 and 2013 to 2015 were reviewed. Of these, 60% were treated without hospitalisation, 37% had orthopaedic hardware and 56% had concurrent infections. *Staphylococcus aureus* was the most common pathogen (78%), primarily methicillin-resistant. The median duration of telavancin treatment in the outpatient setting was 21 days (range 3–105 days). Telavancin was used as first-line therapy in 32% of cases, following prior antibiotic failure in 47% and due to intolerance to previous agents in 22%, predominantly daptomycin or vancomycin. The telavancin dose was 10 mg/kg/day, adjusted for renal function in 25% of patients. The majority of patients self-administered telavancin at home via an elastomeric infusion pump. Overall clinical success was 73%. No significant differences in outcomes were observed with the presence of hardware, concurrent infection, concomitant therapies or type of osteomyelitis. Telavancin-associated adverse events occurred in 57%, with discontinuation in three patients (5%). These data demonstrate the effective and safe OPAT use of telavancin, providing an alternative for successful treatment of patients with osteomyelitis.


## 1. Introduction

Outpatient parenteral antimicrobial therapy (OPAT) has gained wide acceptance for provision of parenteral antimicrobial therapy in the USA and Europe [1–3]. OPAT guidelines recommend the involvement of an infectious diseases physician in patient management, which may result in better adherence to standards of care and improved patient outcomes [1,3]. Osteomyelitis is frequently treated with OPAT owing to the need for prolonged administration of intravenous (i.v.) antimicrobials, however osteomyelitis may require surgical interventions and pose difficult therapeutic challenges [1,4]. Clinical failures have occurred in >30% of osteomyelitis patients treated with OPAT [5]. Gram-positive bacteria are the most common, with *Staphylococcus aureus* accounting for the majority of cases [5,6]. Increasing development of resistance to antimicrobial agents, including vancomycin and daptomycin, in methicillin-resistant *S. aureus* (MRSA) makes optimal patient management more difficult [7,8]. Consequently, alternative agents are needed for the treatment of Gram-positive osteomyelitis.

Telavancin (VIBATIV®), a once-daily intravenously administered lipoglycopeptide antibiotic, is approved in the USA for the treatment of adults with complicated skin and skin-structure infections (cSSSIs) caused by susceptible Gram-positive pathogens [9]. In addition, it is approved for hospital-acquired and ventilator-associated bacterial pneumonia (HABP and VABP) caused by susceptible isolates of *S. aureus* when alternative treatments are not suitable [10]. Telavancin is approved in Europe for nosocomial pneumonia caused by MRSA and in Canada for the treatment of HABP/VABP and cSSSI caused by susceptible Gram-positive pathogens [11]. The drug became unavailable in the USA in December 2011 owing to the inability of the contract manufacturer to supply the drug, and it was re-introduced in August 2013. Telavancin exhibits concentration-dependent bactericidal activity against

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Gram-positive pathogens, including MRSA, via a dual mechanism of action by inhibiting cell wall synthesis and disrupting cell membrane function [12]. Animal data suggest adequate bone penetration of telavancin [13], however clinical data in the treatment of osteomyelitis are limited to case reports [14–16]. Daily dosing as well as administration and stability of telavancin in elastomeric devices lend it to be an ideal OPAT agent, warranting evaluation in osteomyelitis [17].

The purpose of this study was to assess the efficacy and safety of telavancin for the treatment of Gram-positive osteomyelitis in patients receiving OPAT through infectious diseases physician office infusion centres.

## 2. Methods, patients and materials

Eligible patients included adults who received at least three OPAT doses of telavancin for the treatment of osteomyelitis in 2010–2011 and 2013–2015 through 22 infectious diseases physician office infusion centres in the USA. Pertinent data were extracted from medical records and included demographics, prior hospitalisation, co-morbidities, type of osteomyelitis, anatomic location of osteomyelitis and presence of an orthopaedic device. Other concurrent infections (cSSSI, bacteraemia and diabetic foot infection) were recorded along with surgical procedure(s) performed within 12 months prior to the start of telavancin treatment. Microbiological data were collected for all patients. Telavancin therapy characteristics included dosage, length of therapy, type of administration, prior and concomitant antimicrobials, and primary reason(s) for usage.

Clinical outcomes were assessed by the treating physician and were recorded as resolved, improved or unsuccessful. Resolved was defined as resolution of clinical signs and symptoms of infection and/or no additional antibiotic therapy necessary. Improved was defined as partial resolution of clinical signs and symptoms and/or continued oral antibiotic at the end of therapy. Unsuccessful was defined as inadequate response to therapy, worsening or new/recurrent signs and symptoms, or a need for change in antimicrobial therapy. Patient outcomes were identified as non-evaluable if response to therapy was unable to be determined from the record or if the patient was lost to follow-up. The term clinical success was used to describe patients with resolved or improved outcomes.

Safety was assessed by evaluation of all reported adverse events (AEs), regardless of relationship to the study drug. AEs resulting in discontinuation of telavancin were included. Renal impairment was noted as a serum creatinine (SCr) level of ≥1.5 mg/dL or ≥50% above baseline.

Descriptive statistics were used for data assessment. The $\chi^2$ test and analysis of odds ratios were performed for comparison of outcome measures and analysis of risk factors, respectively, using MedCalc v.16.4.3 (MedCalc Software, Ostend, Belgium), with a *P*-value of <0.05 defined as statistically significant. Informed consent from subjects was not necessary owing to the retrospective nature of the study.

## 3. Results

### 3.1. Patient demographics and clinical characteristics

A total of 60 patients treated with outpatient telavancin for Gram-positive osteomyelitis were identified and their demographics and clinical characteristics are described in Table 1. The majority of patients (36; 60%) initiated treatment in the OPAT setting, with the remainder (24; 40%) initiating therapy prior to hospital discharge. Orthopaedic hardware was in place in 22 patients (37%), including 16 patients (27%) with permanent prostheses. Surgical procedure(s) were performed in 44 patients (73%) within 12 months prior to the start of telavancin, including arthroplasty ($n = 8$), debridement ($n = 29$), discectomy ($n = 1$), hardware surgery ($n = 12$), lower limb amputation ($n = 5$) and lumbar spine fusion ($n = 2$). Thirty-four patients (57%) had one or more concurrent infectious diseases, including bacteraemia, cSSSI and diabetic foot infection in 3, 32 and 15 patients, respectively.

**Table 1**
Patient demographics and clinical characteristics.

| Characteristic | Patients ($n = 60$) [a] |
|---|---|
| Age (years) (mean ± S.D.) | 54 ± 12 |
| Age | |
| ≤30 years | 4 (7) |
| 31–64 years | 46 (77) |
| ≥65 years | 10 (17) |
| Sex male | 32 (53) |
| Type of osteomyelitis | |
| Acute | 32 (53) |
| Chronic | 28 (47) |
| Location of osteomyelitis | |
| Foot/toe | 23 (38) |
| Finger | 6 (10) |
| Vertebrae | 6 (10) |
| Knee | 4 (7) |
| Hip | 3 (5) |
| Sternum | 3 (5) |
| Tibia/fibula | 3 (5) |
| Ankle | 2 (3) |
| Shoulder | 2 (3) |
| Other specified sites [b] | 8 (13) |
| Co-morbid conditions [c] | |
| Obesity [d] | 33 (55) |
| Hypertension | 30 (50) |
| Diabetes mellitus | 27 (45) |
| Cardiovascular disease | 23 (38) |
| Rheumatoid arthritis | 17 (28) |
| Chronic renal insufficiency | 4 (7) |
| Renal function [e] | |
| $CL_{Cr}$ > 80 mL/min | 30 (50) |
| $CL_{Cr}$ = 51–80 mL/min | 22 (37) |
| $CL_{Cr}$ = 30–50 mL/min | 5 (8) |
| $CL_{Cr}$ <30 mL/min | 1 (2) |

S.D., standard deviation; CLCr, creatinine clearance.
[a] Data are *n* (%) unless otherwise stated.
[b] Cranium ($n = 1$), elbow ($n = 1$), femur ($n = 1$), hand ($n = 1$), humerus ($n = 1$), mandible ($n = 1$), rib ($n = 1$) and sacrum ($n = 1$).
[c] Patients may have more than one co-morbid condition.
[d] Body mass index (BMI) ≥ 30 kg/m$^2$.
[e] Data available for 58 of 60 patients.

### 3.2. Microbiology and therapy

Of the 60 patients treated with telavancin, 50 (83%) had a total of 63 Gram-positive pathogens isolated. *Staphylococcus aureus* was the most common (78%), with 67% confirmed MRSA. Microbiological data are summarised in Table 2.

**Table 2**
Gram-positive pathogens ($n = 63$) isolated from osteomyelitis patients.

| Primary pathogen [a] | Isolates [*n* (%)] |
|---|---|
| *Staphylococcus* spp. | |
| MRSA | 42 (67) |
| MSSA | 7 (11) |
| CoNS | 8 (13) |
| *Streptococcus* spp. | |
| Group B streptococci | 3 (5) |
| Group D streptococci | 1 (2) |
| *Enterococcus* spp. | 2 (3) |

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *S. aureus*; CoNS, coagulase-negative staphylococci.
[a] More than one pathogen may be derived from the primary site of infection (wound, bone).