Treatment Of Acute Osteomyelitis With Once Weekly Oritavancin

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Background

Osteomyelitis	▪ Acute osteomyelitis in adults remains a clinical challenge with high morbidity and lack of general treatment guidelines except for vertebral osteomyelitis. ▪ Parenteral therapy has traditionally been standard of care, often with multiple daily antibiotic doses given for at least 4 weeks. ▪ Several case reports have described the use of multiple dose regimens with oritavancin for a variety of complex infections, including osteomyelitis, with promising results.
Oritavancin	▪ Semisynthetic lipoglycopeptide antibiotic approved for the treatment of acute Gram-positive skin and soft tissue infections ▪ Approved as a single 1200 mg dose for the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI) ▪ Key covered pathogens: Methicillin resistant Staphylococcus aureus (MRSA), Enterococcus, streptococcus spp. ▪ Rapid bactericidal activity ▪ Cell wall synthesis inhibition ▪ Prevents patients from needing a peripherally inserted central catheter (PICC) or a mid-line catheter, which in turn prevents catheter-associated bacteremia ▪ The long terminal half-life, supports once-weekly administration with logistical advantages over traditional therapies.

Objective

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To characterize the use and safety of oritavancin in patients with acute osteomyelitis in real-world clinical settings.

Primary Outcome:
To evaluate the clinical success of oritavancin for acute osteomyelitis in a multi-dosing regimen scheme over 6 months

Methods

- Consecutive patients who received oritavancin 1200 mg followed by 800 mg once weekly for acute osteomyelitis were included in this retrospective review
- Patients received other dosing regimens, such as 1200 mg followed by 1200 mg once weekly, were not included
- Diagnosis of acute osteomyelitis and antibiotic treatment decisions were determined by board certified infectious diseases physicians at multiple sites throughout the United State
- All patients received a total treatment duration of 4 or 5 weeks. All oritavancin infusions were administered over 3 hours
- Clinical outcomes were assessed at the completion of the entire oritavancin course of therapy at 7 to 10 days after the end of the last dose (ETE) and at 3 months and 6 months post treatment (PTE) using both retrospective electronic medical records assessment and via patient telephone follow up as conducted by an infectious disease trained pharmacist using an approved questionnaire and approved data collection form, see Figure 1.
- Clinical outcome determinations at ETE were based on the following:
  - Clinical success based on resolution of symptoms or improvement in symptoms and no further need for treatment; or
  - Clinical failure based on lack of improvement in symptoms and need for use of additional antibiotics or loss to follow up at ETE Clinical success and failure at PTE were determined during the 3 and 6 month follow up timeframe.
- Clinical failure was defined as:
  - Use of Gram-positive antibiotics during the PTE period;
  - Admission to the hospital for baseline osteomyelitis; or
  - Loss to follow up. All other patients were considered clinical success.
- Safety data, including discontinuation of oritavancin due to safety concerns, infusion events, and other adverse events as noted by patient telephone follow up at 7 to 10 days, 3 months, and 6 months post oritavancin were reported.
- The retrospective study was approved for analysis and publication by an Institution Review Board.

Baseline Characteristics

Male	66 (49.3)
Age , mean years (range)	60 (19 - 97)
Weight, kg, ave, range, SD	78 (38 - 164), 23.8
BMI (kg/m2), mean, (range), SD	27 (15.8 - 48.4), 6.7
Baseline MRI	134 (100)
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Infection confirmed on MRI	128 (95.5)
Baseline CRP	134 (100)
Baseline ESR	132 (98.5)
Previous antibiotic therapy	18 (13.4)
Baseline bacteremia (MRSA)	9 (6.7)
Debridement of bone or joint	121/134 (90.3)
Positive wound, bone, joint culture	119/134 (88.8)
Culture (+) (wound, joint, deep wound) MRSA	92/128 with cultures drawn (71.9)
Prosthetic source	24 (17.9)
Vertebral source	8 (6)

Lower extremity source	74 (55.2)
Upper extremity source	25 (18.7)
Pelvic source	18 (13.4)

Baseline Micro

Culture and Pathogen by Unique Patient	**n/N (%)**
Positive cultures with ≥ 1 Gram-positive result	119/134 (88.8)
Staphylococcus aureus, monomicrobial	
MRSA	92
MSSA	25
S. aureus, mixed	
MRSA + ≥ 1 other GP pathogen [a]	16
MSSA + ≥ 1 other GP pathogen [a]	10
Vancomycin-resistant enterococci (VRE) [b]	7
Vancomycin-intermediate *S. aureus* (VISA) [b]	2
VRE with daptomycin MIC ≥ 4 mg/L	2

Results

Overall Clinical response at Timepoints	n/N (%)
Clinical cure at ETE	118/134 (88.1)
Clinical cure at PTE	109/130 (83.8)
Patient Subgroups	n/N (%)
Overall clinical success according to dosing	
4 weekly doses post initial 1200mg	107/118 (90.7)
5 weekly doses post initial 1200mg	11/16 (68.8)
Prosthetic device infection with osteomyelitis	20/24 (88.3)
Antibiotic therapy prior to first dose of oritavancin	14/18 (77.8)
Osteomyelitis established by MRI	113/128 (90.4)
Baseline history of diabetes	43/51 (84.3)
Baseline history of heart failure	21/25 (84.0)
Baseline history of malignancy or immunosuppression	11/12 (91.7)

Conclusion

- Based on this study, multiple weekly doses of oritavancin is a safe and effective option for the treatment of adult patients with acute osteomyelitis

Disclosure

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation
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