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Real-World Outpatient Use of Omadacycline for Bone and Joint Infections

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Background

Omadacycline (OMC) is approved for the treatment of adult patients with community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections.[1] OMC is often used in outpatient parenteral antimicrobial therapy (OPAT), with increased use in bone and joint infections (BJI). Data regarding real-world use of OMC in BJI are limited. A rat model study of MRSA osteomyelitis showed OMC had improved activity when combined with rifampin[2], which was further evaluated in a PK/PD model[3], abrogating emergence of resistance observed with rifampin monotherapy. Another case report describing the use of PO OMC following 13 days of IV antibiotics showed clinical improvement in a patient with maxillary osteomyelitis.[4] These preliminary findings coupled with promising animal studies showing excellent bone tissue penetration of omadacycline[5] warrant further investigation for the treatment of BJI, including osteomyelitis. We present a multicenter retrospective observational review of OMC use in OPAT for treatment of BJI.

Methods

This study design is a multicenter, real-world experience with a retrospective cohort design. Study locations were 8 Physician Office Infusion Centers (POICs) nationally.

Medical records were reviewed of patients receiving intravenous OMC from 2019 to 2022 for treatment of BJI. Data included demographics, diagnosis, medical history, microbiology, therapy regimen, including transition to oral OMC, adverse events (AEs), clinical outcomes, and 12-month follow-up. Clinical success was defined as complete or partial symptom resolution at completion of OMC with oral antibiotics continued if needed. Persistent and recurrent infection were deemed non-success. Indeterminate outcomes were excluded from outcome assessment. Patients with no recurrence at 12 months were identified as continued success. Analysis of continuous data were reported as mean±SD or range, median (IQR) and categorical data as counts and percentages.

Results

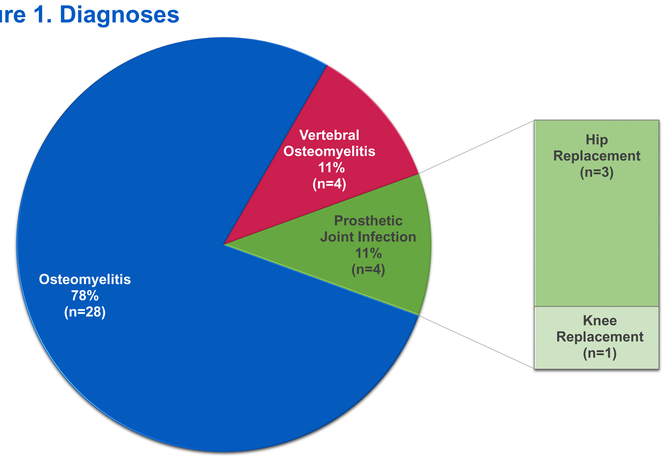
- 36 pts from 8 ID POICs were included in the study

Table 1. Demographics and Baseline Characteristics

Patient Characteristic	N = 36
Age, year, median (IQR)	64 (52-71)
Age ≥65-year	18 (50%)
Male sex	25 (69%)
BMI, kg/m², median (IQR)	33 (28-37)
BMI ≥30 kg/m²	23 (64%)
Charlson comorbidity index, median (IQR)	4.5 (4-6)
Comorbid conditions	
Diabetes mellitus	23 (64%)
Cardiovascular diseases	17 (47%)
Peripheral vascular disease	6 (17%)
Chronic kidney disease	11 (31%)
Immunocompromised[a]	6 (17%)
Malignancy	5 (14%)
Gastrointestinal disease	5 (14%)
Primary Payor	
Medicare	18 (50%)
Commercial Insurance	15 (42%)
Medicaid	3 (8%)
Treatment location prior to omadacycline therapy	
Community	23 (64%)
Hospital	13 (36%)
Hospital length of stay, day, median (IQR)	7 (6-12)
Intravenous antibiotics prior to omadacycline therapy	23 (64%)

Data are presented as n (%), unless otherwise specified.
[a]Due to immunosuppressive medication (chemotherapy, steroids, biologics) or underlying immune deficiency (cancer, acquired immunodeficiency syndrome, genetic disorder, autoimmune disease, organ transplant).
Abbreviations: BMI, body mass index; IQR, interquartile range

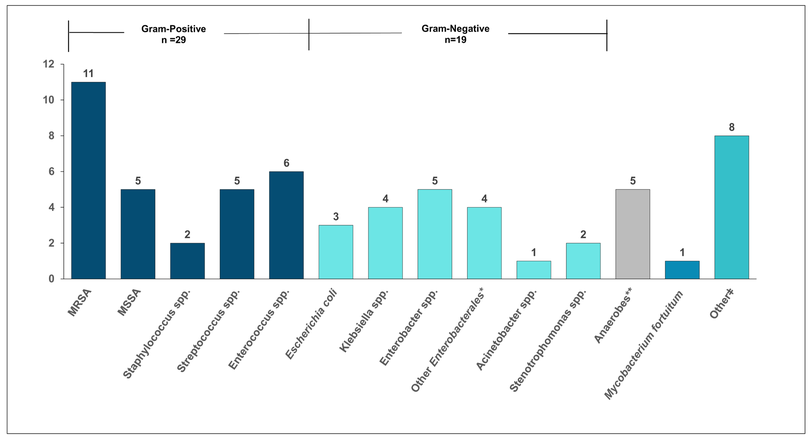
Figure 1. Diagnoses



- 18 of 28 osteomyelitis patients (64%) had underlying diabetic foot infections

Results

Figure 2. Pathogens



*Includes *Serratia marcescens* (n=2), *Citrobacter freundii* (n= 1) and *Morganella morganii* (n=1)
**Includes *Peptostreptococcus* spp. (n=3), *Bacteroides buccae* (n=1) and *Peptoniphilus* sp. (n=1)
‡Includes *Corynebacterium* spp. (n=3), *Pseudomonas aeruginosa* (n=2), *Eikenella* sp. (n= 1), *Haemophilus parainfluenzae* (n=1) and *Prevotella* spp. (n=1)

- MRSA was the predominant organism, followed by Enterococcus spp.
- 21 of 36 pts (58%) had polymicrobial infection. Among these 12 pts (33%) had mixed Gram-positive and Gram-negative infections.

Table 2. Pathogens by Diagnosis

Diagnosis	All	MRSA	MSSA	Staphylococcus spp.	Streptococcus spp.	Enterococcus spp.	*Escherichia coli*	Klebsiella spp.	Enterobacter spp.	Other *Enterobacterales*	Acinetobacter spp.	Stenotrophomonas spp.	Anaerobes	*Mycobacterium fortuitum*	Other[a]
BJI	62	11 (18)	5 (8)	2 (3)	5 (8)	6 (10)	3 (5)	4 (6)	5 (8)	4 (6)	1 (2)	2 (3)	5 (8)	1 (2)	8 (13)
Osteomyelitis	55	9 (16)	5 (9)	2 (4)	4 (7)	6 (11)	2 (4)	3 (5)	4 (7)	4 (7)	1 (2)	2 (4)	5 (9)	0	8 (15)
Vertebral Osteomyelitis	7	2 (29)	0	0	1 (14)	0	1 (14)	1 (14)	1 (14)	0	0	0	0	1 (14)	0

No isolates were identified in prosthetic joint infection. Two patients had no growth in cultures and two had no culture data available.
[a]Other included *Corynebacterium* spp. (n=3), *Pseudomonas aeruginosa* (n=2), *Eikenella* sp. (n= 1), *Haemophilus parainfluenzae* (n=1) and *Prevotella* spp. (n=1)

Figure 3. Median Duration of Therapy

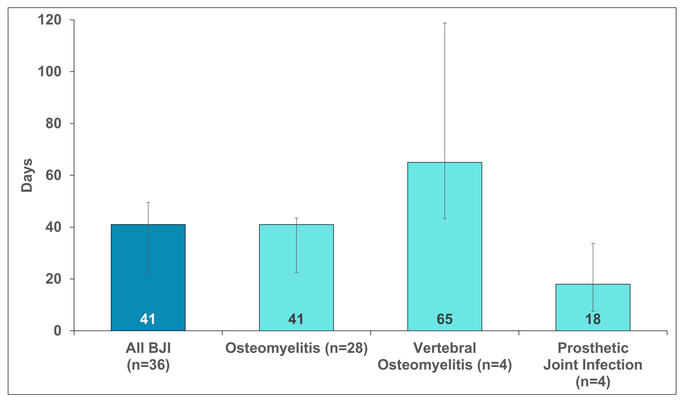


Table 3. Utilization Characteristics

Characteristic	N = 36
Loading dose (200 mg IV once)	35 (97%)
Maintenance dose (100 mg IV every 24 hours)	36 (100%)
Infusion device	
Elastomeric device	13 (36%)
Infusion Pump	23 (64%)
Concomitant intravenous antibiotic therapy	6 (17%)

- 1 pt with vertebral osteomyelitis and 1 with osteomyelitis were transitioned to oral OMC for 2 and 3 weeks, respectively.

Table 4. Adverse Events

Adverse Events	N = 36
Total Adverse Events	16
Nausea	2 (6%)
Dyspepsia	1 (3%)
Abdominal pain	1 (3%)
Fatigue	2 (6%)
AST/ALT elevation, <3X ULN	2 (6%)
AST/ALT elevation, >3X ULN	1 (3%)[a]
ALP elevation, <3X ULN	3 (8%)
ALP elevation, >3X ULN	1 (3%)[a]
Increase in serum creatinine	3 (8%)

[a]AST elevation 8.7X ULN, ALT elevation 5.7X ULN and ALP elevation 4.3X ULN (n=1)
Abbreviations: ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transferase; ULN, upper limit normal

- 16 total adverse events occurred in 12 patients overall.
- No patients discontinued omadacycline due to adverse events.
- The liver enzyme elevations occurred in 6 patients and were transient with no sequelae.

Figure 4. Clinical Outcomes

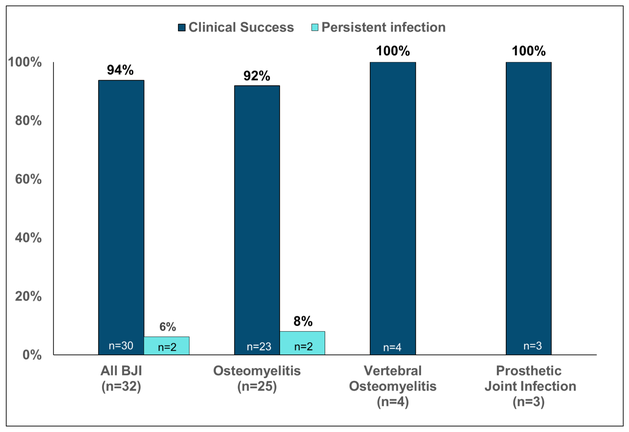
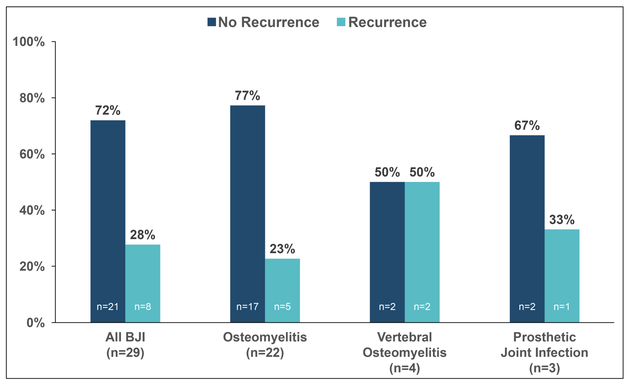


Figure 5. 12-Month Recurrence



- 32 pts were evaluable for outcomes in the study with an overall success rate of 94%. This included one pt with Mycobacterial vertebral osteomyelitis.
- The 2 pts with persistent infection were diabetics with recurrent MRSA osteomyelitis.
- 29/30 with successful outcomes had 12-month follow-up, with sustained success in 72%. Recurrence occurred at a mean of 80 days (range 40 – 140) with polymicrobial infections in four, carbapenem-resistant Enterobacter and Acinetobacter infections in one each.

Discussion / Conclusion

This multicenter study provides real-world data on treatment of BJI with intravenous OMC in POICs.

- 36 adult patients from 8 centers received OMC between 2019 and 2022, with a median age of 64 yrs. Primary payor was Medicare in half, with POIC coverage for intravenous OMC.
- Most patients received other IV antibiotics prior to OMC use. Transition to OMC occurred in the POIC for the majority.
- Single agent therapy with OMC was successfully used in 83% of patients, even with a majority with mixed infections.
- OMC given intravenously was well-tolerated overall with no patient discontinuations.
- Initial success at end of therapy was 94%, with sustained response in 72%.
- Recurrences occurred in 28%, all within 6 months.
- Limitations: Retrospective single arm, small sample size and limited access to patient information regarding oral therapy.

This real-world study of OMC demonstrates successful treatment of complex BJI, including vertebral osteomyelitis, PJI and polymicrobial osteomyelitis with sustained response.

References

1. NUZYRA® (omadacycline) [package insert]. Paratek Pharmaceuticals, Inc. Boston, MA: 2018.
2. Karau MJ et al. *Antimicrob Agents Chemother* 2021; doi:10.1128/AAC.01703-21.
3. Morrisette T, et al. *Antimicrob Agents Chemother* 2023;doi:10.1128/aac.01317-22.
4. Gill GS et al. *Cureus* 2019; 11(8); e5347.
5. Rodvold KA, et al. *Clin Infect Dis* 2019; 69: doi:10.1093/cid/ciz309.

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