Early Experience With Omadacycline For The Treatment Of Diabetic Foot Infections

Abstract #2887 – IDWeek 2023

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Disclosures

- Investigator-initiated Study
- Funded by Paratek Pharmaceuticals, Inc.
- Registered on ClinicalTrials.gov (NCT04714411)

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Background

- Diabetes mellitus is extremely prevalent
  - 12.6% of adults 20 years or older having the disease (U.S.)
  - >170 million people (worldwide)
- Patients with diabetes have at least a 25% lifetime risk of developing a diabetic foot ulcer infection (DFI)
- Osteomyelitis (OM) complicates 20% of moderate and 50-60% of severe DFI
- Lower extremity amputation required in 5% moderate DFI and 20% OM cases
- Often polymicrobial infections with Gram-positive cocci, anaerobes, and *Enterobacterales* are the most commonly identified pathogens
- Frequently used regimens to target likely pathogens are complicated by adverse effects and toxicity including acute kidney injury (AKI)

National Center for Health Statistics. 2017.
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Background – Omadacycline (OMC)

- Tetracycline class antibacterial approved for community-acquired bacterial pneumonia(CABP) and acute bacterial skin and skin-structure infections (ABSSSI)
- Spectrum active against key pathogens frequently causing moderate to severe DFI (*Staphylococcus aureus*, *Enterobacterales*, and anaerobes)
- Animal models demonstrate substantial bone penetration (compared to serum) and efficacy in treating OM
- Not associated with acute kidney injury (AKI) or *Clostridioides difficile* infection (CDI) in phase 3 clinical trials for CABP or ABSSSI
- Gut microbiome modeling suggests a minimal propensity for omadacycline to cause CDI
- Available both intravenously (IV) and orally (PO) which may prove beneficial in minimizing hospital length of stay and avoiding venous catheters

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Methods

- Prospective, open-label, two-center study
- Assess the safety of OMC use in the treatment of patients with moderate or severe DFI (with or without acute OM)
  - Hospitalized adults (≥18 years)
  - High risk for development of CDI, AKI, and/or resistant pathogens
- Clinical success
  - Resolution of the target ulcer and signs/symptoms of infection OR
  - Sufficient clinical improvement in that the majority of signs/symptoms of the infection have abated and no additional antimicrobial therapy is required
- Clinical failure
  - Require longer antibiotic therapy for the target ulcer (more than 42 days)
  - Require an addition/change to another antimicrobial for qualifying enrollment infection through LFU visit (90 days)
  - Develop a new purulent infection while on OMC
  - Require amputation resulting from failure or lack of improvement while on OMC
  - Did not complete the antibiotic course because of an adverse event related to OMC

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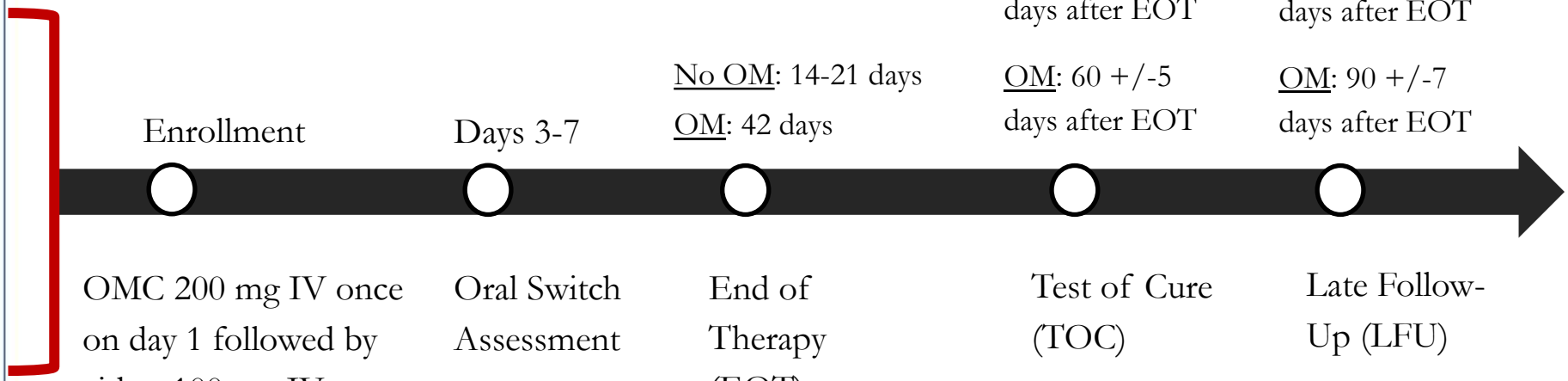
Methods



OMC 200 mg IV once on day 1 followed by either 100 mg IV or 300 mg PO once daily for 14-21 days without OM or 42 days with OM

Oral Switch Assessment

End of Therapy (EOT)

Test of Cure (TOC)

Late Follow-Up (LFU)

Other Antibiotics allowed for up to 48 hours prior to enrollment

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Results

Characteristics	Patients (N=13)
Age (years), median (IQR)	58 (55, 64)
Race, n (%)	
Black	4 (30.7)
White	9 (69.3)
Weight (kg), median (IQR)	90.3 (75.7, 103)
Weight >100 kg, n (%)	5 (38.5)
Body mass index (kg/m^2), median (IQR)	29.9 (27, 32.6)
Body mass index > 30 (kg/m^2), n (%)	7 (53.8)
Hemoglobin A1c, median (IQR)	9.2 (8.3, 10.7)
Chronic heart failure, n (%)	1 (7.7)
Chronic kidney disease, n (%)	6 (46.2)
Hyperlipidemia, n (%)	8 (61.5)
Hypertension, n (%)	11 (84.6)
Peripheral arterial disease, n (%)	5 (38.5)
Solid organ transplant – kidney, n (%)	1 (7.7)

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Results

Infection Characteristics	Patients (N=13)
Acute osteomyelitis, n (%)	8 (61.5)
Abscess, n (%)	2 (15.4)
Systemic inflammatory response syndrome, n (%)	6 (46.2)
White blood cell count, median (IQR)	12.7 (10.9, 15.8)
C-reactive protein, median (IQR)	79 (21, 165)
Erythrocyte sedimentation rate, median (IQR)	105 (73, 126)

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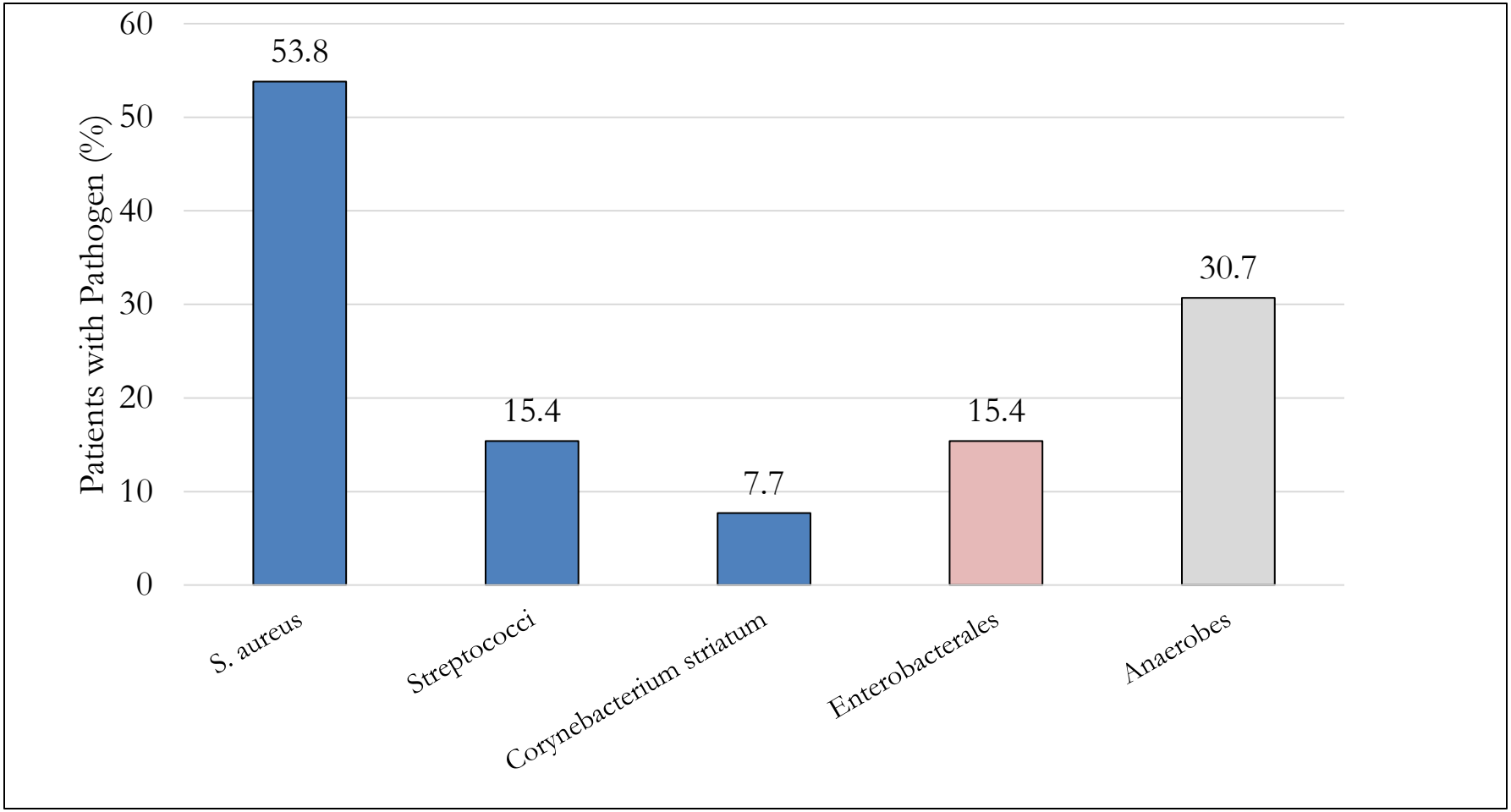
Results - Microbiology



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Results

- A total of 9/13 (69.2%) completed therapy with OMC
  - 4/13 (30.8%) stopped therapy due to identification of OMC resistant pathogen
  - *S. aureus* (n=2);[a] *Proteus mirabilis* (n=1); *Proteus vulgaris* (n=1)

Outcomes	Patients (N=9)
Time to PO switch, median (IQR)	4 (2, 5)
Hospital length-of-stay, median (IQR)	8 (11, 14)
Hospital readmission (90 days), n (%)	2 (22.2)

[a] *S. aureus* isolate susceptibilities precluding completion of therapy

	Isolate 1 MIC (interpretation)	Isolate 2 MIC (interpretation)
MSSA/MRSA	MSSA	MSSA
Tetracycline	>8 (Resistant)	≤4 (Susceptible)
Tigecycline	≤0.25 (Susceptible)	≤0.25 (Susceptible)
Omadacycline	1 (Intermediate)	1 (Intermediate)

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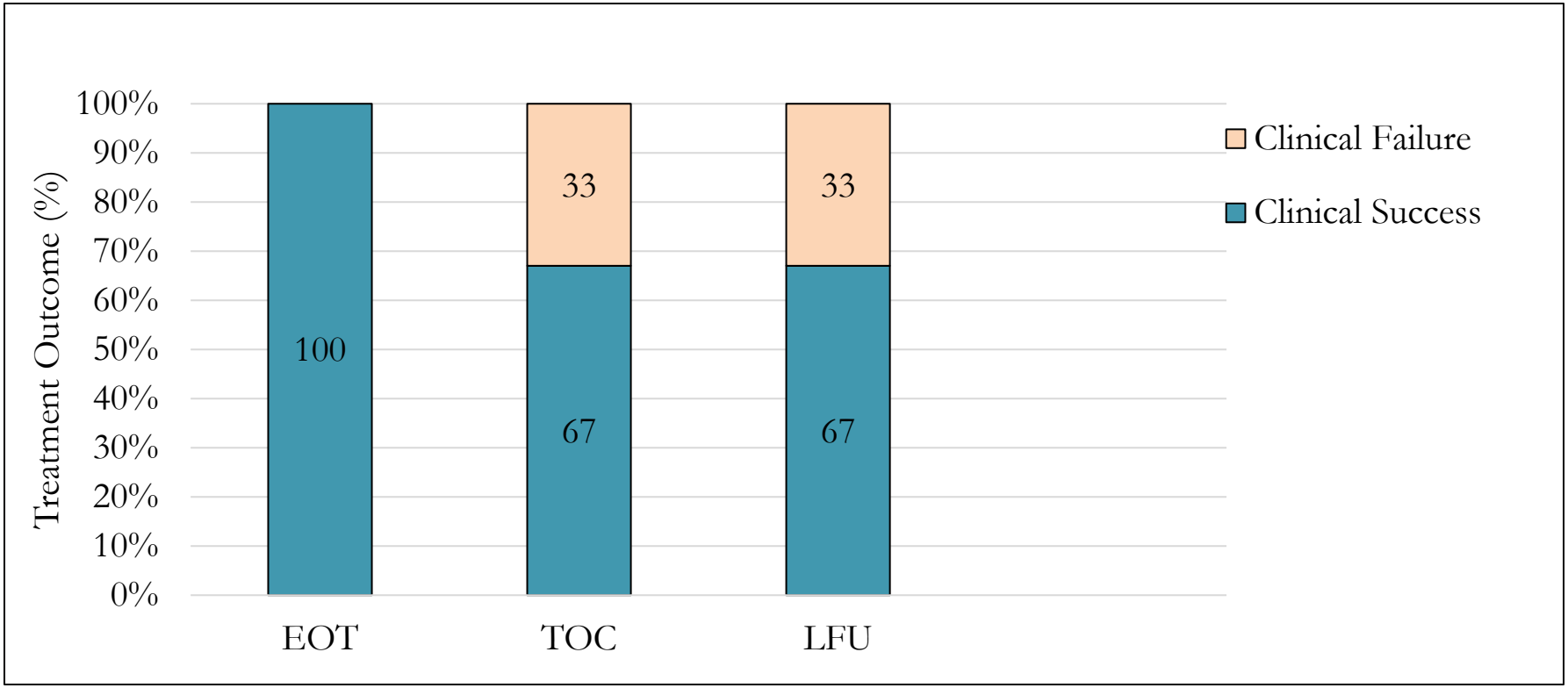
Results – Clinical Outcomes[a]



[a] Clinical outcomes data for patients completing OMC treatment

[b] Reasons for clinical failure: insufficient improvement requiring additional antibiotic treatment during subsequent hospitalization, MRSA bacteremia following treatment, *Proteus mirabilis* infection at same site following treatment and requiring additional antibiotic therapy

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Results - Safety[a]

Outcomes	Patients (N=13)
Adverse drug effect, n (%)	2 (15.4)
Serious adverse drug effect, n (%)	0 (0)
Acute kidney injury, n (%)	0 (0)
C. difficile infection, n (%)	0 (0)

[a] Safety data for all patients receiving OMC treatment

- Adverse drug effects reported
  - Nausea
  - Burning sensation at injection site

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Conclusions

- Early experience with omadacycline suggests it may be a potential treatment for some patients with DFI including acute OM
- Continued investigation for this indication is warranted

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Future Directions

- Ongoing prospective enrollment
- Historical control matching (2:1)
- Further evaluation of *S. aureus* isolates testing susceptible to tetracycline but intermediate or resistant to omadacycline

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