Real-World Experience with Omadacycline for Nontuberculous Mycobacterial and MDR/XDR Gram-Negative Infections: A Multicenter Evaluation

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Background

- Omadacycline (OMC) is an aminomethylcycline antibiotic in the tetracycline class that has been Food and Drug Administration-approved for acute bacterial skin and skin structure infections and community-acquired pneumonia[1]
- OMC has been shown to have potent *in vitro* activity against a broad-spectrum of Gram-positive and Gram-negative organisms, as well as Nontuberculous mycobacteria (NTM)[2-3]
- Due to its spectrum of activity and availability as an oral and intravenous agent, off-label utilization of OMC has been increasing[4]
- We aimed to evaluate the real-world effectiveness and safety of OMC for a variety of infections and pathogens

Methods

- A multicenter, retrospective, observational study conducted at six geographically distinct medical centers in the United States between January 2020 to June 2020
- We included patients ≥18 years of age who received ≥72 hours of OMC for any indication and/or pathogen
- Primary outcome was clinical success, which was defined as a lack of 30-day (non-NTM) or 90-day (NTM) mortality or microbiologic recurrence and absence of therapy alteration
- Secondary objectives were to evaluate reasons for OMC utilization and incidence of potential adverse effects attributable to OMC
- The CLSI breakpoints were applied for minimum inhibitory concentration (MIC) interpretation
- Multidrug-resistance (MDR) was defined as non-susceptibility to ≥1 agent in ≥3 antimicrobial categories, while extensively drug-resistance (XDR) was defined as non-susceptibility to ≥1 in all but ≤2 antimicrobial categories[5]
- Time-dependent outcomes were assessed following OMC initiation for mortality and following OMC discontinuation (if applicable) for microbiologic recurrence
- Microbiologic recurrence was defined as culture positive for the same organism isolated from index culture
- Descriptive statistics were utilized for analysis using SPSS statistics, IBM SPSS software, version 26.0 (IBM Corp., Armonk, NY).

Results

Table 1. Baseline/Clinical Characteristics for Gram-negative (A) and NTM (B) Infections

A

Characteristics	Results (n=7)
Age, years, median (IQR)	49.0 (40.5-55.5)
Male	6 (85.7)
African American	4 (57.1)
Body mass index, mg/kg^2, median (IQR)	24.4 (22.2-24.8)
Comorbid Conditions	----
-Hemiplegia	3 (42.9)
-Heart Failure	1 (14.3)
-CKD	1 (14.3)
-None	2 (28.6)
Insurance	----
-Medicare	4 (57.1)
-Private entity	3 (42.9)
Treatment Setting	----
-Strictly Outpatient	5 (71.4)
-Inpatient, then outpatient	2 (28.6)
Infection Source	---
-Bone/joint	5 (71.4)
-IAI	2 (28.6)
OMC duration, days, median (IQR)	14.0 (13.0-48.5)

B

Characteristics	Results (n=11)
Age, years, median (IQR)	57.0 (54.0-61.0)
Female	6 (54.5)
Caucasian	10 (90.9)
Body mass index, mg/kg^2, median (IQR)	24.0 (20.3-29.5)
Comorbid Conditions	----
-Interstitial lung disease	5 (45.5)
-COPD	3 (27.3)
-None	2 (18.2)
Insurance	---
-Private entity	6 (54.5)
-Medicare	3 (27.3)
Treatment Setting	---
-Strictly Outpatient	10 (90.9)
-Inpatient, then outpatient	1 (9.1)
Infection Source	---
-Nodular bronchiectatic	3 (27.3)
-Fibrocavitary	3 (27.3)
-Bone/joint	2 (18.2)
OMC duration, months, median (IQR)	6.4 (4.5-9.0)

Data reported as n (%) unless otherwise specified

CKD: chronic kidney disease;
IAI: intra-abdominal infection;
COPD: chronic obstructive pulmonary disease

Figure 1. Clinician Reasoning for Omadacycline Utilization

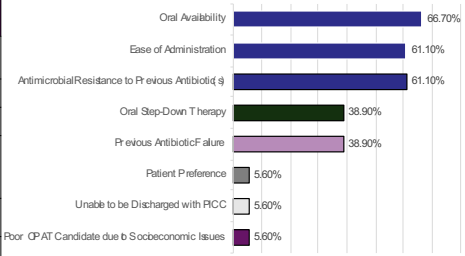
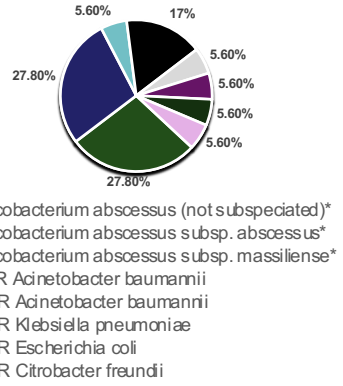


Figure 2. Isolated Bacterial Isolates



**erm* gene genotyping was conducted in 8/11 (72.7%) of *M. abscessus* isolates, with 6/8 (75.0%) of isolates exhibiting functional *erm* gene expression

Results

Table 3. Clinical and Safety Outcomes

Outcomes	Result (Non-NTM: n=7; NTM: n=11)
Overall Composite Clinical Success (n=18)	15 (83.3)
Composite Clinical Success (Gram-negative; n=7)	5 (71.4)
-30-day mortality	0
-30-day microbiologic recurrence*	1 (14.3)
-Alteration of therapy*	2 (28.6)
Composite Clinical Success (NTM; n=11)	10 (91.1)
-90-day mortality	0
-90-day microbiologic recurrence	1 (9.1)
-Alteration of therapy	0
Overall Adverse Effect	3 (16.7)
Gastrointestinal (N/V/D)	1 (5.6)
Serum creatinine increase	1 (5.6)
AST/ALT increase	1 (5.6)

*One patient experience both 30-day recurrence and alteration of therapy

Conclusions

- OMC was effective and well-tolerated in this small sample for a variety of infections caused by various pathogens, including *M. abscessus* and MDR/XDR *A. baumannii* and *Enterobacteriaceae*
- Larger prospective real-world studies are essential to further confirm our early clinical findings

References

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Disclosures

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