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Efficacy and Safety of Omadacycline Oral Step-Down Therapy Following Bloodstream Infection: A Real-World Descriptive Study

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Background

- Recent data support the efficacy of oral step-down therapy for the treatment of bloodstream infections following clinical improvement on intravenous therapy[1]
- Tetracyclines are generally avoided in BSI due to high volumes of distribution and conflicting clinical data
- Omadacycline (OMC) is an oral and intravenous aminomethylcycline tetracycline antibiotic approved in the United States for the treatment of adults with acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia (CABP)[2]
- Omadacycline has a mean volume of distribution approximately threefold lower than that of tigecycline[3,4]

Study objective: To assess the real-world safety and efficacy of omadacycline following bloodstream infections

Methods

Study design
- Multicenter, retrospective, real-world descriptive study of patients treated with omadacycline between 2018 and 2023

Inclusion
- Age ≥ 18 years
- Received omadacycline for ≥72 hours
- Received omadacycline within 60 days of onset of bloodstream infection

Outcomes
- **Primary outcome:** Clinical success (no persistence or re-emergence of infectious signs/symptoms within 14 days of discontinuation of omadacycline)
- **Secondary outcomes**: 90-day all-cause mortality, 90-day microbiologic recurrence, 90-day hospital readmission

Analysis
- Continuous variables are reported as mean (standard deviation [SD]) or median (interquartile range [IQR]), and categorical variables as frequencies. Analyses were performed using SPSS version 30.0 (IBM Corp, Armonk, NY, USA)

Results

Table 1: Baseline characteristics, n (%) (n=14)

Age, mean (SD)	63.6 (20.0)
Male sex	7 (50.0)
Race/ethnicity	
White	9 (64.3)
Black	3 (21.4)
Asian	1 (7.1)
Hispanic/Latino	1 (7.1)
BMI (kg/m^2), median (IQR)	26.7 (22.5 – 32.0)
Baseline SCr (mg/dL), median (IQR)	1.05 (0.75 – 1.67)
APACHE II score, median (IQR)	10.0 (3.8 – 12.0)
Charlson Comorbidity Index, median (IQR)	6.5 (3.8 – 7.3)
Diabetes with end organ damage[a]	3 (21.4)
Peripheral vascular disease	3 (21.4)
Moderate to severe liver disease[b]	3 (21.4)
Malignancy	2 (14.3)
Moderate to severe CKD[c]	2 (14.3)
Immunocompromised	2 (14.3)
Neutropenia (ANC or WBC < 500)	2 (14.3)
Length of hospital admission (days), median (IQR)	16.0 (6.0 – 22.5)

[a]Presence of retinopathy, neuropathy, nephropathy, or brittle diabetes. [b]Portal hypertension or cirrhosis. [c]KDOQI CKD stages 3-5 or GFR < 60 mL/min or on chronic dialysis. Abbreviations: ANC, absolute neutrophil count; APACHE, acute physiology and chronic health evaluation; BMI, body mass index; CKD, chronic kidney disease; ICU, intensive care unit; IQR, interquartile range; SCr, serum creatinine; SD: standard deviation; WBC, white blood cell count.

Table 2: Infection characteristics, n (%) (n=14)

OMC susceptibility[a]	
Susceptible[b]	5 (35.7)
Resistant	0 (0.0)
Not tested	9 (64.3)
Polymicrobial index bacteremia	4 (28.6)
Source control intervention	8 (57.1)
Incision and drainage	3 (21.4)
Debridement	2 (14.3)
Amputation	1 (7.1)
Intravenous catheter removal	1 (7.1)
Invasive device removal	1 (7.1)

[a]Determined using breakpoints established by the United States Food and Drug Administration (FDA). For *Stenotrophomonas maltophilia*, minocycline breakpoints were utilized.
[b]OMC susceptibility performed in *Enterococcus faecium* (n=3), *Stenotrophomonas maltophilia* (n=1), and *Escherichia coli* (n=1)
Abbreviations: OMC: omadacycline

Figure 1: Organisms isolated in index blood culture

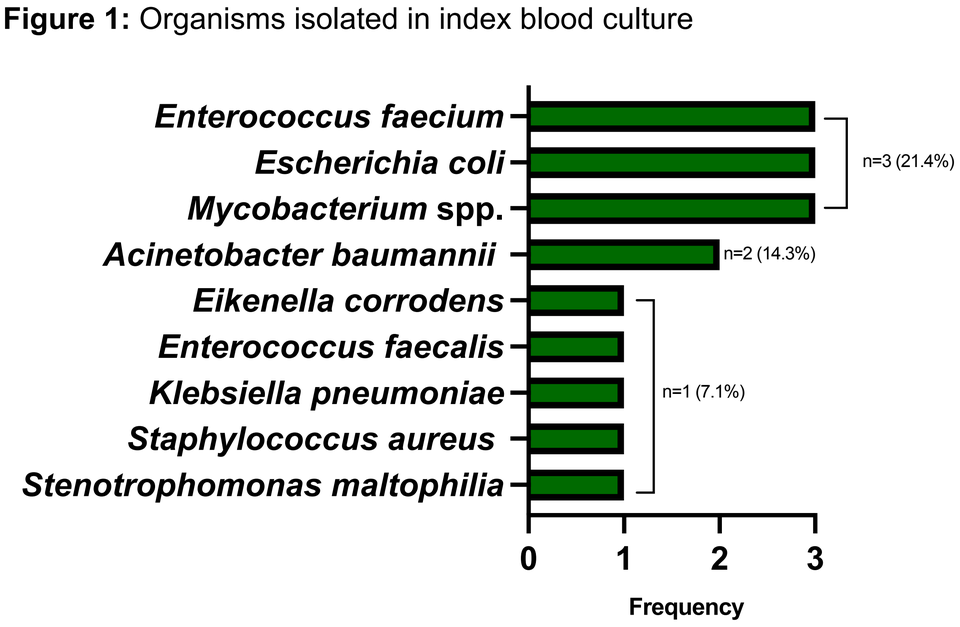


Figure 2: Source of index bacteraemia

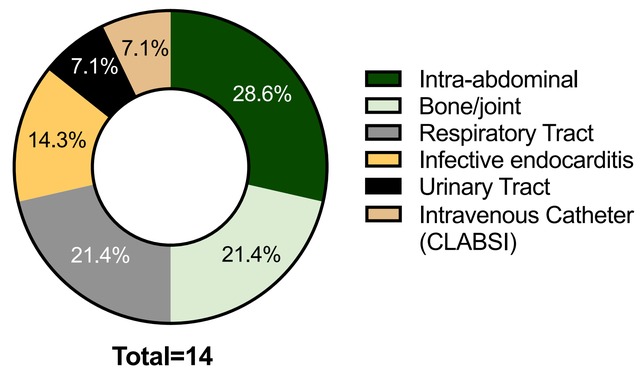


Figure 3: Reason for omadacycline utilization

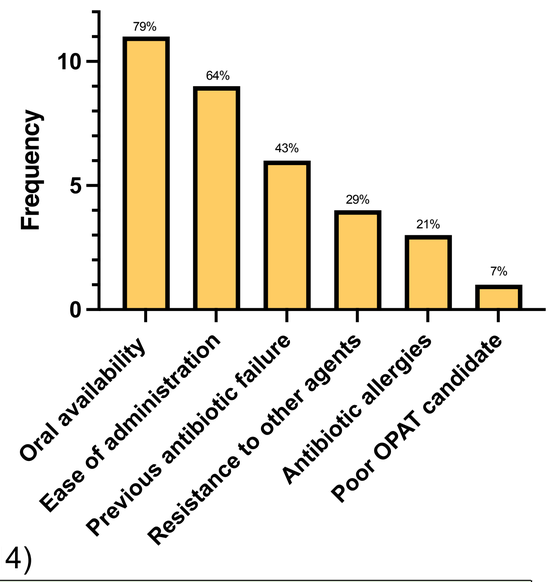
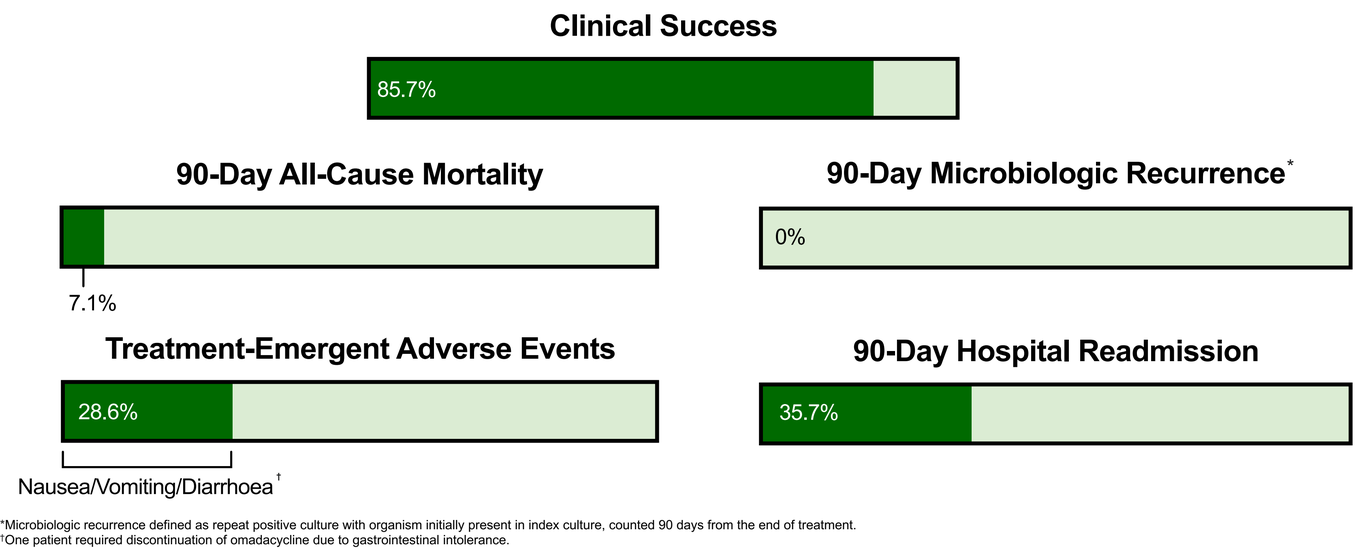


Table 3: Treatment characteristics, n (%) (n=14)

Treatment setting	
Inpatient	4 (28.6)
Ambulatory	10 (71.4)
Received OMC loading dose	6 (42.9)
OMC maintenance dose	
300 mg PO daily	13 (92.9)
450 mg PO daily	1 (7.1)
Time to OMC from index blood culture (days), median (IQR)	33.4 (12.2 – 44.6)
Length of OMC therapy (days), median (IQR)	81.0 (20.8 – 307.2)
Combination therapy ≥ 48 hours with OMC	8 (57.1)
Amikacin, systemic	2 (14.3)
Amikacin, inhaled	1 (7.1)
Amoxicillin/clavulanate	1 (7.1)
Azithromycin	1 (7.1)
Cefepime	1 (7.1)
Ciprofloxacin	1 (7.1)
Imipenem	1 (7.1)
Levofloxacin	1 (7.1)
Tedizolid	1 (7.1)
Tigecycline[a]	1 (7.1)

[a]For treatment of non-tuberculous mycobacterium infection. Patient received four drug regimen of IV amikacin, imipenem, tigecycline, and omadacycline for a total of 281 days.
Abbreviations: OMC: omadacycline; IQR: interquartile range.

Figure 4: Clinical outcomes



*Microbiologic recurrence defined as repeat positive culture with organism initially present in index culture, counted 90 days from the end of treatment.
†One patient required discontinuation of omadacycline due to gastrointestinal intolerance.

Conclusions

- This study described the real-world efficacy and safety of omadacycline as oral therapy following the treatment of bloodstream infections.
- Further investigations with larger sample sizes are required to corroborate these findings

References: 1. Sutton JD et al. *JAMA Netw Open.* 2020;3(10):e2020166. 2. Gallagher JC. *Clin Infect Dis.* 2019;69:S1-5. 3. Rodvold KA et al. *Clin Infect Dis.* 2019;69(Suppl 1):S16-S22. 4. Muralidharan G et al. *Antimicrob Agents Chemother.* 2005;49(1):220-9.
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