Oritavancin for the treatment of complicated gram-positive infection in persons who inject drugs

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Abstract

Background: Treatment of complicated infections in persons who inject drugs (PWID) and patients experiencing homelessness poses a unique challenge to clinicians. Long-acting lipoglycopeptide antibiotics, such as oritavancin, may facilitate extended courses of outpatient intravenous therapy while avoiding the need for central lines, improving compliance and thus increasing the chance of clinical cure.

Methods: Retrospective chart review of adult PWID who received at least one dose of oritavancin for a gram-positive infection between 1/1/17 and 6/30/19 at a large safety net hospital.

Results: Twenty three PWID received 24 courses of at least one dose of oritavancin for a gram-positive infection; 16 were experiencing homelessness at the time of diagnosis. Methicillin resistant Staphylococcus aureus (MRSA) was the most common infecting pathogen and bone or joint the most frequent infection site. Nineteen encounters resulted in clinical cure, including 5 whose conditions improved despite non-adherence to their prescribed regimen. Three patients experienced a non-favorable outcome. Two patients experienced mild adverse drug reactions that did not interfere with therapy; no patients died while on therapy.

Conclusion: Oritavancin may be a clinically effective treatment option for the management of complicated gram-positive infections in PWID and patients experiencing homelessness. Further studies should be performed to validate these results.

Introduction

Effective strategies to improve serious infection treatment outcomes in non-adherent patients are lacking and complicated by injection drug use (IDU) and homelessness. Up to 70% of persons who inject drugs (PWID) experience at least 1 bacterial skin infection in their lifetime, but it is difficult to accurately describe the true breadth of the problem as a recent study found that more than half of all IDU-associated bacterial infections (ABIs) may be unrecorded [1–4]. Adding further complexity to treatment, the prevalence of homelessness among PWID has been reported to be as high as 59% [5]. Homelessness significantly increases the risk of relapse in those who have previously stopped injecting, promoting initial and recurrent IDU-ABIs [6].

Complex socioeconomic factors often limit the ability to administer first-line therapies. Outpatient parenteral antibiotic therapy (OPAT) is controversial due to concerns of inappropriate central line access and treatment failure risk [7]. Eaton et al. challenged this apprehension by employing a 9-point risk assessment to successfully administer OPAT to PWID, reducing average length of stay from 42 to 22 days [8].
However, after providers form trusting relationships with patients, home infusion services may still refuse to provide therapy to patients they deem high risk. When oral antibiotics are therapeutically appropriate, drug interactions (e.g. with rifampin), cost and repeated non-adherence may preclude use of this route. Thus, at times patients must remain admitted for multiple weeks to complete therapy, or leave against medical advice (AMA) and risk the potentially life-threatening consequences of inadequately treated infections. Additionally, prolonged admissions delay patient enrollment in outpatient rehabilitation programs, which in turn slows substance use disorder (SUD) treatment.

Oritavancin (ORI) is a long-acting lipoglycopeptide (LAL) that covers a broad range of gram-positive pathogens including methicillin-resistant and methicillin susceptible *Staphylococcus aureus* (MRSA, MSSA), *Streptococcus* species, and vanA-mediated vancomycin-resistant *Enterococcus* species and was FDA approved in 2014 for the treatment of acute bacterial skin and skin structure infections (ABSSSI) as a one-time 3 hour 1200 mg intravenous (IV) infusion [9]. Its long terminal half-life, large volume of distribution and penetration to bone and joint spaces make it appealing for treatment of deep seated infections that require IV therapy, but in whom this route may not be feasible in the outpatient setting. At our institution, ORI was selected as the formulary LAL due to patient assistance programs that were more relevant to our patient population and a lack of evidence demonstrating clinical superiority of dalbavancin (DAL), the other LAL, over oritavancin.

Hennepin County Medical Center (HCMC) is the largest safety net hospital in the state of Minnesota and a Level 1 Trauma and Burn destination caring for patients across the upper Midwest. Providers at our 484 bed institution routinely face challenges providing IV therapy for patients afflicted with serious mental health issues, SUD and homelessness. In 2018, HCMC providers treated over 130 cases of *Staphylococcus aureus* bacteremia, of which approximately one-third were attributed to IDU. Additionally, during 2018 alone, at least 10% of patients were readmitted with recurrent *S. aureus* bloodstream infections primarily due to non-adherence and/or re-infection. In an effort to provide adequate treatment courses, single- or multiple-dose regimens of ORI have been employed in select patients at our institution. We describe our clinical experience utilizing ORI for the treatment of complicated gram-positive infections in adult PWID, many of whom experienced homelessness.

### Methods

We performed a retrospective cohort analysis of PWID treated with ORI for gram-positive infection. Patients were included if they were 18 years of age or older and received at least one dose of ORI for the treatment of documented or presumed gram-positive endocarditis, bone/joint infection, bacteremia, or skin and soft tissue infection between 1/1/17 and 6/30/19. For patients who received more than one course of oritavancin during the study period, each course was assessed separately for inclusion. All patients in this study were evaluated by an infectious diseases (ID) physician as prescription of ORI is restricted to ID physicians at our institution due to its high drug acquisition cost and broad gram-positive spectrum of activity; pharmacy does not release ORI unless authorized by ID. Infection indication was identified by the ID consult note. Susceptibility testing for ORI was not performed on any isolates, but was inferred from vancomycin susceptibility based on previous studies’ findings [10]. Patients who received concomitant antibiotics were included in the analysis; their additional therapy is included in Table 1. For multiple dose regimens, doses were administered once weekly until completed. Patients were excluded if more than 14 days elapsed between administered doses, their care was palliative in nature, they were pregnant or a prisoner at the time of treatment, or had declined use of their information for research purposes.

Both authors independently reviewed each case and made a determination of outcome. Results were categorized as clinical cure or failure based on manual chart review. Outcomes were further described as incomplete adherence/cure (I/C) or incomplete adherence/failure (I/F) if a dose was missed based on the initially planned regimen. Clinical cure was defined as resolution of signs and symptoms of infection (fever, white blood cell count, C-reactive protein) without need for additional antimicrobial therapy following completion of ORI, excluding long term suppressive antibiotics for patients with retained hardware. Failure was defined as progression of gram-positive infection and need for alternative therapy. Outcomes were reviewed out to 60 days after the final ORI infusion.

Adverse drug reactions (ADRs) were collected up to 6 weeks from the last dose or up to the point that a patient was lost to follow up. All notes available in the institution’s electronic medical record (EMR) were examined for mention and description of ADRs. Outside hospital records were reviewed if available at the time of review by way of Epic’s Care Everywhere. The Naranjo Adverse Drug Reaction Probability Scale (NADRPS) was
| #  | Sex, Age range, BMI | Additional Social History | Infection Location, Source Control Achieved? | Pathogen(s) | Gram-Positive Antibiotics Prior to ORI (days) | Abx DOT before ORI | Concurrent antibiotics with ORI | ORI Doses Planned (received) | Outcome |
|----|-------------------|--------------------------|----------------------------------------------|-------------|-----------------------------------------------|-------------------|-------------------------------|-------------------------------|---------|
| 1  | M, 40–49, 22.9    | Homeless                 | BSI; SSTI Yes                                | MRSA        | VAN × 8                                       | 8                 | None                          | 1200 × 1 (1) CC               |          |
| 2  | M, 40–49, 30.1    | Homeless                 | Joint Yes                                    | MRSA + Enterobacter | VAN × 1                                      | 1                 | LVX - Enterobacter             | 1200 × 2 (2) CC               |          |
| 3  | M, 40–49, 20.9    | Homeless ETOH            | SSTI N/A                                     | Unknown      | None                                          | 0                 | None                          | 1200 × 1 (1) CC               |          |
| 4  | F, 40–49, 23.6    | Homeless ETOH            | SSTI N/A                                     | MRSA         | VAN × 2                                       | 2                 | None                          | 1200 × 1 (1) CC               |          |
| 5  | M, 30–39, 24.5    | ETOH                     | Joint Yes                                    | MSSA; GAS    | CRO × 2, VAN × 1                              | 2                 | None                          | 1200 × 1 (1) CC               |          |
| 6  | F, 50–59, 39.5    | Homeless ETOH            | BSI; SSTI Yes                                | MSSA         | VAN + Tzp × 2, NAF × 3, CFZ × 2               | 25                | None                          | 1200 × 2 (1) VC               |          |
| 7  | F, 40–49, 196     | Homeless ETOH            | BSI; Bone Yes                                | MSSA         | LVX × 1, VAN + Tzp × 2, CFZ × 24              | 25                | None                          | 1200 × 2 (2) CC               |          |
| 8  | M, 40–49, 22.8    | Homeless ETOH            | BSI; Bone No                                 | MRSA         | VAN × 6, DAL × 1                             | 13                | None                          | 1200 × 1 (1) CC               |          |
| 9  | M, 40–49, 32.2    | Homeless                 | Joint; HW Yes                                | Strep mitis; Strep oralis | Tzp × 3, VAN × 4, CRO × 8, LVX × 8–17 | 36                | None                          | 1200 × 1 (1) CC               |          |
| 10 | F, 30–39, 26.5    | BSI; IE No               |                                | MSSA         | VAN + Tzp × 2, NAF × 2, CFZ × 16–23, VAN + Tzp × 2, CFZ × 6 | 30                | None                          | 1200 × 1 (1) CC               |          |
| 11 | M, 50–59, 26.0    | BSI; IE Bone No          |                                | MRSA         | VAN × 9, CPT + DAP × 14, *none × 4 days*, CPT × 5, DAP × 22 | 47                | None                          | 1200 × 2 (2) F                |          |
| 12 | F, 30–39, 32.5    | Homeless ETOH            | BSI N/A                                     | MSSA         | CRO × 2, VAN × 3, CFZ × 15, None × 2 CFZ × 2 | 20                | None                          | 1200 × 1 (1) CC               |          |
| 13 | M, 40–49, 34.1    | Homeless ETOH            | BSI N/A                                     | MSSA         | VAN × 3, CFZ × 7, CRO × 1                    | 10                | None                          | 1200 × 1 (1) LTFU             |          |
## Table 1 Antibiotic course and clinical outcomes of patients who inject drugs treated with oritavancin (Continued)

| #   | Sex, Age range, BMI | Additional Social History | Infection Location, Source Control Achieved? | Pathogen(s) | Gram-Positive Antibiotics Prior to ORI (days) | Abx DOT before ORI | Concurrent antibiotics with ORI | ORI Doses Planned (received) | Outcome |
|-----|---------------------|---------------------------|----------------------------------------------|-------------|---------------------------------------------|-------------------|--------------------------------|--------------------------------|---------|
| 14  | M, 30–39, 28.9      | Homeless ETOH             | BSI; SSTI N/A                                | MRSA        | VAN × 15 DAP × 1                            | 16                | None                           | 1200 × 2 (2)                   | LTFU    |
| 15  | M, 60–69, 44.6      | Joint; HW No              | MRSA, MRSE                                  |             | VAN × 6 DOX × 5                             | 13                | None                           | 1200 × 1 (1) 800 × 5 (5)       | CC      |
| 16  | F, 20–29, 24.2      | Homeless ETOH             | Bone No                                     | MRSA        | VAN × 1                                     | 1                 | None                           | 1200 × 2 (2)                   | I/C     |
| 17  | M, 20–29, 22.1      | Homeless                   | Bone; HW No                                 | MSSA        | VAN + TZP × 2 CFZ × 2                        | 3                 | RIF                            | 1200 × 2 (2)                   | CC      |
| 18  | M, 30–39, 19.6      | Homeless ETOH             | Bone; SSTI Yes                              | MRSA        | VAN × 5 DOX × 2                             | 7                 | DOX                            | 1200 × 2 (1)                   | I/C     |
| 19  | F, 30–39, 36.2      | BSI; Bone No              | MRSA                                         | VAN × 9     | 9                                            | 13                | None                           | 1200 × 1 (1) 800 × 3 (1)       | I/C     |
| 20  | F, 20–29, 23.0      | Bone No                    | MRSA                                         | VAN × 13    | 4                                            | None                           | 1200 × 2 (1)                   | I/F     |
| 21  | M, 20–29, 23.4      | BSI; SSTI N/A              | MSSA                                         | VAN × 2 CFZ × 4 | 4                | None                           | 1200 × 2 (1)                   | I/C     |
| 22  | M, 40–49, 32.2      | Joint Yes                  | MRSA                                         | VAN × 2     | 2                                            | RIF                            | 1200 × 1 (1) 800 × 5 (5)       | CC      |
| 23  | M, 30–39, 22.8      | ETOH                       | BSI N/A                                     | MRSA        | VAN × 6                                     | 6                 | None                           | 1200 × 1 (1)                   | F       |
| 24  | M, 60–69, 18.0      | Homeless                   | Bone No                                     | MRSA        | DAP × 4                                     | 4                 | None                           | 1200 × 1 (1) 800 × 3 (3)       | CC      |

**Heading abbreviations:** Abx antibiotic, BMI body mass index, DOT days of therapy  
**Social history abbreviations:** ETOH ethanol  
**Infection location abbreviations:** BSI bloodstream infection, HW hardware, IE infective endocarditis, SSTI skin and soft tissue infection  
**Pathogen abbreviations:** GAS group A strep, MRSA methicillin resistant staph aureus, MSSA methicillin susceptible staph aureus, MRSE methicillin resistant staph epidermidis  
**Antimicrobial abbreviations:** CFZ cefazolin, CRO ceftriaxone, FEP cefepime, CPT ceftaroline, DAL dalbavancin, DAP daptomycin, DOX doxycycline, LVX levofloxacin, LZD linezolid, MTZ metronidazole, MEM meropenem, NAF nafcillin, ORI oritavancin, TZP piperacillin-tazobactam, RIF rifampin, SXT trimethoprim-sulfamethoxazole, VAN vancomycin  
**Treatment evaluation outcomes:** CC clinical cure, F failure, I/C incomplete (patient did not adhere to intended regimen but appears to have been cured), I/F incomplete adherence and clinical failure, LTFU lost to follow up
employed to determine the probability the ADR was attributable to oritavancin [11].

This study was reviewed and approved by the Human Subjects Research Committee of the Hennepin Healthcare Research Institute.

Results
A list of all 37 encounters in which a patient received one or more doses of oritavancin within the specified time frame supplied the starting point for review. Thirteen encounters were excluded; the primary reason for exclusion was no known history of injection drug use \( (n = 9) \); other reasons included a diagnosis outside of the inclusion criteria \( (n = 2) \) and greater than 14 days elapsed between administered doses \( (n = 2) \). Twenty four courses, prescribed to 23 different patients, were included in the analysis. One patient (numbers 2 and 22 in Table 1) received 2 separate courses of treatment, with the second course administered 20 months after the final dose of the initial course. At the time of infection diagnosis, 16/24 (67%) encounters were for patients experiencing homelessness. Most patients were male (16/23, 70%) and the average age was 41 years old (range 22–64). The median body mass index (BMI) was 24.3; 8/24 (33%) were considered obese with a BMI of greater than 30. Sixteen of 23 patients (70%) had a history of significant psychiatric illness defined as schizophrenia, bipolar disorder, major depressive disorder, schizoaffective disorder or borderline personality disorder. Nine (39%) patients left AMA during care, most due to homelessness. Most patients were male (16/23, 70%) and the average age was 41 years old (range 22–64). The median body mass index (BMI) was 24.3; 8/24 (33%) were considered obese with a BMI of greater than 30. Sixteen of 23 patients (70%) had a history of significant psychiatric illness defined as schizophrenia, bipolar disorder, major depressive disorder, schizoaffective disorder or borderline personality disorder. Nine (39%) patients left AMA during care, most due to homelessness.

MRSA was the most common infecting pathogen occurring in 14/24 (58%) of encounters. Bone or joint was the most frequent infection location occurring in 14/24 (58%) encounters, and the spine was the most common site of bone infection (4/9, 44%). Half of all encounter patients (12/24, 50%) were bacteremic with either MRSA (6/12, 50%) or MSSA (6/12, 50%). Of the two patients diagnosed with infective endocarditis, both involved native tricuspid valves and neither underwent surgical valve replacement.

Patients received a median of 9.5 days of effective gram-positive therapy based on susceptibility, when available, prior to ORI initiation. Number of ORI doses ranged from 1 to 6; initial doses were universally 1200 mg. Subsequent dosing was at the discretion of the clinician and was always administered weekly. Eleven patients received more than one dose. Of those, 4 received 800 mg doses and 7 received 1200 mg doses. The majority of doses were administered in the outpatient infusion center. Twelve patients received 1 dose as inpatient; 3 of these patients received additional outpatient doses thereafter. Twenty three of 24 encounters utilized ORI for therapy completion, having received prior gram-positive treatment for their infections. Patient 8 was the only patient to also receive DAL; the patient received a single dose at an outside hospital prior to transferring care to our institution.

Clinical cure was achieved in 19/24 (79%) encounters and failure in 3/24 (13%); 2/24 (8%) were lost to follow-up after their last infusion. The two patients lost to follow-up were not noted to have any signs of worsening of infection at their final infusion, however, documentation was limited at each of those visits and thus no assessments can be made. Of the 4 patients with osteomyelitis involving the spine, 3/4 (75%) experienced clinical cure and 1/4 (25%) treatment failure. Of the 6 patients who had incomplete adherence to the planned regimen, cure was seen in 5 patients and failure in 1. Three patients received only the first of two planned doses; including the patient deemed to be a clinical failure in the group with partial adherence. The remaining 3 patients with partial adherence experienced an unexpected delay of 14 days between doses, but received all planned doses (3 to 5 doses total).

Two patients (8%) experienced ADRs within 6 weeks of receiving ORI. One patient presented to the Emergency Department (ED) 5 days after receiving ORI complaining of sharp, non-radiating abdominal pain, however, the patient eloped prior to evaluation. Four days after her ED visit she was admitted to the jail medical ward, which is overseen by our institution, without documentation of infection, pain or further antibiotics. One patient experienced an infusion-related reaction becoming visibly flushed and complaining of a headache 20 min into the first dose. After an infusion pause, the remaining drug was administered without symptom recurrence and she received a second dose 1 week later without issue. Employing the NADRPS harm scale, the former patient’s ADR was classified as possible and the latter as probable.

Three patients (patients 11, 21, and 23) were determined to have failed therapy with ORI, with 1 of 3 possibly related to incomplete adherence. Patient 11 was being treated for MRSA (vancomycin minimum inhibitory concentration (MIC) 2, confirmed by two methods, Vitek and Microscan) bacteremia with vertebral osteomyelitis and was initially bacteremic for 14 consecutive days. Source control was unable to be achieved due to location of fluid collections and proximity to spinal cord. After blood culture clearance, he was discharged and returned for daily infusions of high-dose daptomycin (>10 mg/kg) but was transitioned to weekly ORI 3 weeks later due to loss of IV
P. aeruginosa was cultured from the pre-ORI blood cultures and post-ORI intraoperative cultures, had a vancomycin MIC of 1 μg/mL via Vitek.

Discussion

We describe our real-world experience using ORI for the treatment of complicated gram-positive infections in PWID, many of whom were also experiencing homelessness. Despite having limited treatment options for patients that are noncompliant with oral therapies or otherwise not candidates to receive IV antibiotics, alternative therapeutic regimens are often discredited or avoided due to a lack of robust clinical evidence. Although more data are emerging regarding LAL use for complicated infections, studies specific to ORI use in vulnerable populations remain limited.

When comparing our study to others that included outcomes specific to persons who use drugs (PWUD), it is important to note that each investigation evaluated outcomes differently. In an effort to compare findings despite methodological differences, data specific to PWUD in similar studies are outlined in Table 2. Overall, our rates of clinical cure (79%) and failure (13%) were similar to other reports.[12–16]

A comparable study focused on complicated infections in vulnerable patients treated with LALs but outcomes were specific to DAL.[16]. Although ORI and DAL are similar, it is important to highlight their differences to further appreciate our study’s contribution to existing literature. While both boast an exceptionally long half-life (t½) based on population pharmacokinetic analyses, ORI’s terminal t½ is slightly longer, 10.2 vs. 8.5 days and the plasma protein binding of DAL is 93% as compared to 85% with ORI. Oritavancin has a large volume of distribution (Vd) (1.25 L/kg) indicating extensive tissue distribution, whereas DAL’s smaller Vd (0.11 L/kg) indicates it primarily remains in the plasma compartment.[9,17]. Although we acknowledge the presence of these and other differences, the clinical impact is unclear as both drugs have been associated with successful outcomes in the treatment of complicated infections.[12,13,14–16]. In addition, clinical scenarios exist where DAL may be preferred, such as for genitourinary sources as < 5% of ORI is recovered unchanged in the urine compared to 33% of DAL.[9,17].

Our study is not without limitations. All but one patient received ORI as secondary therapy and all bacteremic patients received the drug following clearance of blood cultures, so no determination may be made regarding the utility of this agent for primary therapy. Patients received varying regimens for similar indications and thus it is not possible to evaluate a specific regimen for a given indication. Finally, generalizability may be limited due to the single center design of the study.

Conclusion

In conclusion, we report our real-world experience using ORI in PWID primarily for treatment completion of complicated gram-positive infections. We acknowledge the delicate balance between antimicrobial stewardship efforts and financial considerations in providing a high cost, broad spectrum agent to ensure patients receive a safe, effective regimen that avoids extended hospitalizations and incomplete treatment courses. We believe ORI may be considered in patients who require prolonged therapy courses but are unable to receive OPAT, including PWID and patients experiencing homelessness. Randomized controlled studies should be conducted to determine optimal dosing regimens for off-label indications and to compare LAL therapy to standard of care.
| Citation, year, LAL(s) | Patients | Organisms | Indications | Number of doses | Results | Outcomes & Definitions |
|------------------------|----------|-----------|-------------|-----------------|---------|-----------------------|
| Stewart et al. 2017 [12] ORI | • Total: 10 | PWID | ▪ MSSA: 2  
▪ GBS: 1  
▪ Enterococci: 1 | PWID | ▪ GBS: BSI + IE  
▪ E. faecalis BSI  
▪ BSI + bone/joint  
▪ BSI + psoas abscess | PWID | ▪ 1 dose = 4/4 | PWID (n = 4) | • Cure: 1/4  
▪ Failure: 2/4  
▪ LTFU: 1/4 | • Clinical cure: resolution of all clinical signs/symptoms of infection (febrile, normalization of WBC/ESR), no additional infection-related hospital admissions, no additional antibiotic therapy required for the initial indication treated with ORI, infection clearance with sterile blood cultures where indicated.  
• Failure: worsening of current infection or new/recurrent signs or symptoms of infection requiring a change in antibiotics or additional antibiotic therapy.  
• Not clinically evaluable: patients who were LTFU.  
• ADRs: based on reporting by prescribing physician and follow-up with patients after administration (timeframe not specified). |
| Morrisette et al. 2019 [14] DAL + ORI | • Total: 56 | PWUD | ▪ MSSA: 8 (47%)  
▪ MRSA: 5 (29%)  
▪ E. faecalis: 1 (6%)  
▪ VRE: 1 (6%)  
▪ Other: 2 (12%) (unknown or mixed) | PWUD | ▪ ABSSSI: 6 (35%)  
▪ OM: 6 (35%)  
▪ IE: 3 (18%)  
▪ Other: 2 (12%) | PWUD | ▪ Median = 1 (IQR 1–2) | PWUD (n = 17) | • Success: 13/17 (77%)  
▪ Failure: 1/17 (6%)  
▪ Unknown: 3/17 | • Clinical success: no further clinical or microbiological evidence of active infection (resolution of signs/symptoms related to bacterial infection and clearance of cultures if applicable) without need for further gram-positive therapy due to clinical worsening within 60 days of last dose of LAL.  
• Clinical failure: lack of clinical response, relapse with the primary infection within 60 days of last LAL dose, need for alternative gram-positive therapy due to clinical worsening during LAL therapy, or death.  
• ADRs: any potential ADR occurring during or within 7 days of LAL infusion. |
| Bork et al. 2019 [15] DAL | • Total: 28 | All patients | All patients | All patients | Substance Abusers (n = 19) | Primary outcome: proportion of patients with... |
### Table 2: Comparison of long acting lipoglycopeptide studies that included persons who use drugs (Continued)

| Citation, year, LAL(s) | Patients | Organisms | Indications | Number of doses | Results | Outcomes & Definitions |
|------------------------|----------|-----------|-------------|----------------|---------|-----------------------|
| **PWID: 16/19 (57%) All patients** | Males: 26 (93%) Median age: 52 years (IQR 21.5) | MSSA: 6 (21%) CoNS: 4 (14%) Mixed GP: 8 (29%) Unknown: 5 (18%) | Endovascular: 6 (21%) BSI: 4 (14%) Other: 5 (18%) | Site 1: 1.5 Site 2: 5.5 | Success: 10/13 (77%) Failure: 3/13 (23%) LTFU: 6/19 | 30 day clinical cure (30 days after planned DAL course). **Secondary outcomes:** 90 day clinical cure; ADRs **Clinical cure:** composite of resolution of clinical signs of infection (erythema, swelling, pain), afibrile; normalization of CRP/ESR/WBC source control; resolution of radiographic signs of infection and/or microbiologic clearance of organisms. If readmitted for infection then considered failure. **Clinical failure:** due to (1) death, (2) intolerance or AE, (3) lack of access to subsequent DAL, (4) lack of source control, (5) worsening signs of infection or relapse. **ADRs:** anything likely to be associated w/ DAL based on specific ADE and temporal relationship with DAL (specific timeframe not provided). |
| **PWUD: 28 (88%) Homeless: 15 (47%) All patients (PWUD)** | Males: 23 (72%) Average age: 38 years (IQR 25–50) | MSSA: 28 (88%) | IE-9 | 1 dose = 22 2 doses = 7 3 doses = 2 5 doses = 1 | Cure: 34/73 (466%) Improvement: 34/73 (466%) | **Clinical response:** patient had a follow-up visit within 1 year at HMC or a neighboring hospital, linked through a common EMR, without evidence for an ongoing or relapsed infection, regardless of whether they completed the intended course of therapy. **LTFU:** patient did not have a subsequent encounter to evaluate their infection at either the ID clinic or another institution linked via EMR within 1 year. **All-cause readmission:** hospital readmission within 30 days from previous discharge. **ADRs:** not defined/reported. |
| **PWUD: 75 safety analysis 73 efficacy analysis** | MSSA: 23 (31.5%) MRSA: 13 (17.8%) | ABSSSI: 25 Diabetic foot infection: 3 | 1–32 | n = 73 Cure: 34/73 (466%) Improvement: 34/73 (466%) | **Clinical outcomes** were reviewed within 28 days of the end of therapy. Safety outcomes were reviewed within 28 days of the end of therapy. |
| Citation, year, LAL(s) | Patients | Organisms | Indications | Number of doses | Results | Outcomes & Definitions |
|------------------------|----------|-----------|-------------|----------------|---------|------------------------|
| PWID: 10 (13.3%)       |          | CoNS: 4 (5.8%) | IE: 4 Line infection: 2 | Failure: 5/73 (6.8%) | PWID (n = 10) | reviewed out to 30 days after ORI. |
| PWID: 24 (100%)        |          | MSSA: 8 (33%) | Other: 5 OM/Septic arthritis: 10 | Cure or improvement: 7/10 (70%) |         | Clinical cure: resolution of signs and symptoms of infection without the need for further treatment after the completion of ORI. |
| PWID: 24 (100%)        |          | Streptococci: 2 | Pneumonia: 5 Prosthetic device infection: 3 |         |         | Clinical improvement: recovery from infectious signs and symptoms with the need for subsequent gram-positive therapy after the completion of the ORI. |
| PWID: 24 (100%)        |          | Unknown: 1 | Sepsis: 5 Surgical wound infection: 12 |         |         | Clinical failure: progression of infectious signs and symptoms and need for alternative gram-positive therapy during the ORI course. |
| Total = 24             |          | PWUD        | Bone/Joint: 14 | PWUD (n = 24) | Success: 19/24 (79%) |         |
| PWUD: 24 (100%)        |          | MSSA: 8 (33%) | Bone: 9 | - I/C = 5 |         | Outcomes were reviewed out to 60 days after the final ORI infusion. |
| PWUD: 24 (100%)        |          | Streptococci: 2 | Spine: 5/9 | Failure: 3/24 (13%) | - I/F = 1 | Clinical cure: resolution of signs and symptoms of infection (fever, WBC, ESR) without need for additional antimicrobial therapy following completion of ORI (excluding long term suppressive antibiotics for retained hardware). |
| PWUD: 24 (100%)        |          | Unknown: 1 | Joint: 5 | - LTFU: 2/24 (8%) |          | Failure: progression of infection and need for alternative therapy. |
| PWUD: 24 (100%)        |          | PWUD        | BSi: 12 IE: 2 | Completed therapy: 19/24 (79%) |         | Incomplete cure/failure: incomplete adherence to therapy. |
| PWUD: 24 (100%)        |          | PWUD        | Patients may be counted in multiple categories |         |         | LTFU: no notes or data available in EMR after final ORI dose. |
| PWUD: 24 (100%)        |          | PWUD        | 1 dose = 13 |         |         | ADRs: collected up to 6 weeks from last dose or until LTFU. |
| PWUD: 24 (100%)        |          | PWUD        | 2 doses = 7 |         |         | |
| PWUD: 24 (100%)        |          | PWUD        | 3 doses = 1 |         |         | |
| PWUD: 24 (100%)        |          | PWUD        | 4 doses = 1 |         |         | |
| PWUD: 24 (100%)        |          | PWUD        | 6 doses = 2 |         |         | |

**Abbreviations:** ABSSSI acute bacterial skin and skin structure infection, BSI bloodstream infection, CC clinical cure, CoNS coagulase-negative staphylococci, DAL dalbavancin, EMR electronic medical record, ESR erythrocyte sedimentation rate, GBS Group B Streptococcus, GP gram-positive, HW hardware, IE infective endocarditis, I/C incomplete adherence with cure, I/F incomplete adherence with failure, IQR interquartile range, LTFU lost to follow-up, MSSA methicillin-susceptible Staphylococcus aureus, MRSA methicillin-resistant Staphylococcus aureus, OM osteomyelitis, ORI oritavancin, PWID persons who inject drugs, PWUD persons who use drugs, VRE vancomycin-resistant Enterococcus faecium, WBC white blood cell count.
Abbreviations
PWID: Persons who inject drugs; MRSA: Methicillin resistant Staphylococcus aureus; IDU: Injection drug use; ABIs: Associated bacterial infections; OPAT: Outpatient parenteral antibiotic therapy; AMA: Against medical advice; SD: Substance use disorder; ORI: Oritavancin; LAL: Long-acting lipoglycopeptid; MSSA: Methicillin susceptible Staphylococcus aureus; ABSSSI: Acute bacterial skin and skin structure infections; IV: Intravenous; DAL: Dalbavancin; HCMC: Hennepin County Medical Center; ID: Infectious diseases; I/C: Incomplete adherence/cure; I/F: Incomplete adherence/failure; ADRs: Adverse drug reactions; EMR: Electronic medical record; NADR: Adverse drug reactions. Clarification for using vancomycin as a surrogate to infer oritavancin susceptibility. Antimicrob Agents Chemother. 2016;60(3):3174–7.  https://doi.org/10.1128/AAC.03029-15.

Authors’ contributions
AA and HR both made substantial contributions to the conception and design of the work, the analysis and interpretation of data and equally contributed to the development of the manuscript. AA and HR have both approved the submitted version and have agreed both to be personally accountable for their contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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Availability of data and materials
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The study was reviewed and approved by the Hennepin Healthcare Research Institute, study # 19–4633.

Consent for publication
Not applicable.

Competing interests
On behalf of both authors, the corresponding author states that there is no conflict of interest.

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