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BRIEF REPORT

# Use of a Standardized Dalbavancin Approach to Facilitate Earlier Hospital Discharge for Vulnerable Patients Receiving Prolonged Inpatient Antibiotic Therapy

**Axel A. Vazquez Deida,[1] Katherine C. Shihadeh,[1] Candice R. Preslaski,[1] Heather L. Young,[2,3] David L. Wyles,[2,3] and Timothy C. Jenkins[2,3]**

[1]Pharmacy Department, Denver Health Medical Center, Denver, Colorado, USA, [2]Division of Infectious Diseases, Department of Medicine, Denver Health Medical Center, Denver, Colorado, USA, and [3]Division of Infectious Diseases, Department of Medicine, University of Colorado School of Medicine, Aurora, Colorado, USA

Twenty-seven patients receiving prolonged inpatient antibiotic therapy for a serious bacterial infection received a single dose of dalbavancin 7–10 days before the planned end date to facilitate earlier hospital discharge. Eighty-one percent met criteria for clinical success, 7% experienced a potential adverse event, and 182 hospital days were averted.

**Keywords.** dalbavancin; persons experiencing homelessness; persons who use injection drugs; *Staphylococcus aureus*; substance use disorder.

## INTRODUCTION

Vulnerable populations including people who inject drugs (PWID), people experiencing homelessness, and those with alcohol use disorder are at increased risk of developing serious bacterial infections such as infective endocarditis (IE) and osteomyelitis (OM). Injection drug use–related IE hospitalizations have been on the rise since 2000, with a doubling in prevalence in the last decade [1–3]. Many patients with these infections are not considered candidates for outpatient parenteral antimicrobial therapy (OPAT) and are therefore kept in the hospital to complete prolonged parenteral antibiotic courses [4]. Extended hospitalizations for completion of antibiotic therapy in patients who are otherwise stable for discharge lead to negative consequences for patients, including feelings of isolation, financial stress, inability to maintain family responsibilities, and the potential for nosocomial infections while straining the finite resources of hospitals. Although recent randomized trials have demonstrated that oral antibiotics are effective for bone and joint infections and endocarditis, these studies have included few patients with substance use disorders, and concerns about nonadherence may limit use of oral therapy in this population [5, 6]. A recent retrospective study showed similar readmission rates among PWID with invasive infections who completed inpatient parenteral therapy and those who received partial oral therapy, but published evidence with oral therapy in this population remains scarce [7]. Novel care models to successfully treat these patients while shortening durations of hospitalization are urgently needed.

Parenteral lipoglycopeptides, such as dalbavancin, have a long half-life and are approved for single-dose treatment of acute bacterial skin and skin structure infections (ABSSSIs). Off-label use of dalbavancin for more complicated, deep-seated infections such as IE and OM has been supported by an increasing number of case series, especially among vulnerable populations who are not suitable candidates for OPAT [8–14]. However, to date, there has been only 1 published randomized trial in which a multidose dalbavancin regimen was as effective as standard of care for osteomyelitis [13]. In February 2018, we implemented a standardized approach in which a single dose of dalbavancin was given 7–10 days before the planned end date of therapy for vulnerable patients receiving prolonged inpatient parenteral antibiotic therapy for bloodstream infection, IE, or OM, thus allowing an earlier hospital discharge with no further therapy needed. In this report, we describe the clinical outcomes, adverse events, and cost avoidance associated with this standardized treatment approach.

## METHODS

### Setting and Population

This was a retrospective observational case series conducted at Denver Health Medical Center in Denver, Colorado. Denver Health Medical Center is a 525-bed, academic, tertiary care, level 1 trauma center that serves as the primary safety net institution for the city and county of Denver. Adult patients ≥18 years of age hospitalized from February 1, 2018, to November 30, 2019, with a gram-positive infection in which a single dose of dalbavancin was used to complete the planned antibiotic course were included. Patients who received dalbavancin in the outpatient setting were excluded. Refer to the Supplementary Data for our specific institutional approach for use of dalbavancin.

### Data Collection

Data extracted from the electronic health record included patient demographics, medical comorbidities, microbiology,

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Correspondence: Axel A. Vazquez Deida, PharmD, Pharmacy Department Denver Health Medical Center, 790 Delaware St, MC 0056, Denver, CO 80204 (axel.vazquez.deida@gmail.com).

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indication for antibiotics, antibiotics administered, hospital length of stay, time to follow-up, and dalbavancin-related adverse events. Hospital readmissions, emergency department or urgent care visits, and deaths occurring within 90 days of the dalbavancin dose were recorded.

#### Definitions

Clinical failure was defined as the need for additional antibiotic therapy related to the primary infection or clinical or microbiological evidence of active infection within 90 days of the dalbavancin dose. Cases not meeting criteria for clinical failure were classified as clinical success. For the primary analysis, patients lost to follow-up, defined as having no clinical encounters within 90 days of the dalbavancin dose, were classified as clinical failure. Potential dalbavancin-related adverse events were defined as hypersensitivity, dermatologic, gastrointestinal, hepatic, hematologic, or other reactions documented in the electronic health record within 7 days of the dose. Potential adverse events were adjudicated by 3 study authors (A.V.D., K.S., H.Y.) to determine relatedness to dalbavancin.

#### Statistical and Cost Analyses

The projected hospital length of stay (LOS) was the date of admission to the planned end date of antibiotic therapy as documented by the Infectious Diseases service. For each hospitalization, hospital days averted were determined by subtracting the actual LOS from the projected LOS. Estimated cost avoidance was determined by multiplying the total hospital days averted by the estimated cost of 1 hospital day ($1800) minus an estimated $3000 for each dalbavancin dose.

#### Ethical Approval

This programmatic evaluation was reviewed by the Quality Improvement Review Committee of Denver Health and Hospital Authority (authorized by the Colorado Multiple Institutional Review Board) and deemed not to constitute human subjects research.

## RESULTS

Of 28 patients who received an inpatient dose of dalbavancin, 27 met criteria for inclusion. One patient was excluded because treatment was planned to be completed with a second outpatient dose of dalbavancin and therefore did not meet the institutional criteria for use being evaluated. The median age (interquartile range [IQR]) was 49 (40–54) years. A large proportion of patients were PWID (67%), were experiencing homelessness (56%), or had alcohol use disorder (22%). Twenty-five (93%) were bacteremic at hospital admission. Other baseline and clinical characteristics are shown in Table 1.

The most common indications for the prolonged inpatient antibiotic course included uncomplicated *Staphylococcus aureus* bacteremia (26%), right-sided IE (26%), and bone or joint infection with concurrent bacteremia (15%). *S. aureus* was isolated in all 27 patients; 48% were methicillin-resistant *S. aureus* (MRSA). Four cases (15%) involved a polymicrobial infection.

**Table 1. Baseline and Clinical Characteristics (n = 27)**

| | |
|---|---|
| Age, median (IQR), y | 49 (40–54) |
| Male | 17 (63) |
| White/Caucasian | 25 (93) |
| Experiencing homelessness | 15 (56) |
| Substance use disorder[a] | |
| People who inject drugs | 18 (67) |
| Noninjection drug use | 7 (26) |
| Alcohol use disorder | 6 (22) |
| Concomitant diseases | |
| Hepatitis C virus infection | 13 (48) |
| HIV infection | 4 (15) |
| Diabetes mellitus | 2 (7) |
| Cirrhosis | 1 (4) |
| Chronic kidney disease | 0 |
| Bacteremia | 25 (93) |
| Infection | |
| Documented bacteremia | |
| Uncomplicated bacteremia | 7 (26) |
| Complicated bacteremia | 4 (15) |
| Right-sided infective endocarditis | 7 (26) |
| Bone or joint infection with bacteremia | 4 (15) |
| Pneumonia with bacteremia | 2 (7) |
| Left-sided infective endocarditis | 1 (4) |
| Bone or joint infection without bacteremia | 2 (7) |
| Microorganisms | |
| Methicillin-susceptible *Staphylococcus aureus* | 12 (44) |
| Methicillin-resistant *Staphylococcus aureus* | 11 (41) |
| Polymicrobial | 4 (15) |
| MRSA and group A streptococci | 1 |
| MSSA and *Streptococcus anginosus* | 1 |
| Methicillin-resistant *Staphylococcus epidermidis* and group A streptococci | 1 |
| MRSA, *Enterococcus durans* or *hirae*, and alpha-hemolytic streptococci | 1 |
| Days of antibiotic therapy before dalbavancin administration, median (IQR) | 21 (8.5–35) |
| Hospital length of stay, actual, median (IQR) | 26 (10–34.5) |
| Hospital days averted per patient, median (IQR) | 7 (6–7) |
| 90-d inpatient re-admission, all-cause | 4 (15) |
| 90-d inpatient re-admission due to initial infection | 1 (4) |
| 90-d re-presentation to the emergency department/urgent care, all-cause | 10 (37) |
| 90-d re-presentation to the emergency department/urgent care due to initial infection | 0 |
| Follow-up appointment with either ID clinic, primary care provider, or other outpatient clinic to assess infection | 13/25 (52) |
| Loss to follow-up | 4 (15) |
| Potential dalbavancin-related adverse events | 2 (7) |
| 90-d mortality, all-cause | 0 |
| 90-d mortality due to initial infection | 0 |
| Clinical success | 22 (81) |

Data reported as No. (%) unless otherwise noted.

Abbreviations: ID, infectious diseases; IQR, interquartile range; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.

[a]Categories are not mutually exclusive.

Dalbavancin was administered a median (IQR) of 21 (8.5–35) days after clearance of blood cultures or source control was achieved. The median length of hospital stay (IQR) was 26 (10–34.5) days.

Of the 27 patients, 2 planned to follow up at a clinic outside of the Denver Health system. Of the remaining 25 patients, 52% followed up in the infectious diseases clinic, with a primary care provider, or in another clinic in which the initial infection was assessed. Within the 90-day follow-up period, 37% of patients had an emergency department or urgent care visit, and 15% were re-hospitalized. Only 1 of these encounters was likely due to recurrence of the primary infection. Four (15%) patients, including 2 with planned follow-up outside of Denver Health, had no documented clinical encounters and were classified as lost to follow-up. Overall, 22 (81%) patients met criteria for clinical success. When excluding the 4 patients lost to follow-up, 96% achieved clinical success. Two patients experienced adverse effects potentially related to dalbavancin within 1 day of dose administration. Both reported self-resolving dizziness, and 1 reported nausea requiring ondansetron. Additional details of the cases are presented in Table 2.

The total number of hospital days averted was 182 (median [IQR], 7 [6–7]). The projected LOS cost was $1 467 000, and the actual LOS plus dalbavancin drug cost was $1 220 400. Thus,

**Table 2. Case Descriptions**

| Patient | Experiencing Homelessness | Substance Use Disorders | | | Indication | Pathogen | Culture Source | Days of Antibiotic Therapy Before Dalbavancin[a] | Inpatient Re-admission, Reason | Emergency Department or Urgent Care Representation, Reason | Clinical Failure or Loss to Follow-up |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Noninjection Drug Use | Injection Drug Use | Alcohol Use Disorder | | | | | | | |
| 1 | Yes | No | No | Yes | Osteomyelitis, foot | MRSA | Bone | 35 | No | Yes, foot pain with no evidence of infection | No |
| 2 | Yes | No | No | Yes | Osteomyelitis, hand | MRSE, Group A Streptococci | Bone | 34 | Yes, hand pain, no evidence of infection and alcohol intoxication | Yes, alcohol intoxication with delirium | No |
| 3 | Yes | Yes | No | Yes | Complicated bacteremia with septic superficial thrombophlebitis | MSSA | Blood | 21 | No | No | No |
| 4 | Yes | Yes | No | No | Complicated bacteremia with pneumonia | MRSA, Group A Streptococci | Blood, sputum | 21 | No | No | No |
| 5 | Yes | No | Yes | Yes | Bacteremia with septic arthritis, skin abscesses, pyomyositis, and osteomyelitis of the humerus complicated by septic pulmonary emboli concerning for tricuspid valve endocarditis | MRSA | Blood, joint synovial fluid, soft tissue, bone, wound abscess | 35 | Yes,[b] MRSA bacteremia with shoulder osteomyelitis | Yes, fatigue and pain due to assault | Clinical failure |
| 6 | No | No | Yes | No | Complicated bacteremia with psoas abscess | MSSA | Blood, wound abscess | 27 | No | No | Lost to follow-up |
| 7 | Yes | No | Yes | No | Bacteremia with left upper extremity abscess | MSSA, *S. anginosus* | Blood, wound abscess | 14 | No | Yes, upper respiratory infection | No |
| 8 | No | No | Yes | No | Bacteremia with osteomyelitis, left shoulder | MSSA | Blood | 35 | No | No | No |
| 9 | Yes | No | Yes | No | Bacteremia with neck abscess, septic thrombophlebitis, and concern for L4-L5 septic joint facet and epidural phlegmon | MRSA | Blood, wound abscess | 28 | No | Yes, labial abscess | No |
| 10 | Yes | No | Yes | No | Tricuspid valve endocarditis | MSSA | Blood | 8[c] | No | No | Lost to follow-up |
| 11 | Yes | No | Yes | No | Uncomplicated bacteremia with gluteal abscess | MSSA | Blood | 9 | No | No | Lost to follow-up |

**Table 2. Continued**

| Patient | Experiencing Homelessness | Substance Use Disorders | | | Indication | Pathogen | Culture Source | Days of Antibiotic Therapy Before Dalbavancin[a] | Inpatient Re-admission, Reason | Emergency Department or Urgent Care Representation, Reason | Clinical Failure or Loss to Follow-up |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Noninjection Drug Use | Injection Drug Use | Alcohol Use Disorder | | | | | | | |
| 12 | Yes | No | Yes | No | Uncomplicated bacteremia secondary to bilateral upper extremity abscesses | MRSA | Blood, wound abscess | 7 | Yes, hypoxia | Yes, phlebitis | No |
| 13 | Yes | No | Yes | No | Complicated bacteremia with probable septic pulmonary embolism and right-sided endocarditis | MRSA | Blood | 21 | No | Yes, chest pain | No |
| 14 | Yes | No | Yes | No | Uncomplicated bacteremia secondary to cutaneous abscess | MRSA | Blood | 7 | No | No | No |
| 15 | No | No | Yes | No | Tricuspid valve endocarditis with septic thrombophlebitis of right external jugular | MRSA | Blood | 35 | No | No | Lost to follow-up |
| 16 | Yes | No | Yes | No | Uncomplicated bacteremia secondary to purulent cellulitis | MSSA | Blood | 7 | No | Yes, wound check | No |
| 17 | No | Yes | Yes | No | Bacteremia with tricuspid valve endocarditis complicated by acute pacer lead infection status postextraction | MRSA | Blood | 35 | No | No | No |
| 18 | No | Yes | No | No | Bacteremia with sternomanubrial septic arthritis and osteomyelitis | MSSA | Blood | 35 | No | No | No |
| 19 | No | No | Yes | No | Uncomplicated bacteremia with cellulitis, foot | MSSA | Blood | 7 | No | No | No |
| 20 | No | No | No | Yes | Complicated bacteremia of unknown source | MSSA | Blood | 21 | No | No | No |
| 21 | No | Yes | No | No | Bacteremia with necrotizing pneumonia with pleural effusion and septic emboli suggestive of right-sided endocarditis | MRSA | Blood, sputum | 21 | No | Yes, left-sided Bell's palsy | No |
| 22 | Yes | Yes | Yes | No | Tricuspid-valve endocarditis status post–valve replacement | MRSA, *E. durans* or *hirae*, alpha-hemolytic Streptococci | Blood | 35 | No | No | No |
| 23 | No | No | No | No | Uncomplicated bacteremia secondary to abscess, left buttock | MSSA | Blood | 6 | No | No | No |
| 24 | Yes | No | Yes | No | Bacteremia with aortic valve endocarditis status post–valve replacement complicated by multiple septic emboli | MRSA | Blood | 35 | Yes, presyncope and dizziness, urinary tract infection | No | No |
| 25 | No | No | No | Yes | Bacteremia of unknown source | MSSA | Blood | 14 | No | No | No |
| 26 | No | Yes | Yes | No | Uncomplicated bacteremia secondary to cellulitis, left lower extremity | MSSA | Blood | 7 | No | Yes, upper respiratory tract infection | No |
| 27 | No | No | Yes | No | Bacteremia with tricuspid valve endocarditis complicated by septic emboli likely secondary to abscess, right upper extremity | MRSA | Blood | 35 | No | No | No |

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; MRSE, methicillin-resistant *Staphylococcus epidermidis*; MSSA, methicillin-susceptible *Staphylococcus aureus*.

[a]After clearance of blood cultures or appropriate surgical source control.

[b]Patient was readmitted 60 days after dalbavancin administration with MRSA bacteremia and shoulder osteomyelitis in the setting of continued injection drug use. During the initial encounter, the patient had received 50 days of parenteral antibiotics (35 days with regards to when source control was achieved). The patient did not show up to the infectious diseases clinic appointment but did show up to a primary care provider appointment, and there was documentation of no concern of infection recurrence. The patient also had multiple emergency department encounters between the discharge date and the subsequent readmission, with normal laboratory tests and imaging not suggestive of infection.

[c]The patient had received 2 weeks of parenteral therapy at an outside hospital before being transferred to Denver Health Medical Center.

the overall estimated cost avoidance was $246 600 (average of $9600 per patient).

## DISCUSSION

To our knowledge, this is the first description of outcomes associated with a standardized approach for use of dalbavancin to facilitate earlier hospital discharge for patients with a serious bacterial infection. Administration of dalbavancin 7–10 days before the planned end date of therapy led to clinical success in 81% of cases, appeared to be safe, and averted about 7 hospital days per patient. This was associated with an estimated cost avoidance of $9600 per patient. Only 1 case was deemed to be a true clinical failure due to recurrent bacteremia and osteomyelitis, but this occurred 2 months after dalbavancin administration in the setting of continued injection drug use, making it difficult to determine if this was a recurrence of the initial infection or reinfection.

There have been an increasing number of reports of off-label dalbavancin use for the treatment of serious infections caused by gram-positive organisms [8–14]. These reports have been heterogeneous with respect to the types of infections treated, timing of dalbavancin dosing, and number of doses given. Our standardized approach represented a relatively conservative off-label use of dalbavancin in that patients were medically stable, nearing the end of their planned antibiotic course, and otherwise ready for discharge when the dose was given. This case series is also unique in that all patients had bloodstream or deep-seated infection (93% were bacteremic); several previous studies included a large proportion of patients of less severe infections such as ABSSSIs or bone or joint infection without bacteremia [10, 13]. The high rate of clinical success and low rate of potential dalbavancin-related adverse events were notable and support the ongoing use of this approach to shorten hospitalizations in these vulnerable patients.

There are several limitations to this report. First, given that this is a description from a single center, the results are not generalizable. Second, the sample size was small, which limits the evaluation of both safety and effectiveness. Third, the retrospective assessment of clinical success was limited to follow-up care in our system and relied on documentation in the medical record. Fourth, we did not perform a formal cost analysis of the program; the results presented are only general estimates. Finally, it is unknown whether any clinical failures were related to the use of dalbavancin or would have also occurred if treatment was completed with parenteral therapy.

In summary, our experience shows that a standardized approach to administer dalbavancin 7–10 days before the planned end date of therapy for vulnerable patients with serious gram-positive infections receiving prolonged inpatient therapy appears to be safe and effective, facilitates earlier hospital discharge, and results in cost avoidance as compared with completion of the full parenteral antibiotic course in the hospital. Until additional clinical data are available demonstrating the safety and efficacy of multiple-dose long-acting lipoglycopeptides for bloodstream or deep-seated infections, this relatively conservative off-label treatment approach may be considered to shorten hospitalizations in vulnerable patients who may not be candidates for OPAT.

### Supplementary Data

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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