



## Brief Report

# Evaluation of Dalbavancin in Vancomycin Allergic Patients: A Case Series

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## ABSTRACT

**Purpose:** There is a paucity of data regarding dalbavancin use in patients with a vancomycin allergy because of potential cross-reactivity between the 2 glycopeptide antibiotics.

**Methods:** A retrospective medical record review was performed between February 2016 and February 2021 in patients with a listed vancomycin allergy who received dalbavancin as an outpatient infusion and had a listed vancomycin allergy in the electronic health record.

**Findings:** There were 559 unique patients during the study period who received dalbavancin as an outpatient infusion, 10 of whom had a documented vancomycin allergy in the electronic health record. Four of the 10 patients had a history of a type I IgE-mediated reaction to vancomycin, 1 patient reported delayed rash, 2 patients reported a vancomycin infusion reaction, 2 patients reported acute kidney injury, and 1 patient reported intolerance with general malaise. All 10 patients received at least 1 dose of dalbavancin with no reported adverse events.

**Implications:** This case series displays that all patients who received dalbavancin tolerated the infusion well with no adverse events reported. Dalbavancin may be a viable option for patients with a listed vancomycin allergy. (*Clin Ther.* 2022;44:e59–e63.) © 2022 Elsevier Inc.

**Key Words:** allergy, dalbavancin, outpatient parenteral antimicrobial therapy, vancomycin.

## INTRODUCTION

Dalbavancin, a semisynthetic lipoglycopeptide antibiotic structurally related to vancomycin, is indicated for treatment of acute bacterial skin and skin structure infections (ABSSSIs) caused by susceptible gram-positive bacteria and provides a full course of therapy in a single 30-minute infusion, usually as an outpatient.<sup>1</sup> Clinical use has demonstrated utility in settings necessitating prolonged antimicrobial therapy, including osteomyelitis, prosthetic joint infections, infective endocarditis, catheter-related blood stream infections, and spontaneous bacterial peritonitis.<sup>2</sup> The spectrum of activity covers gram-positive bacteria, most notably, methicillin-resistant *Staphylococcus aureus*. Antibiotics in the glycopeptide class, such as vancomycin, also contain a heptapeptide core, which raises concern for possible cross-sensitivity reactions. Because of this risk and the extended plasma  $t_{1/2}$  of dalbavancin (14.4 days), the package insert contains a warning for use in patients with a glycopeptide allergy. Conversely, dalbavancin has lipophilic side chains that reduce the risk of cross-sensitivity to vancomycin.<sup>1,3–5</sup> Successful dalbavancin use in patients with a prior hypersensitivity reaction to vancomycin has been described previously in a case report using graded challenge and a case series of patients with probable diagnosis of drug reaction with eosinophilia and systemic symptoms due to vancomycin that were

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tested *ex vivo* to dalbavancin and suggested cross-reactivity to be very low to none.<sup>4,5</sup> We report a case series of real-world patients with a vancomycin allergy documented in their electronic health record (EHR) who received at least 1 dose of dalbavancin in the outpatient setting.

## METHODS

We generated a computerized list of all adult patients who received dalbavancin at 2 distinct health systems in the southeastern United States: St. Joseph's/Candler Health System and Methodist Healthcare of Memphis. A retrospective medical record review was performed from February 2016 through February 2021 for patients who received dalbavancin as an outpatient infusion and had a listed vancomycin allergy in the EHR. Patient characteristics were collected on each patient to include age, sex, race, weight, height, white blood cell count, specifics of any allergies or adverse drug reactions, serum creatinine level, and temperature at baseline. Specifics of the dalbavancin infusion were also collected to include dose, volume, infusion rate, intravenous access, and receipt of any premedication. Reports of adverse events were evaluated by review of dalbavancin infusion in the EHR and review of any possible emergency department visits. This study only used preexisting, deidentified data and was exempt from local institutional review board review.

## RESULTS

There were 559 unique patients during the study period who received dalbavancin as an outpatient infusion, 10 of whom had a documented vancomycin allergy in the EHR. Patient characteristics and specifics of the dalbavancin infusion are summarized in the [Table 1](#). The mean age of the patients was 62.8 years, 50% were female, and a majority were White. The mean height and weight were 171.11 cm and 103.87 kg, respectively. All patients were afebrile at baseline and most had white blood cell counts within normal limits. Eight patients had normal baseline renal function and received the full 1500-mg dose, with 2 patients receiving the reduced 1125-mg dose for impaired baseline renal function. Five patients received 1 dose and 2 patients received 2 doses for treatment of cellulitis. Two patients received 2 doses for off-label treatment of osteomyelitis or bacteremia. One patient received 3 doses to treat both an abscess and bacteremia. All 5 patients who received multiple doses

received the same 1500-mg dose and tolerated each dose without issue.

Four of the 10 patients had a history of a type I IgE-mediated reaction to vancomycin, 1 patient reported delayed rash, 2 patients reported a vancomycin infusion reaction, 2 patients reported acute kidney injury, and 1 patient reported intolerance with general malaise. All 10 patients were able to tolerate dalbavancin during the recommended 30-minute infusion, with no adverse events reported with no receipt of premedication.

## DISCUSSION

This case series outlines the successful use of dalbavancin in patients with a self-reported vancomycin allergy. Vancomycin has been a long-standing first-line agent for treating ABSSSIs as well as invasive methicillin-resistant *S aureus* infections. Vancomycin-associated adverse effects, such as nephrotoxicity, have increased because of targeting of higher trough concentrations. Recent guidelines now recommend AUC monitoring to maintain efficacy while limiting acute kidney injury, but adoption of this new strategy is not universal, likely because of significant training and education needed to overhaul the current trough-based approach.<sup>6,7</sup> Long-acting lipoglycopeptides, such as dalbavancin and oritavancin, are attractive options in clinical practice because of their convenience of 1-time doses for ABSSSIs or weekly doses for off-label use for invasive gram-positive infections. ABSSSIs continue to be a common indication for hospital admission, which in certain circumstances could be managed with long-acting lipoglycopeptide therapy, avoiding hospitalization altogether. Oritavancin has no specific warning in its labeling regarding vancomycin allergies and therefore could be a potential option for patients who normally would receive glycopeptide therapy. However, depending on the formulation, a longer infusion time of between 1 and 3 hours is required compared with 30 minutes for dalbavancin. The manufacturer also recommends initiating alternative antimicrobial therapy in patients with suspected or confirmed osteomyelitis, a common off-label indication.<sup>8</sup> Oral linezolid specifically may be an attractive option for moderate to severe ABSSSIs once clinically improved with intravenous vancomycin, but a number of patients may be better candidates for lipoglycopeptide therapy to ensure medication adherence and avoid drug-drug interactions and

Table 1. Patient characteristics and dalbavancin infusion specifics.

| Patient No. | Date                        | Dose, mg | Route (intra-venous) | Infection(s)        | Age, y | Sex    | Race             | Height, cm | Weight, kg | BMI, kg/m <sup>2</sup> | SCr, mg/dL | Reaction to Vancomycin       | Other ABX Allergies/ADRs               |
|-------------|-----------------------------|----------|----------------------|---------------------|--------|--------|------------------|------------|------------|------------------------|------------|------------------------------|----------------------------------------|
| 1           | 12/15/16<br>12/28/16        | 1500     | C                    | Cellulitis          | 76     | Female | White            | 163        | 95.6       | 36                     | 1.0        | Vancomycin infusion reaction | Ceftriaxone, doxycycline, linezolid    |
| 2           | 1/1/17<br>3/4/17<br>3/13/17 | 1500     | P                    | Bacteremia, abscess | 41     | Female | White            | 173        | 104.3      | 34.9                   | 0.5        | Acute kidney injury          | Daptomycin, erythromycin, sulfonamides |
| 3           | 5/24/18                     | 1125     | C                    | Cellulitis          | 68     | Male   | Unknown          | 170        | 60.5       | 20.9                   | 4.1        | General malaise              | None                                   |
| 4           | 8/24/18                     | 1500     | P                    | Cellulitis          | 27     | Male   | White            | 175        | 121.1      | 39.4                   | 0.8        | Acute kidney injury          | None                                   |
| 5           | 7/8/19                      | 1500     | P                    | Cellulitis          | 50     | Male   | African American | 185        | 221.8      | 64.8                   | 1.1        | Anaphylaxis                  | None                                   |
| 6           | 10/10/19<br>10/16/19        | 1500     | P                    | Cellulitis          | 77     | Female | White            | 168        | 119.4      | 42.4                   | 0.8        | Vancomycin infusion reaction | None                                   |
| 7           | 1/15/20<br>1/22/20          | 1500     | C                    | Osteomyelitis       | 63     | Male   | White            | 185        | 116.6      | 34.1                   | 2.1        | Hives, rash                  | Penicillin                             |
| 8           | 12/24/17<br>1/7/18          | 1500     | C                    | Bacteremia          | 43     | Female | African American | 157.5      | 75         | 30.2                   | 0.9        | Anaphylaxis, hives           | None                                   |
| 9           | 12/18/17                    | 1500     | P                    | Cellulitis          | 95     | Female | White            | 162.6      | 61.7       | 23.3                   | 0.6        | Delayed rash                 | Sulfonamides                           |
| 10          | 9/18/18                     | 1125     | P                    | Cellulitis          | 88     | Male   | White            | 172        | 62.7       | 21.7                   | 1.8        | Hives, rash                  | None                                   |

ABX = antibiotics; ADRs = adverse drug reactions; BMI = body mass index; C = central; P = peripheral; SCr = serum creatinine.

increased adverse effects with prolonged use, such as bone marrow suppression or neurotoxicity.

Dalbavancin was well tolerated overall in clinical trials. The median duration of adverse reactions was 4 days within a pooled analysis of 7 Phase II and III studies reported by the manufacturer at the time. Within this same analysis, rash and pruritis occurred in 2.7% and 2.1% of participants receiving dalbavancin compared with 2.4% and 3.3% of participants receiving a comparator drug, which often was vancomycin.<sup>1</sup> Because of the nature of the dalbavancin registry trials involving vancomycin within the comparator, such as the DISCOVER 1 and DISCOVER 2 trials evaluating treatment for ABSSSIs, patients with known hypersensitivity to glycopeptides were excluded from the study population. A study evaluating single-dose versus 2 weekly doses of dalbavancin for ABSSSIs did not specifically exclude patients with known glycopeptide hypersensitivity. Therefore, it is not known how many of these nearly 700 patients who participated had previous vancomycin allergies. Of note, none of the patients who experienced treatment-emergent adverse events reported any hypersensitivity reaction, including rash or pruritis.<sup>9</sup> A recent study of patients with vancomycin-induced drug reaction with eosinophilia and systemic symptoms had their saliva tested for *ex vivo* response, and all 15 patients tested did not have cross-reactivity specifically to dalbavancin.<sup>10</sup> Of the 10 patients who received dalbavancin in our case series, none had immediate hypersensitivity or any report of adverse reaction, including those with documented type I IgE-mediated hypersensitivity reactions. The product labeling for dalbavancin states that because of possible cross-sensitivity with other glycopeptides, its use should be carefully monitored for signs of hypersensitivity during treatment.<sup>1</sup>

A limitation to our finding is the subjective nature of the reporting of allergies. Because of the retrospective nature of our study, we were unable to verify specifics of the patients' allergies beyond what was documented in the EHR. This is, however, the scenario commonly faced by treating clinicians. In addition, 4 of the 10 patients reported IgE-mediated immunologic pathogenesis. Evidence indicates that approximately 80% of patients specifically with a penicillin allergy lose their sensitivity in 10 years.<sup>11</sup> No data are available on whether this would be similar with an allergy to vancomycin, and how long ago these 4 patients had their reaction to vancomycin is not known.

We have previously reported a decreased length of stay and associated decreased direct costs at our institution for inpatients discharged to receive dalbavancin, while maintaining 30-day readmissions similar to published national means.<sup>12</sup> We have also reported a decrease in direct and indirect costs specifically in a self-pay population receiving dalbavancin after discharge.<sup>13</sup> A recent publication documented numerically but not statistically significant cost savings, reduced length of stay, and similar efficacy outcomes of dalbavancin compared with standard-of-care antibiotics in the management of invasive gram-positive infections.<sup>14</sup> Therefore, the presence of vancomycin allergy in the patient health record could prevent receipt of a potentially useful option if the assumption is made by prescribers to not use dalbavancin in vancomycin allergic patients.

## CONCLUSIONS

With the increase in use of dalbavancin as a viable option for hospital admission avoidance and/or early discharge, along with potential increased time required to monitor vancomycin to prevent adverse effects, these data may increase clinician confidence in the use of dalbavancin for patients with a self-reported vancomycin allergy.

## DECLARATION OF INTEREST

Bruce M. Jones has served on the speaker's bureau for AbbVie, Paratek, and La Jolla and performed consulting for Merck and Melinta. Kerry O. Cleveland has served on speaker's bureau for AbbVie, Cumberland, Merck, Paratek, and Pfizer. Christopher M. Bland has served on the speaker's bureau for Merck. The authors have indicated that they have no other conflicts of interest regarding the content of this article.

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Bruce M. Jones and Kennedy J. Freeman contributed to the literature search, table creation, study design, data collection, data interpretation, and writing of manuscript. Kerry O. Cleveland contributed to the study design, data collection and data interpretation. Christopher M. Bland contributed to the study design, data interpretation, and writing of manuscript. All authors read and approved the manuscript.

## REFERENCES

1. . *Dalvance (dalbavancin) [prescribing information]*. Madison, NJ: Allergan USA, Inc.; 2021 Accessed 22 Apr 2022.
2. Gatti M, Andreoni M, Pea F, Viale P. Real-World Use of Dalbavancin in the Era of Empowerment of Outpatient Antimicrobial Treatment: A Careful Appraisal Beyond Approved Indications Focusing on Unmet Clinical Needs. *Drug Des Devel Ther*. 2021;15:3349–3378.
3. Bambeke FV. Glycopeptides in clinical development: pharmacological profile and clinical perspectives. *Curr Opin Pharmacol*. 2004;4:471–478.
4. Ishizuka KT, Tran TK, Ayars AG, Chau AS, Chan JD. Graded dalbavancin challenge in a patient with severe vancomycin hypersensitivity reaction. *Clin Infect Dis*. 2020;70:1230–1232.
5. Nakkam N, Gibson A, Mouhtouris E, et al. Cross-reactivity between vancomycin, teicoplanin, and telavancin in patients with HLA-A\*32:01-positive vancomycin-induced DRESS sharing an HLA class II haplotype. *J Allergy Clin Immunol*. 2021;147:403–405.
6. Rybak MJ, Le J, Lodise TP, et al. Therapeutic monitoring of vancomycin for serious methicillin-resistant *Staphylococcus aureus* infections: a revised consensus guideline and review by the American Society of Health-system Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. *Clin Infect Dis*. 2020;71:1361–1364.
7. Bland CM, Crosby CM, Orvin DL, Smith SE, Jones BM. Transitioning from guideline approval to practical implementation of AUC-based monitoring of vancomycin. *Am J Health Syst Pharm*. 2021;78:1270–1272.
8. . *Orbactiv (oritavancin) [prescribing information]*. Melinta Therapeutics, Inc.; 2019 Accessed April 22, 2022.
9. Dunne MW, Puttagunta S, Giordano P, Krievins D, Zelasky M, Baldassarre J. A randomized clinical trial of single-dose versus weekly dalbavancin for treatment of acute bacterial skin and skin structure infection. *Clin Infect Dis*. 2016;62:545–551.
10. Nakkam N, Gibson A, Mouhtouris E, Kovinse K, et al. Cross-reactivity between vancomycin, teicoplanin and telavancin in HLA-A\*32:01 positive vancomycin DRESS patients sharing an HLA-Class II haplotype. *J Allergy Clin Immunol*. 2021;147:403–405.
11. Solensky R, Khan DA, Bernstein IL, et al. Drug allergy: an updated practice parameter. *Ann Allergy Asthma Immunol*. 2010;105:259–273.
12. Jones BM, Hersey R, Taylor C, Bland CM. Evaluation of dalbavancin on length of stay in acute bacterial skin and structure infections. *J Am Coll Clin Pharm*. 2019; 2:477–481.
13. Pizzuti AG, Murray EY, Wagner JL, Gaul GA, Bland CM, Jones BM. Financial analysis of dalbavancin for acute bacterial skin and skin structure infections for self-pay patients. *Infect Dis Ther*. 2020;9:1043–1053.
14. Antosz K, Al-Hasan MN, Lu ZK, et al. Clinical utility and cost effectiveness of long-acting lipoglycopeptides used in deep-seated infections among patients with social and economic barriers to care. *Pharmacy*. 2021;10:1.

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