

# Dalbavancin as Consolidation Therapy in Elderly Patients

Lucia Corral Sastre<sup>1</sup>, Anna Gallotti<sup>2</sup>, Belén Loeches-Yagüe<sup>3</sup>, Francisco Moreno-Ramos<sup>4</sup>, Alicia Rico-Nieto<sup>3</sup>

<sup>1</sup>La Paz University Hospital, Department of Geriatric, Madrid, Spain

<sup>2</sup>External Rotation Doctor, Severo Ochoa University Hospital, Madrid, Spain

<sup>3</sup>La Paz University Hospital, Infectious Disease Unit, Madrid, Spain

<sup>4</sup>La Paz University Hospital, Department of Clinical Pharmacology, Madrid, Spain

## Abstract

**Objective:** The goal of this study was to show the clinical characteristics, tolerability, safety and outcomes of geriatric patients treated with dalbavancin.

**Materials and Methods:** A retrospective and observational study was conducted in a tertiary-level hospital. All patients over 80 years old who received at least one dose of dalbavancin from June 2016 to December 2021 were included. Demographic and clinical data, microbiological, indication for dalbavancin prescription, adverse effects and evolution of the infection were collected in this study. Geriatric assessment of the patient on admission was also documented, including Barthel index and the presence of polypharmacy in their treatments.

**Results:** A total of 25 patients were included (mean age =87), mostly were female (64%), coming from their usual residence (72%), independent for the activities of daily living "ADLs" (68%) and in a hyperpolypharmacy regimen (up to 44%). Fourteen patients presented endovascular infections like endocarditis/vascular device infections (53%), the other 13 patients (47%) debuted with locomotor system infections such as joint prosthetic infection or septic arthritis. Regarding the microbiological data, 56% of the patients were infected by *streptococcus/enterococcus* group, followed by methicillin-resistant coagulase-negative *Staphylococci* (24%) and methicillin-resistant *S. aureus* (20%). No patient experienced adverse effects.

**Conclusion:** Dalbavancin is presented as an attractive antibiotic in the geriatric population due to its potential uses in complex pathologies, showing safety and efficacy in short treatments or in prolonged regimens.

**Keywords:** Clinical geriatrics, dalbavancin, early discharge, elderly patients, hospitalization, safety and toxicity

## Introduction

Dalbavancin is a long-acting lipoglycopeptide approved by European Medicines Agency since March 2015 for the treatment of acute bacterial skin and skin-structure infections (ABSSSIs) (1,2), with excellent activity against Gram-positive pathogens, including multi-drug resistant isolates. While dalbavancin is approved for ABSSSIs, it has subsequently been used in serious, Gram-positive infections requiring long-term intravenous (IV) antibiotics, such as osteoarticular and endovascular infections, showing efficacy and a favorable safety profile. Dalbavancin's pharmacokinetics characteristics, with a half-life of 14.4 days, permits an IV dosing regimen of 1.500 mg as a single infusion or 1.000 mg followed by 500 mg one week apart, without

the need of daily in-hospital IV or outpatient antimicrobial regimens (3-10).

The rapid and constant population ageing represents a worldwide challenge. For that reason, it is essential to effectively manage elderly patients with a tailor-made treatment approach. However, there are not enough evidence available to guide clinicians in the appropriate antimicrobial treatment strategy for this aged population. In addition, the high prevalence of comorbidities in the elderly and the loss of functional capacity due to prolonged hospitalization, results in complex medical treatments (11). According to the statistical data of the Continuous Register published in December 2019, there are 9,057,193 people over 65 years old in Spain, which

**Address for Correspondence:** Corral Sastre Lucia, La Paz University Hospital, Geriatric Department, Madrid, Spain

**E-mail:** lucia771@hotmail.com **ORCID:** orcid.org/0009-0004-1729-9253

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represents approximately 19% of the total national population. The population of octogenarians represents about 6.1%, while there are about 16,300 people over 100 years old (12). The number of residential health and social care institutions in Spain is estimated to be 5,500, which stands for approximately 384,251 beds with an average occupancy pattern of 81.4% (13,14). The numbers of these residential institutions, as well as the number of beds is increasing in the last years, reaching 116% more residential beds than 10 years ago (15).

Given the unique pharmacokinetic/pharmacodynamic properties of dalbavancin, this long-acting lipoglycopeptide could be an effective therapeutic strategy, in an outpatient setting, in residential health and social care institutions. Therefore, the goal of this study is to show the clinical characteristics, tolerability, safety, and clinical outcomes of geriatric patients treated with dalbavancin in a tertiary hospital in Spain.

## Materials and Methods

A retrospective and observational study was conducted in a tertiary-level hospital. All patients over 80 years old who received at least one dose of dalbavancin from June 2016 to December 2021 were included in the study. Dalbavancin was administered intravenously with the following doses: 1,500 mg as a single infusion, 1,500 mg every two weeks (most frequent regimen), 1,500 mg every 3 weeks or 1,500 mg per month if estimated glomerular filtration rate <30 mL/min/1.73 m<sup>2</sup>.

The following variables were included in the study: Demographics (age, gender, usual residence), clinical characteristics (location of infection), microbiological features (microorganism), indication for dalbavancin prescription (drug toxicity, interactions, allergies, poor adherence to first-line therapy, indication for suppressive therapy or early hospital discharge), adverse effects and evolution of the infection. Geriatric assessment of the patient on admission was also documented, including Barthel index (dependency if <60 points or independent for the activities of daily living if >60 points), polypharmacy (between 5 and 10 drugs) or hyperpolypharmacy (more than 10 drugs).

## Statistics

A descriptive-univariate analysis was performed for all clinical variables studied. Qualitative variables were presented in absolute and relative frequencies, and quantitative variables were presented with the main measures of centralization and dispersion (average, standard deviation).

## Ethics Committee

The work was evaluated by the Ethics Committee of La Paz University Hospital and was carried out in accordance with the

protocol and ethical considerations outlined in the Declaration of Helsinki, and the ethical guidelines of the Council for International Organizations of Medical Science.

## Results

Twenty-five elderly patients treated with dalbavancin were documented at our hospital since its approval in 2016. The average patient age was 87 years old (range: 81-96 years). Patients were predominantly female (64%), from their usual residence (72%), considered independent for the activities of daily living "ADLs" (68%), and following a hyperpolypharmacy regimen (up to 44%). Demographic data and clinical characteristic are shown in Table 1.

Fourteen patients presented endovascular infections (endocarditis/vascular device infections) (53%), and the remaining 13 patients (47%) debuted with locomotor system infections (prosthetic joint infections or septic arthritis). Out of the total patient population, 6 patients (24%) had associated bacteremia at the time of diagnosis and 2 patients (8%) presented both clinical infections (endocarditis and osteoarticular infection).

<b>Variable</b>	
Total	25
<b>Mean age</b>	87, (81-96 years old)
<b>Sex</b>	
Male	9 (36)
Female	16 (64)
<b>Place of residence</b>	
Home	18 (72)
Nursing home	7 (28)
<b>Barthel index</b>	
>60 points	17 (68)
<60 points	8 (32)
<b>Treatment</b>	
Polypharmacy	14 (56)
Hyperpolypharmacy	11 (44)
<b>Chronic kidney disease</b>	
Yes	11 (44)
No	14 (56)
<b>Infection type</b>	
Endocarditis/endovascular	14 (56)
Chronic prosthesis infection	5 (20)
Acute prosthesis infection	4 (16)
Infectious arthritis	3 (12)
Skin and soft tissue infection	1 (4)
Bacteremia	6 (24)

Regarding the processed samples, 29 types of samples were collected from the 25 patients included in the study, since some patients had several positive cultures, e.g., blood and joint cultures. Samples were obtained from skin abscesses (1/29; 4%); from blood cultures (15/29; 60%); from joint fluid cultures (3/29; 10%); from intraoperative samples: Tissues and joint fluid (8/29; 28%); from IV catheters (1/29; 4%); from surgical wounds (1/29; 4%) Figure 1.

Overall, all patients had positive cultures, and 25 microorganisms were isolated in the study. The most common isolated pathogens belonged to the *Streptococcus/Enterococcus* group, followed by methicillin-resistant coagulase-negative staphylococci, methicillin-resistant *S. aureus*, methicillin sensitive coagulase-negative staphylococci and methicillin sensitive *S. aureus*. The isolated microorganisms are summarized in Figure 2.

The main indications for initiating treatment with dalbavancin were early discharge in 10 patients (40%), toxicity to previous antibiotics in 7 patients (28%), or allergy to the antibiotic of choice in 6 patients (24%). Up to 44% of the patients had more than one indication to support the prescription of dalbavancin. A total of 16 patients (64%) received concomitant treatment with another antibiotic against Gram-positive pathogens Figure 3. The number of doses administered ranged from 1 administration to 29 administrations (mean: 6 administrations; median: 2 administrations).

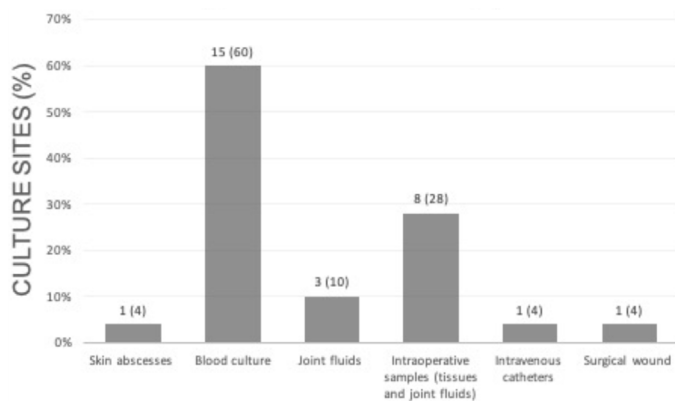


Figure 1. Culture sites n (%)

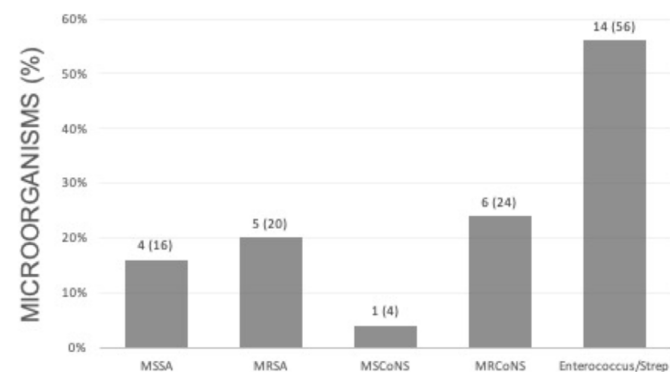


Figure 2. Microbiological isolation n (%)

Chronic kidney disease was present in 44% of the patients in whom dalbavancin dose was appropriately adjusted. There was a wide variability in the doses prescribed from 500 mg-1.500 mg in fortnightly doses to 1.500 mg monthly. Regarding the range of administrations, it ranged from patients who received a single dose (11 patients) to patients who received up to 29 doses. No patient experienced dalbavancin-related adverse effects; one patient suffered a reversible angioedema during dalbavancin infusion. However, after further investigation by our allergy department, it was concluded that there was no correlation between the study drug and the adverse event.

Overall, most patients (24/25; 96%) showed a favorable clinical outcome compared to a patient (1/25; 4%) who experienced a treatment failure due to a dalbavancin-resistant microorganism. There were no infection-related deaths.

### Discussion

In the literature, dalbavancin has shown great clinical efficacy, achieving clinical cure or infection control in more than 96% of patients, as well as safety and tolerability in both, elderly patients over 80 years old and in the general adult population (3,16). Several multicenter cohort studies [Bouza et al. (3), Morata et al. (8) and Hidalgo-Tenorio et al. (5)] assessed the efficacy of dalbavancin for the treatment of different type of Gram-positive infections, resulting in a clinical success rate ranging 80-96% (4,16). Consistently with previous reported data, 96% achieved clinical success in our study. According to the systematic review and meta-analysis on the safety of dalbavancin published by Monteagudo-Martínez et al. (16), adverse events, mainly gastrointestinal alterations, may occur in 13-55% of patients as reported by different studies (8,17). However, our patients presented excellent adherence, tolerance, and safety, only one patient reported a side effect of angioedema, which was assessed as not directly related to the study drug.

In our study, dalbavancin was mainly used for endovascular infections (53%), followed by osteoarticular infections (47%), which is not consistent with previously published series in

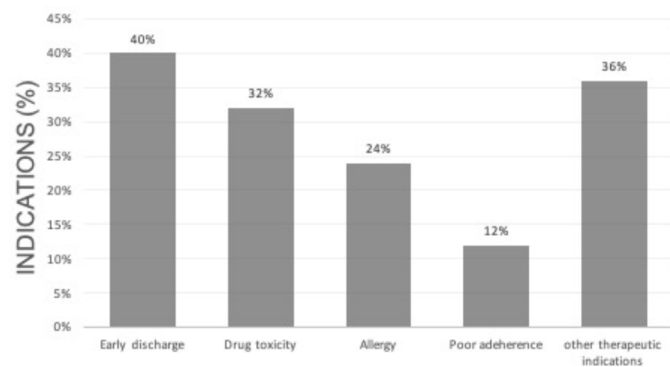


Figure 3. Main indications for the use of treatment with dalbavancin n (%)

which osteoarticular infections were the most common type of infection (3,18). Of note, 83% of bacteremia reported in the study was secondary to catheter/endovascular devices, which possibly reflects the challenge in the clinical management of elderly population due to several factors such as frailty, atypical presentation of symptoms, presence of comorbidity and polypharmacy (19,20). Regarding the type of microorganisms, staphylococcus is frequently the most prevalent microorganism in previous published series. However, 56% of the total infections were caused by *Enterococci/Streptococci* in our study, which were responsible from 40% of all endovascular infections reported (5). Given that elderly population over 80 years old presents greater intestinal flora colonization than the overall adult population, it might explain the microbiological difference reported in our study versus the literature (19). We have only found one recent publication by Wackenheim et al. (20) reviewing the use of dalbavancin in elderly population. Among the 65 patients included in the study, 51% (33) were considered old (over 75 years old, or over 65 years old, but associated with a CIRS-G score of 7 or more). Patients presented mainly with bone and joint infections (52%), while infective endocarditis was the less common type of infection (8%). The most frequently isolated microorganism was *Staphylococcus* spp. Overall, the study showed similar results to those described in the literature, achieving clinical cure of the infection in approximately 80% of patients, with only 9% of patients reporting side effects (20).

Moreover, chronic kidney disease is relatively common in the elderly. According to our data, 44% patients had impaired kidney function in whom dalbavancin dose was appropriately adjusted. One of the unmet needs in clinical practice is to establish the appropriate dosing regimen in patients with altered kidney function. DUR001-303 clinical trial demonstrated that single-dose regimen (1.500 mg) or a two-dose regimen, as administered in DISCOVER 1 and 2 pivotal trials (1.000 mg on day 1.500 mg on day 8), achieved similar efficacy and safety results, avoiding nephrotoxicity, both in healthy patients and chronic kidney diseases patients in whom dose adjustment is required (21). However, real-world clinical experience has showed potential variability at different doses (3,4,8,16). In our study, elderly patients with a glomerular filtration rate <20 mL/min received monthly doses of 500 mg achieving therapeutic success, which ensures the efficacy and convenience of a single monthly administration without secondary nephrotoxicity.

An important aspect of dalbavancin in the elderly population is that it allows the treatment of complex infections on an outpatient basis: three different hospitalization methods could be used such as home care units, day hospitals or medicalized nursing homes. Some of the infections reviewed in our study (prosthetic joint infections and infective endocarditis) require prolonged courses of antibiotics (4-6 weeks). Given the impact of long-term hospitalization in geriatric patients, resulting in

loss of functionality and muscle mass, in-hospital delirium, catheter-associated infections, pressure sores, pneumonia, and nosocomial urinary tract infections, among other health-related problems, it is essential to decrease the number of unnecessary hospitalizations, especially in this patient population (18). Dalbavancin could be a valuable therapeutic approach to facilitate hospital discharge, providing reliable systemic antimicrobial exposure for multiple weeks, avoiding nosocomial infections, optimizing therapeutic compliance, and ensuring a favorable safety profile. For that reason, analyzing the efficacy and safety of dalbavancin in the elderly population represents an unmet need, and studies in this line would be of great interest for the medical community. In addition, dalbavancin has shown to reduce the average hospital patient stay, lowering the impact on healthcare associated costs. Therefore, it would be of great interest to extend these cost-effectiveness studies to the geriatric population (22).

This study presents some limitations. First, as per the intrinsic retrospective nature of the study, we lacked relevant information such as patient frailty, which is currently an important tool for geriatric assessment (23,24). Second, the relatively small sample size highlights the need to conduct additional multicenter studies with larger sample sizes to further advance the knowledge of dalbavancin in the geriatric population.

## Conclusion

In conclusion, unlike previous published data, *Streptococci* and *Enterococci* isolates were responsible from most of the infections reported in our elderly patients over 80 years old, followed by endovascular infections as the most prevalent infection type described in the study.

Dalbavancin is an attractive antibiotic for the geriatric population due to its potential use in deep and complex infections, showing efficacy and a favorable safety profile, both in short and prolonged treatment regimens. Dalbavancin may thus facilitate early hospital discharge or referral to support units, reducing hospital stay, along with the subsequent reduction in nosocomial-related infections derived from prolonged hospitalization. Therefore, the use of dalbavancin not only reduces hospitalization, but also residential social health centers could benefit from its easy and convenient administration.

## Ethics

**Ethics Committee Approval:** The work was evaluated by the Ethics Committee of La Paz University Hospital and was carried out in accordance with the protocol and ethical considerations outlined in the Declaration of Helsinki, and the ethical guidelines of the Council for International Organizations of Medical Science.

**Informed Consent:** Retrospective study.

**Peer-review:** Internally and externally peer-reviewed.

### Authorship Contributions

Concept: L.C.S., A.G., A.R.N., B.L.Y., F.M.R., Design: C.S.L., A.R.N., Data Collection or Processing: C.S.L., A.G., A.R.N., Analysis or Interpretation: C.S.L., A.G., Literature Search: C.S.L., Writing: C.S.L.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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