Infectious diseases now 56 (2026) 105268

Contents lists available at ScienceDirect

Infectious Diseases Now

journal homepage: www.sciencedirect.com/journal/infectious-diseases-now

Original article

Efficacy and safety of dalbavancin as suppressive therapy in chronic implant-associated infections

Tomaso Beringheli [a,b,c], Céline Dupieux [a,d,e], Sylvain Goutelle [a,f,g], Tiphaine Roussel-Gaillard [a,d], Carole Dhelens [h], Pauline Rascle [i], Charlotte Doudet [j], Sandrine Roux [a,b], Clément Javaux [a,b], Claire Triffault-Fillit [a,b], Evelyne Braun [a,b], Tristan Ferry [a,b,g], Florent Valour [a,b,e,*], on behalf of the Lyon BJI study group

[a] *Reference center for the management of complex bone and joint infection (CRIOAc Lyon, www.crioac-lyon.fr), Hospices Civils de Lyon, Lyon, France*
[b] *Department of infectious diseases, Hospices Civils de Lyon, Lyon, France*
[c] *School of Infectious and Tropical Diseases, University of Milan, Milan, Italy*
[d] *Laboratory of bacteriology, National Reference Center for staphylococci, Hospices Civils de Lyon, Lyon, France*
[e] *CIRI - Centre International de Recherche en Infectiologie, Inserm, U1111, Université Claude Bernard Lyon 1, CNRS, UMR5308, Ecole Normale Supérieure de Lyon, Univ Lyon, Lyon, France*
[f] *Pharmacy department, Hôpital Croix-Rousse, Hospices Civils de Lyon, Lyon, France*
[g] *LBBE - Laboratoire de Biométrie et Biologie Evolutive, CNRS, UMR 5558, Université Lyon 1, Villeurbanne, France*
[h] *Department of pharmacy, Groupement Hospitalier Centre, Hospices Civils de Lyon, Lyon, France*
[i] *Department of pharmacy, Groupement Hospitalier Est, Hospices Civils de Lyon, Lyon, France*
[j] *Department of pharmacy, Groupement Hospitalier Sud, Hospices Civils de Lyon, Lyon, France*

ARTICLE INFO

Keywords:
Bone and joint infection
Dalbavancin
Prosthetic joint infection
Suppressive antimicrobial therapy

ABSTRACT

Introduction: Long-acting lipoglycopeptides represent an innovative suppressive antimicrobial therapy (SAT) for Gram-positive chronic infections. We aimed to describe the off-label use of dalbavancin SAT.
Methods: Retrospective cohort including all patients receiving dalbavancin SAT.
Results: Thirty-three patients received dalbavancin SAT for bone/joint (n = 27, 81.8%) or cardiovascular (n = 6, 18.2%) implant-related infections, mostly caused by coagulase-negative staphylococci (n = 27/44, 61.4%). After initial surgery (n = 29, 87.9%) and 83 (IQR, 70–125) days of curative therapy, SAT was prescribed because of the impact of a potential relapse (n = 13, 39.4%), incomplete surgical source control (n = 9, 27.3%), or previous failures (n = 7, 21.3%). The initial dalbavancin dose was most commonly 1,500 mg (n = 28, 84.8%), with a second dose of 1,500 mg (n = 19, 57.6%) 14 (IQR, 7–15) days apart. The third administration was carried out 28 (IQR, 27–31) days later (1,000 [n = 13, 39.4%] or 1,500 [n = 12, 36.4%] mg). A median of 7 (IQR, 5–11; min–max, 3–49) infusions were performed over a period of 210 (IQR, 107–532) days, with a last dose of 1,500 (n = 13, 39.4%), 1,000 (n = 13, 39.4%) or 500 (n = 7, 21.2%) mg at a 42 (IQR, 28–56) days interval. At the last follow-up, 21 patients were still on dalbavancin SAT with favorable outcome. Dalbavancin was discontinued in three patients with no sign of infection. Six relapses were observed with the same pathogen including four with increased dalbavancin MIC. No dalbavancin-related adverse events were observed.
Conclusion: Dalbavancin SAT for implant-related infections was overall safe and effective, despite failures with emergence of resistance, advocating for close monitoring of treatment response.

1. Introduction

Dalbavancin is a semi-synthetic lipoglycopeptide labelled for the treatment of acute skin and soft tissue infections. However, dalbavancin is currently mainly used in off-label contexts, especially in patients with Gram-positive chronic infections, justified by [1]: *i)* a good *in vitro* activity against most Gram-positive bacteria [2]; *ii)* a prolonged half-life (149–250 h) and documented good tissue (especially bones) penetration, predicting prolonged *in situ* exposition [3], with specific dosing regimens based on therapeutic drug monitoring (TDM) in osteomyelitis

* Corresponding author at: Department of infectious diseases, Hôpital Croix-Rousse, 103 Grande Rue de la Croix-Rousse, 69004 Lyon, Italy.
E-mail address: florent.valour@chu-lyon.fr (F. Valour).

https://doi.org/10.1016/j.idnow.2026.105268
Received 21 January 2026; Received in revised form 25 March 2026; Accepted 3 April 2026
Available online 4 April 2026

[4]; *iii)* an antibiofilm activity *in vitro* and in experimental models of bone and joint infection (BJI) and infective endocarditis [5–7]; and *iv)* a randomized clinical trial which supports its use in BJI, with no difference compared with the standard-of-care [8].

Suppressive antimicrobial therapy (SAT) is increasingly used in patients with device-associated Gram-positive infections, consisting in prolonged—and sometimes lifelong—antibiotic treatment. SAT indication is driven by the evaluation of the risk and impact of a potential relapse, related to the patients' age and comorbidities, and the quality of surgical infection source control [9].

The pharmacokinetics of dalbavancin makes it an attractive SAT option for Gram-positive chronic infections. However, this prolonged and off-label use has poorly been evaluated. Some studies with small sample sizes have reported conflicting results, suggesting a potential role for therapeutic drug monitoring [10–12]. We report our experience with dalbavancin used as SAT in patients with chronic implant-associated Gram-positive infections.

2. Patients and methods

2.1. Study design, included population and collected data

All adults (≥ 18 years) receiving dalbavancin as SAT at our tertiary care center were included in a retrospective observational cohort from the time dalbavancin became available (July 2019) to December 2024. Patients were identified using the exhaustive dispensing register of the pharmacy departments.

The total number of dalbavancin infusions was recorded for each patient, and information regarding treatment initiation (the first three infusions) and the last administration during follow-up were specified, including dosage and dosing intervals.

SAT was defined as prolonged antibiotic therapy beyond the usually recommended treatment duration (mainly 3 months for chronic device-associated infections).

The surgical strategy was considered adequate if it achieved effective source control using the preferred technique for the specific infectious condition. In particular, debridement, antibiotics, and implant retention (DAIR) were considered appropriate for acute (symptom duration ≤ 4 weeks) orthopedic device-associated infections, whereas one- or two-stage implant replacement was required for chronic infections.

Outcome and SAT continuation, as well as modification or discontinuation reasons, were assessed at the last follow-up visit. Clinical status was considered favorable when infection–related symptoms remained stable or improved while on SAT. Treatment failure included infection symptom relapse or worsening, superinfection (documented new surgical site infection with a different pathogen), need for unplanned surgical procedure for septic reason, or death.

2.2. Microbiological data

Microbiological diagnosis was based on deep surgical samples inoculated on various enriched media for prolonged (14 days) aerobic and anaerobic cultures. Two or more culture-positive samples were considered significant for low virulent pathogens and/or potential contaminants (non-*aureus* staphylococci, *Corynebacterium* spp., *Cutibacterium acnes*), and at least one culture-positive sample for more virulent pathogens (*Staphylococcus aureus,* streptococci/enterococci, or Gram-negative bacilli [GNB]). Dalbavancin susceptibility testing was performed by broth microdilution (Sensititre, ThermoFisher Scientific) for staphylococci and enterococci, and E-test® gradient strips (bioMérieux) for other bacteria. According to the current French antibiogram guidelines (CA-SFM/EUCAST), isolates were considered susceptible if dalbavancin MIC was ≤ 0.25 mg/L for staphylococci and enterococci, and ≤ 0.125 mg/L for streptococci.

2.3. Statistical analysis

Population characteristics were described using percentages for dichotomous variables and median (interquartile range, IQR) for quantitative variables. Data were analyzed using Jamovi software [13].

3. Results

3.1. Included population

A total of 33 patients received a dalbavancin-based SAT (23 [69.7%] males, median age 71 [IQR, 59–80] years). Main baseline characteristics of patients are shown in Table 1. The median age-adjusted Charlson comorbidity index was 4 (IQR, 3–6). The most common comorbidities were diabetes (n = 13, 39.4%), peripheral vascular disease (n = 8, 24.2%), and chronic renal failure (n = 8, 24.2%).

Twenty-two (66.7%) patients were treated for a prosthetic joint infection (PJI)—including 15 total knee PJIs, six total hip PJIs, one total femur arthroplasty—six (18.2%) had a cardiovascular device-related infection (five vascular implants and one ventricular assist device), three (9.1%) had orthopedic device-associated osteomyelitis, and two (6.1%) had spinal implant-related infection. Of note, upon retrospective review, all prosthetic joint infections fulfilled the European Bone and Joint Infection Society (EBJIS) criteria [14].

3.2. Microbiological data

All infections were documented. Thirteen (39.4%) infections were polymicrobial, including eight (24.2%) with at least two Gram-positive pathogens. The 44 dalbavancin-targeted pathogens were coagulase-negative staphylococci (n = 27, 61.4%), *S. aureus* (n = 8, 18.2%,

Table 1
Baseline characteristics of the 33 patients included.

Demographics	
Sex (male)	23 (69.7%)
Age (years)	71 (59–80)
Main comorbidities	
Adjusted Charlson's comorbidity index	4 (3–6)
Diabetes mellitus	13 (39.4%)
Peripheral arterial disease	8 (24.2%)
Chronic renal failure	8 (24.2%)
Chronic pulmonary disease	7 (21.2%)
Congestive heart failure	5 (15.2%)
Index infection	
Bone and joint infection	27 (81.8%)
Prosthetic joint infection	22 (66.7%)
Chronic device-associated osteomyelitis	3 (9.1%)
Spinal implant-related infection	2 (6.1%)
Cardiovascular device-related infection	6 (18.2%)
Vascular prosthetic graft infection	5 (15.2%)
Left ventricular assist device infection	1 (3.0%)
Microbiological results	
Microbiological documentation	33 (100%)
Polymicrobial infection	13 (39.4%)
Dalbavancin-targeted pathogens (n = 44)	
Coagulase negative staphylococci	27 (61.4%)
S. aureus	8 (18.2%)
Streptococci	4 (9.1%)
E. faecium	2 (4.5%)
C. acnes	2 (4.5%)
Corynebacterium spp.	1 (2.3%)
Dalbavancin MIC (mg/L)	0.03 (0.03–0.047)
Initial management	
Surgery	29 (87.9%)
Appropriate surgical strategy for infection source control	17 (51.5%)
Duration of targeted antimicrobial therapy before suppressive antimicrobial treatment (days)	83 (70–125)

Data are presented as numbers and percentages for dichotomous variables, and as median (interquartile range) for continuous variables.

including two MRSA), streptococci (n = 4, 9.1%), *E. faecium* (n = 2, 4.5%), *C. acnes* (n = 2, 4.5%) and *Corynebacterium* spp. (n = 1, 2.3%). All isolates were susceptible to dalbavancin (median MIC value: 0.03 [IQR, 0.03–0.047 mg/L]). Nine (27.3%) patients were co-infected with one or more pathogens not susceptible to dalbavancin, including Enterobacterales (n = 4), non-fermenting Gram-negative bacilli (n = 4), and *Candida* spp. (n = 4).

3.3. Initial management

Twenty-nine (87.9%) patients underwent surgery at the initial management phase; 12 (41.4%) were deemed inadequate for properly addressing the infectious focus. DAIR, prosthesis replacement, and abstention were respectively proposed in 13 (59.1%), eight (36.4%), and one (4.5%) patients with PJI. Device-associated osteomyelitis or spinal infections were managed by DAIR (n = 4, 80%) or complete implant removal (n = 1, 20%). Among patients with cardiovascular device-related infections, only three (50%) underwent surgery for abscess drainage (n = 2) and vascular allograft after prosthesis removal (n = 1).

All patients received an empirical broad-spectrum antimicrobial therapy at infection onset or at the time of surgery. After microbiological documentation, targeted antimicrobial therapy was initiated. Dalbavancin was initiated at this stage in four (12.2%) patients only. Among the remaining patients, 13 (44.8%) were switched to dalbavancin during the initial treatment phase, after a median of 24 (IQR, 11–40) days of other targeted therapies. Among these, 11 (84.6%) received a combination therapy, mostly with rifampicin (n = 4, 36.4%). Reasons for using dalbavancin at this stage were the need for parenteral SAT with inability to maintain long-term venous access or the need for ambulatory care (n = 7, 41.2%), or poor compliance (n = 6, 35.3%), failure (n = 2, 11.8%) or toxicity (n = 2, 11.8%) of previous antimicrobials.

3.4. Suppressive antibiotic therapy

SAT was initiated after a median of 83 (IQR, 70–125) days of targeted antibiotic therapy. Reasons for initiating SAT were the absence of appropriate surgical infection control (n = 13, 39.4%), the high impact of a potential relapse (n = 13, 39.4%), and multiple previous treatment failures (n = 7, 21.3%). In the BJI group, only one patient had a sinus tract at the time of SAT initiation. Dalbavancin was used as first-line SAT in 29 (87.9%) patients, including the 17 for whom dalbavancin had been started during the initial phase. In the remaining four patients, initial SAT was based on oxazolidinones, with switch to dalbavancin after a median of 527 (IQR, 360–633) days due to hematologic or neurologic toxicity.

3.5. Dalbavancin administration and therapeutic drug monitoring

The reason for using dalbavancin as SAT were poor compliance to previous oral antibiotic therapy (n = 8, 24.2%), the need for parenteral SAT with inability to maintain long-term venous access (n = 7, 21.2%), failure of previous therapies (n = 7, 21.2%), the need for outpatient antimicrobial therapy (n = 6, 18.2%), and toxicity to a previous treatment (n = 5, 15.2%).

The 33 included patients received a median of 7 (IQR, 5–11; min–max, 3–49) infusions over a period of 210 (IQR, 107–532) days from the first to the last administration. Excluding the infusion performed as part of the initial curative treatment, the median number of infusions of dalbavancin specifically as SAT was six (IQR, 4–11; min–max, 1–49), over a total period of 175 (IQR, 70–561) days. Dalbavancin regimens are detailed in Table 2.

The first three administrations more frequently occurred in an ambulatory care unit (n = 90, 91%). Only one (3%) patient started outpatient parenteral antibiotic therapy (OPAT) at the third administration.

The first infusion dose was most often 1,500 mg, in 28 (84.8%) patients. Four (12.1%) received 1,000 mg and one (3.0%) patient received 500 mg. The second dose of 1,500 mg (n = 19, 57.6%), 1,000 mg (n = 7, 21.2%) or 500 mg (n = 7, 21.2%) was administered after a median interval of 14 (IQR, 7–15) days. The third dose of 1,500 mg (n = 12, 36.4%), 1,000 mg (n = 13, 39.4%) or 500 mg (n = 8, 24.2%) was administered after a median interval of 28 (IQR, 27–31) days following the second infusion. Subsequent doses were guided by therapeutic drug monitoring in most patients. The last infusion during follow-up was administered with a median interval of 42 (IQR, 28–56; min–max, 20–84) days after the previous one, with doses of 1,500 mg (n = 13, 39.4%), 1,000 mg (n = 13, 39.4%) or 500 mg (n = 7, 21.2%).

Table 2
Summary of dalbavancin regimens.

Number of dalbavancin infusions per patient	
Total number of infusions	7 (5–11; min–max, 3–49)
Period of time (days)	210 (107–532)
Number of infusions as suppressive antimicrobial treatment	6 (4–11; min–max, 1–49)
Period of time	175 (70–561)
First three administrations	
1st infusion	
Dose	
1,500 mg	28 (84.8%)
1,000 mg	4 (12.1%)
500 mg	1 (3.0%)
2nd infusion	
Dose	
1,500 mg	19 (57.6%)
1,000 mg	7 (21.2%)
500 mg	7 (21.2%)
Interval between 1st and 2nd infusion (days)	14 (7–15)
3rd infusion	
Dose	
1,500 mg	12 (36.4%)
1,000 mg	13 (39.4%)
500 mg	8 (24.2%)
Interval between 2nd and 3rd infusion (days)	28 (27–31)
Last infusion during follow-up	
Dose	
1,500 mg	13 (39.4%)
1,000 mg	13 (39.4%)
500 mg	7 (21.2%)
Interval after the previous infusion (days)	42 (28–56; min–max, 20–84)

Data are presented as numbers and percentages for dichotomous variables, and as median (interquartile range) for continuous variables.

3.6. Outcomes

After a median of 477 (IQR, 127–839) days after SAT initiation, 28 patients (84.8%) were still on SAT at the last follow-up visit. Among these, 21 (75.0%) remained on dalbavancin with stable (n = 16) or improved (n = 5) clinical condition compared with SAT initiation. Dalbavancin was discontinued in three patients who were considered cured (two benefited from an additional curative surgery, one from a functional imaging showing no argument for persistent infection), with no relapse at the end of follow-up (22, 24, and 56 months after the last dalbavancin infusion). Overall, a success rate of 72.7% (n = 24/33) was recorded.

Unplanned discontinuation of dalbavancin occurred in nine (27.3%) patients: *i)* six (18.2%) experienced relapse caused by the same pathogen, including three in whom a dalbavancin–resistant isolate emerged, and one who showed an increase in dalbavancin MIC that remained below the resistance breakpoint; and *ii)* three developed a superinfection, including one with a dalbavancin-resistant Methicillin-resistant *Staphylococcus epidermidis* (MRSE) (and two caused by non-Gram-positive pathogens). Characteristics of patients who experienced relapses associated with an increased dalbavancin MIC are shown in

Table 3
Main characteristics of patients who discontinued dalbavancin due to failure (relapse) caused by a microorganism with a high dalbavancin MIC.

Patient	**1**	**2**	**3**	**4**	**5**
Demographics					
Age (years), sex	64, M	90, F	87, M	81, M	69, M
Charlson Index Score	4	4	6	7	8
Index infection					
Type	PJI, knee	PJI, knee	PJI, knee	PJI, knee	PJI, hip
Surgical strategy	Partial exchange	DAIR	DAIR	No surgery	DAIR
Appropriate surgical source control	No	Yes	Yes	No	No
Microbiological data (dalbavancin MIC, mg/L)					
Index pathogens	MRSE (0.032)	MSSE (≤ 0.03) *Abiotrophia defectiva* (0.012)	MSSE (≤ 0.03)	MRSA (≤ 0.03)	*S. capitis* (≤ 0.03) MRSE (≤ 0.03)
Failure type and pathogens	RelapseMRSE (0.500)	Relapse *Abiotrophia defectiva* (0.032)	Superinfection MRSE (0.250) MRSE (0.500) MRSE (2)	Relapse MRSA (0.500)	Relapse *S. capitis* (0.500) *S. capitis* (0.125) Gram-negative
Dalbavancin therapy					
Dalbavancin initiation	Second-line targeted therapy	Second-line targeted therapy	First-line SAT	Second-line targeted therapy	First-line SAT
Combination therapy	Rifampicin	Rifampicin	No	Rifampicin	No
Reason for SAT	Inappropriate surgical source control	High impact of a potential relapse	Multiple previous failures	Inappropriate surgical source control, multiple previous failures	Inappropriate surgical source control
Clinical status on SAT	Good	Sinus tract	Good	Persistent signs of infection	Good
Dalbavancin doses (n)	7	10	8	5	4
Time from first to last infusion (days)	134	360	324	171	59
Last dalbavancin trough concentration (mg/L)	8.0	4.8	7.9	4.1	14.8
Outcome					
Time from dalbavancin start to relapse (days)	134	360	324	171	59
Additional surgical procedure	Yes	No	Yes	Yes	Yes
New SAT	Doxycycline	Amoxicillin	Tedizolid and rifampicin	Pristinamycin	No
Clinical status	Relapse	Persistent signs of infection	Good	Good	Relapse

DAIR, debridement, antibiotics, and implant retention; F, Female; M, Male; MIC, Minimum inhibitory concentration; MRSA, Methicillin-resistant *Staphylococcus aureus*; MRSE, Methicillin-resistant *Staphylococcus epidermidis*; MSSE, Methicillin-susceptible *Staphylococcus epidermidis*; PJI, Prosthetic joint infection; SAT, Suppressive antimicrobial therapy.

Table 3. Of note, all these patients had benefited from repeated therapeutic drug monitoring, with dalbavancin trough concentrations exceeding 100-fold the initial MIC at all time-points for all patients.

No dalbavancin-related adverse event was observed.

4. Discussion

Dalbavancin has been considered an appealing option for Gram-positive infections requiring prolonged antimicrobial therapy such as BJI or cardiovascular infections, which represent its primarily real-life use, ahead of its marketing authorization in skin and soft tissue infections [1]. Its pharmacokinetics features—including its prolonged half-life—also allows to consider dalbavancin as a SAT option, but this indication has been poorly described.

At our center, well-tolerated, narrow-spectrum and less costly oral SAT options such as doxycycline are preferred whenever possible. In our series, reasons for using dalbavancin mostly included issues with compliance or intolerance to oral therapies, or multidrug-resistant pathogens requiring prolonged parenteral treatment. We consequently presented here our experience with 33 patients receiving dalbavancin used as SAT for chronic implant-associated infections, with no adverse events. Six relapses were observed with the same pathogen including four with increased dalbavancin MICs, and three superinfections, including one with dalbavancin-resistant MRSE. Our study has several limitations, such as its sample size, retrospective design, and population heterogeneity—inherent to chronic infections where standardized approaches are not used—but it is the largest cohort of patients receiving dalbavancin SAT to date.

The most frequent initial regimen was based on two infusions of 1,500 mg one week apart, with a third infusion on Day 28, and subsequent dosing adjustment based on therapeutic drug monitoring. Data on dalbavancin therapeutic drug monitoring PK/PD targets are largely derived from a neutropenic mouse thigh model, in which a 24-hour fAUC/MIC values of 27, 49, and 111 were associated with stasis, 1-log kill, and 2-log-kill, respectively [15]. Based on the 24-hour AUC values and assuming a free fraction of 7%, PK/PD targets for total concentration in patients are usually set at a mean AUC > 1,000 to 1,500 (over the interdose interval) and minimal AUC > 500 (on the last day before the next administration). Therapeutic drug monitoring appears particularly valuable for dalbavancin SAT management, considering the lack of approved dosage for this off-label use. Indeed, observational studies suggested that therapeutic drug monitoring-guided dosing allows extended dosing intervals while maintaining effective therapeutic levels, particularly for *Staphylococcus* spp. BJI [4,12]. Using this approach, the dalbavancin dose could be reduced to 500 mg and the dosing interval increased beyond 1 month in some patients, resulting in lower treatment cost and reduced infusion burden. Supporting this approach, Lafon-Desmurs *et al.* published a retrospective study in 2024 reporting 15 patients with prosthetic-related infections (12 PJI, two vascular prosthesis infections, and one valvular prosthesis infection) predominantly caused by staphylococci receiving a median of four (IQR, 2–7) dalbavancin infusions [16]. Therapeutic drug monitoring enabled

the extension of dosing intervals (median interval: 57 [IQR, 28–82] days, up to 142 days), while targeting a dalbavancin concentration > 4 mg/L for SAT in dalbavancin-susceptible *Staphylococcus* spp. infections. Moreover, the use of dalbavancin as OPAT could represent an interesting option, provided patients are carefully selected according to current guidelines [17]. However, its restriction to hospital–only prescription and its high cost—borne by home–hospitalization services—limit the feasibility of this approach in France, such that only one patient in our study was able to benefit from it.

Evaluating SAT effectiveness is challenging, as this non-curative strategy is typically used in the most complex situation and in highly heterogeneous patients, where multiple outcome determinants hinder the standardization of evaluation endpoints. The most frequently reported indication is chronic PJI treated by DAIR, with a global success rate ranging between 60% and 93% [9]. In our series of patients with chronic infections involving orthopedic or cardiovascular devices, but no endocarditis or prosthetic valve infections, we observed a consistent and acceptable infection control rate of 72.7%. In a retrospective multicentric cohort study of patients with osteoarticular (n = 6) or vascular (n = 2) device-associated infections treated with dalbavancin used as SAT between 2016 and 2018, Ruiz-Sancho *et al.* reported a similar efficacy rate of 75%, with a median of 29 (IQR, 9–61) administrations [10]. Other case series present mixed results regarding infection control with dalbavancin used as SAT, mostly in device-associated cardiovascular infections, with relatively long periods of infection suppression. For example, Cooper *et al.* described eight patients with a median of 229 (IQR, 107–372) days of dalbavancin SAT for endovascular infections, with five relapses [11]. Another study involving 10 patients with left ventricular assist device-related infections found a 60% rate of successful infection suppression over 12 (IQR, 13.7–124.9 weeks) months [18]. The impact of therapeutic drug monitoring-guided dalbavancin SAT on outcome has poorly been evaluated. Gallerani *et al.* retrospectively described dalbavancin therapeutic drug monitoring in 14 cardiovascular prosthetic infections mostly caused by *Staphylococcus* spp. with a median of 3.5 (IQR, 2–9) doses over a period of 8 (IQR, 1–45) weeks [19]. In the therapeutic drug monitoring-guided group, dosing intervals ranged from 4 to 9 weeks. After a median of 65 (IQR, 23–144) weeks of follow-up, infection control was maintained in 10 (76.9%) patients, with success rates of 87.5% and 60% in the therapeutic drug monitoring-guided and control groups, respectively. However, infection source control differed significantly between the two groups, making it difficult to interpret any differences.

The observation of relapses caused by the same pathogen, accompanied by increased dalbavancin MICs, raises specific concerns about the selection of dalbavancin resistance during treatment, a phenomenon already reported *in vitro* [20]. Increased MICs during treatment have already been described specifically during SAT in two strains of methicillin-resistant *S. aureus* and *S. epidermidis* with a risk of cross-resistance with vancomycin and daptomycin [21,22]. Determinants of dalbavancin resistance selection *in vivo* are unclear, but a preexposure to vancomycin/daptomycin, a high inoculum and/or an insufficient surgical source control, and biofilm-associated infections have been suggested, as observed in most of our patients [21,23]. Almost all patients in our cohort had been exposed to daptomycin before starting dalbavancin, at least during the empirical treatment phase, preventing any conclusion on the impact of this prior therapy. Dalbavancin underexposure has also been suggested. However, exposure was adequate in all patients who experienced relapses with increased dalbavancin MICs, with trough concentrations exceeding the initial MIC by more than 100–fold.

Regarding the safety profile, no dalbavancin-related adverse event was observed in our cohort. Similarly, all studies previously cited reported an excellent tolerance of multiple dalbavancin doses, with few adverse reactions, all non-severe. Increased creatinine and liver enzyme levels were observed in one patient, leading to dalbavancin discontinuation [10]. Another patient discontinued dalbavancin due to a bronchospasm during infusion [16].

Finally, dalbavancin has been associated with reduced overall treatment-associated costs in Gram-positive infection requiring prolonged antimicrobial therapy [24]. The economic impact of dalbavancin used as suppressive antimicrobial therapy has not been specifically assessed, but it could be substantial for multidrug-resistant Gram-positive pathogens when compared with the few available oral alternatives, such as tedizolid.

5. Conclusion

Our series shows that the use of dalbavancin as suppressive antimicrobial therapy is well tolerated and associated with an acceptable success rate in patients with chronic Gram-positive implant-associated infections. However, relapses with increased dalbavancin MICs advocate for close monitoring of patients—especially in case of insufficient surgical source control—and dalbavancin therapeutic drug monitoring to guide dosing and to avoid underexposure.

Declaration of generative AI and AI-assisted technologies in the writing process

The authors declare that they did not use generative AI and AI-assisted technologies.

Ethics approval

The study was subject to declaration with the local commission for data protection and liberties and received the approval of the Scientific and Ethical Committee of Hospices Civils de Lyon, France (reference number 25–5019). In accordance with French legislation regarding retrospective observational studies, all patients received written information about the study and their possibility to decline to participate, but the need for written informed consent was waived.

Contribution of authors.

FV and TF designed and supervised the study. All authors contributed to data collection: CDu and TRG for microbiological data; SG, CDh, PR, and CDo for pharmacological and PK/PD data; SR, CJ, CTF, EB, TF, and FV for clinical data. TB centralized and computed the data. SR, CJ, CTF, EB, TF, and FV provided medical care to participants. TB and FV performed the descriptive analysis and drafted the paper. All authors read, revised, and approved the final version of the manuscript.

Funding

This study was carried out as part of our routine work, with no specific funding.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: FV and CDu received a grant from Correvio Pharma for a previous *in vitro* study, with no relation or impact on the present work. SG was a speaker in a symposium supported by Correvio in 2019 and was a member of an advisory board for Advanz Pharma in 2024, without personal fee.

Acknowledgements

Lyon BJI study group: *Coordinator*: Tristan Ferry. *Infectious Diseases Specialists:* Claire Triffault-Filit, Florent Valour, Agathe Becker, Anne Conrad, Evelyne Braun, Florence Ader, Isabelle Eberl, Joanna-Isabelle Kurban Bessa Lippman, Lorena Van-Den-Bogaart, Marie Simon, Pierre Chauvelot, Sandrine Roux, Sarah Soueges, Thomas Perpoint, Tristan Ferry, Clément Javaux, Marie Wan. *Surgeons:* Cécile Batailler, Sébastien Lustig, Elvire Servien, Gerald Delfosse, Guillaume Mesnard, Jean

Baltzer, Julien Erard, Nicolas Cance, Sébastien Martres, Franck Trouillet, Stanislas Gunst, Alexandre Couraudon, Anthony Viste, Fabien Ewald, Jean-Luc Besse, Matthieu Cotte, Michel Fessy, Philippe Chaudier, Thomas Cuinet, Vianney Derreveaux, Antoine Bertani, Antoine Colas, Frédéric Rongieras, Jean-Baptiste Masson, Léonard Vézole, Maxime Rarchaert, Vincent Pibarot, Aram Gazarian, Arnaud Walch, Christophe Gaillard, Gaetan Vanpoulle, Louis Ducharne, Lyliane Ly, Nael Ben-Hadid, Selma Lahlali, Thibault Druel, Victor Rutka, Alain-Ali Mojallal, Abdulrahman Hashim, Guillaume Henry, Hélène Person, Mathilde Lherm. *Anesthesiologists:* Audrey Chevreau-Ciliberti, Caroline Macabéo, Frédéric Aubrun, Kaissar Rouhana, Mikhail Dziadzko. *Microbiologists:* Laetitia Beraud, Matthieu Curtil-Dit-Galin, Tiphaine Roussel-Gaillard, Ani Horikian, Anne-Lise Maucotel, Céline Dupieux, Jean-Philippe Rasigade, Camille Kolenda. *Imaging specialists:* David Gicquel, Grégoire Vervust, Isabelle Morelec, Jean-Baptiste Pialat, Joris Lavigne, Nicolas Stacoffe. *PK/PD specialists:* Agnes Henry, Noémie Vieux, Romain Garreau, Sylvain Goutelle, Thomas Briot. *Clinical research assistant and database manager*: Johanna Boulant.

References

[1] De Vito A, Fiore V, Colpani A, Zauli B, Fanelli C, Tiseo G, et al. The current and future off-label uses of dalbavancin: a narrative review. Eur Rev Med Pharmacol Sci 2023;27:1222–38. https://doi.org/10.26355/eurrev_202302_31233.

[2] Jones RN, Sader HS, Flamm RK. Update of dalbavancin spectrum and potency in the USA: report from the SENTRY Antimicrobial Surveillance Program (2011). Diagn Microbiol Infect Dis 2013;75:304–7. https://doi.org/10.1016/j.diagmicrobio.2012.11.024.

[3] Dunne MW, Puttagunta S, Sprenger CR, Rubino C, Van Wart S, Baldassarre J. Extended-duration dosing and distribution of dalbavancin into bone and articular tissue. Antimicrob Agents Chemother 2015;59:1849–55. https://doi.org/10.1128/AAC.04550-14.

[4] Cojutti PG, Rinaldi M, Zamparini E, Rossi N, Tedeschi S, Conti M, et al. Population pharmacokinetics of dalbavancin and dosing consideration for optimal treatment of adult patients with staphylococcal osteoarticular infections. Antimicrob Agents Chemother 2023;65: e02260 –20:AAC.02260-20. https://doi.org/10.1128/AAC.02260-20.

[5] Oliva A, Stefani S, Venditti M, Di Domenico EG. Biofilm-Related Infections in Gram-positive Bacteria and the potential Role of the Long-Acting Agent Dalbavancin. Front Microbiol 2021;12:749685. https://doi.org/10.3389/fmicb.2021.749685.

[6] Barnea Y, Lerner A, Aizic A, Navon-Venezia S, Rachi E, Dunne MW, et al. Efficacy of dalbavancin in the treatment of MRSA rat sternal osteomyelitis with mediastinitis. J Antimicrob Chemother 2016;71:460–3. https://doi.org/10.1093/jac/dkv357.

[7] Lefort A, Pavie J, Garry L, Chau F, Fantin B. Activities of dalbavancin in vitro and in a rabbit model of experimental endocarditis due to *Staphylococcus aureus* with or without reduced susceptibility to vancomycin and teicoplanin. Antimicrob Agents Chemother 2004;48:1061–4. https://doi.org/10.1128/AAC.48.3.1061-1064.2004.

[8] Rappo U, Puttagunta S, Shevchenko V, Shevchenko A, Jandourek A, Gonzalez PL, et al. Dalbavancin for the Treatment of Osteomyelitis in Adult patients: a Randomized Clinical Trial of Efficacy and Safety. Open Forum. Infect Dis 2019;6: ofy331. https://doi.org/10.1093/ofid/ofy331.

[9] Horne M, Woolley I, Lau JSY. The use of long-term Antibiotics for suppression of Bacterial Infections. Clin Infect Dis Off Publ Infect Dis Soc Am 2024;79:848–54. https://doi.org/10.1093/cid/ciae302.

[10] Ruiz-Sancho A, Núñez-Núñez M, Castelo-Corral L, Martínez-Marcos FJ, Lois-Martínez N, Abdul-Aziz MH, et al. Dalbavancin as suppressive antibiotic therapy in patients with prosthetic infections: efficacy and safety. Front Pharmacol 2023;14: 1185602. https://doi.org/10.3389/fphar.2023.1185602.

[11] Cooper MM, Preslaski CR, Shihadeh KC, Hawkins KL, Jenkins TC. Multiple-Dose Dalbavancin Regimens as the Predominant Treatment of Deep-Seated or Endovascular Infections: a Scoping Review. Open Forum. Infect Dis 2021;8: ofab486. https://doi.org/10.1093/ofid/ofab486.

[12] Gatti M, Viale P, Cojutti PG, Zamparini E, De Paolis M, Giannella M, et al. A descriptive case series of the relationship between maintenance of conservative PK/PD efficacy thresholds of dalbavancin over time and clinical outcome in long-term treatment of staphylococcal osteoarticular infections. Int J Antimicrob Agents 2023;61:106773. https://doi.org/10.1016/j.ijantimicag.2023.106773.

[13] Jamovi [Internet]. n.d. Jamovi [cited April 3, 2026]. Available from: https://www.jamovi.org/.

[14] McNally M, Sousa R, Wouthuyzen-Bakker M, Chen AF, Soriano A, Vogely HC, et al. The EBJIS definition of periprosthetic joint infection. Bone Jt J 2021;103-B:18–25. https://doi.org/10.1302/0301-620X.103B1.BJJ-2020-1381.R1.

[15] Lepak A, Marchillo K, VanHecker J, Andes D. Impact of Glycopeptide Resistance in *Staphylococcus aureus* on the Dalbavancin *In Vivo* Pharmacodynamic Target. Antimicrob Agents Chemother 2015;59:7833–6. https://doi.org/10.1128/AAC.01717-15.

[16] Lafon-Desmurs B, Gachet B, Hennart B, Valentin B, Roosen G, Degrendel M, et al. Dalbavancin as suppressive therapy for implant-related infections: a case series with therapeutic drug monitoring and review of the literature. Eur J Clin Microbiol Infect Dis Off Publ Eur Soc Clin Microbiol 2024;43:1475–80. https://doi.org/10.1007/s10096-024-04849-0.

[17] Tometten L, Trost U, Jürgens L, Achterberg S, Arenz L, Audebert F, et al. Practice guidelines for outpatient parenteral antimicrobial therapy (OPAT) in Germany. Infection 2025;53:2701–15. https://doi.org/10.1007/s15010-025-02619-4.

[18] Mansoor A-E-R, Krekel T, Cabrera NL. Experience with dalbavancin for long-term antimicrobial suppression of left ventricular assist device infections. Transpl Infect Dis Off J Transplant Soc 2023;25:e14068. https://doi.org/10.1111/tid.14068.

[19] Gallerani A, Gatti M, Bedini A, Casolari S, Orlando G, Puzzolante C, et al. Long-Term Suppressive Therapeutic-Drug-Monitoring-Guided Dalbavancin Therapy for Cardiovascular Prosthetic Infections. Antibiot Basel Switz 2023;12:1639. https://doi.org/10.3390/antibiotics12111639.

[20] Werth BJ, Ashford NK, Penewit K, Waalkes A, Holmes EA, Ross DH, et al. Dalbavancin exposure in vitro selects for dalbavancin-non-susceptible and vancomycin-intermediate strains of methicillin-resistant *Staphylococcus aureus*. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis 2021;27:910.e1–8. https://doi.org/10.1016/j.cmi.2020.08.025.

[21] Ruffier d'Epenoux L, Barbier P, Fayoux E, Guillouzouic A, Lecomte R, Deschanvres C, et al. Dalbavancin-resistant *Staphylococcus epidermidis* in vivo selection following a prosthetic joint infection: phenotypic and genomic characterization. JAC-Antimicrob Resist 2024;6:dlae163. https://doi.org/10.1093/jacamr/dlae163.

[22] Kussmann M, Karer M, Obermueller M, Schmidt K, Barousch W, Moser D, et al. Emergence of a dalbavancin induced glycopeptide/lipoglycopeptide non-susceptible *Staphylococcus aureus* during treatment of a cardiac device-related endocarditis. Emerg Microbes Infect 2018;7:202. https://doi.org/10.1038/s41426-018-0205-z.

[23] Werth BJ, Jain R, Hahn A, Cummings L, Weaver T, Waalkes A, et al. Emergence of dalbavancin non-susceptible, vancomycin-intermediate *Staphylococcus aureus* (VISA) after treatment of MRSA central line-associated bloodstream infection with a dalbavancin- and vancomycin-containing regimen. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis 2018;24:429.e1–5. https://doi.org/10.1016/j.cmi.2017.07.028.

[24] Poliseno M, Bavaro DF, Brindicci G, Luzzi G, Carretta DM, Spinarelli A, et al. Dalbavancin Efficacy and Impact on Hospital Length-of-Stay and Treatment costs in Different Gram-positive Bacterial Infections. Clin Drug Invest 2021;41:437–48. https://doi.org/10.1007/s40261-021-01028-3.