



**HAL**  
open science

## French national cohort of first use of dalbavancin: A high proportion of off-label use

Aurélien Dinh, Clara Duran, Patricia Pavese, Lydie Khatchatourian, Boris Monnin, Alexandre Bleibtreu, Eric Denis, Cédric Etienne, Nicolas Rouanes, Rafael Mahieu, et al.

### ► To cite this version:

Aurélien Dinh, Clara Duran, Patricia Pavese, Lydie Khatchatourian, Boris Monnin, et al.. French national cohort of first use of dalbavancin: A high proportion of off-label use. *International Journal of Antimicrobial Agents*, 2019, 54, pp.668 - 672. 10.1016/j.ijantimicag.2019.08.006 . hal-03488868

**HAL Id: hal-03488868**

**<https://hal.science/hal-03488868>**

Submitted on 20 Jul 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

1 **French national cohort of first use of dalbavancin: a high proportion of off-label use**

2 Aurélien Dinh<sup>1</sup>, Clara Duran<sup>1</sup>, Patricia Pavese<sup>2</sup>, Lydie Khatchatourian<sup>3</sup>, Boris Monnin<sup>4</sup>,

3 Alexandre Bleibtreu<sup>5</sup>, Eric Denis<sup>6</sup>, Cédric Etienne<sup>7</sup>, Nicolas Rouanes<sup>8</sup>, Rafael Mahieu<sup>9</sup>,

4 Frédérique Bouchand<sup>10</sup>, Benjamin Davido<sup>1</sup>, Romain Lotte<sup>11</sup>, Philippe Cabaret<sup>12</sup>, Fabrice

5 Camou<sup>13</sup>, Pascal Chavanet<sup>14</sup>, Assi Assi<sup>15</sup>, Silvia Limonta<sup>16</sup>, Catherine Lechiche<sup>17</sup>, Raphaëlle

6 Riou<sup>18</sup>, Johan Courjon<sup>11</sup>, Gabriela Illes<sup>19</sup>, Flore Lacassin-Beller<sup>19</sup>, Eric Senneville<sup>20</sup>, on behalf of

7 the Dalbavancin French study group

8

9 <sup>1</sup> Infectious disease unit, Raymond Poincaré University Hospital, AP-HP, Versailles Saint-

10 Quentin University, Garches, France

11 <sup>2</sup> Infectious disease unit, University Hospital of Grenoble, Grenoble, France

12 <sup>3</sup> Infectious disease unit, Cornouaille Hospital, Quimper, France

13 <sup>4</sup> Infectious disease department, University Hospital of Montpellier, Montpellier, France

14 <sup>5</sup> Infectious disease unit, La Pitié-Salpêtrière University Hospital, AP-HP, Paris, France

15 <sup>6</sup> Infectious disease unit, Hospital of Antibes, Antibes, France

16 <sup>7</sup> Infectiologie transversale, Hospital of Grasse, Grasse, France

17 <sup>8</sup> Infectious disease unit, Hospital of Périgueux, Périgueux, France

18 <sup>9</sup> Infectious disease unit, University Hospital of Angers, Angers, France

19 <sup>10</sup> Pharmacy department, Raymond Poincaré University Hospital, AP-HP, Versailles Saint-

20 Quentin University, Garches, France

21 <sup>11</sup> Infectious disease unit, University Hospital of Nice, Nice, France

22 <sup>12</sup> Antimicrobial stewardship team, Saint Philibert - Saint Vincent de Paul hospitals, GHICL,

23 Lille, France

24 <sup>13</sup> Intensive care unit, University Hospital of Bordeaux, Bordeaux, France

25 <sup>14</sup> Infectious disease department, University Hospital of Dijon, Dijon, France

26 <sup>15</sup> Antimicrobial stewardship team, Les Fleurs Clinic, Toulon, France

27 <sup>16</sup> Infectious disease unit, Pontchaillou University Hospital, Rennes, France

28 <sup>17</sup> Infectious disease unit, Caremeau University Hospital, Nîmes, France

29 <sup>18</sup> Infectious disease unit, Hotel-Dieu University Hospital, Nantes, France

30 <sup>19</sup> Infectious disease unit, Hospital of Mont-de-Marsan, Mont-de-Marsan, France

31 <sup>20</sup> Infectious disease unit, Hospital of Tourcoing, Tourcoing, France

32

33 **Running title:** National cohort of first use of dalbavancine

34

35 Corresponding author:

36 Aurélien Dinh

37 Infectious disease unit

38 Raymond Poincaré University Hospital, AP-HP

39 Versailles Saint-Quentin University

40 104 Bd Raymond Poincaré, 92380 Garches

41 Tel: +33147104432

42 Fax: +33147107790

43 aurelien.dinh@aphp.fr

44

45 **Abstract**

46 Dalbavancin is a glycopeptide antibiotic with a long half-life, recently marketed in Europe for  
47 skin and soft tissue infections (SSTI), but real-life use is not well-known. We aimed to  
48 describe all first prescriptions in France over an 18-month period.

49 We performed a retrospective study on all adult patients who received at least one dose of  
50 dalbavancin from July 1<sup>st</sup>, 2017 to September 31<sup>st</sup>, 2018. Data were collected thanks to a  
51 standard questionnaire. Failure was defined as: persistent or reappearance of signs of  
52 infection; and/or switch to suppressive antibiotic treatment; and/or death from infection.

53 We included 75 patients from 29 French hospitals.

54 Main indications were bone and joint infections (BJIs) (64.0%), endocarditis (25.3%), and  
55 SSTIs (17.3%).

56 Main bacteria involved were: *Staphylococcus aureus* (51.4%), including methicillin-resistant  
57 *S. aureus* (MRSA) (19.4%); and coagulase-negative staphylococci (CNS) (44.4%).

58 Median MICs for staphylococci to vancomycin and dalbavancin ranged from 0.875 mg/L to  
59 2.0 mg/L, and 0.040 mg/L to 0.064 mg/L, respectively.

60 Dalbavancin was used after a mean of  $2.3 \pm 1.2$  lines of antimicrobial treatment.

61 Main treatment regimens for dalbavancin were a weekly 2-dose regimen (1500mg each) in  
62 38 (53.2%) cases, and a single-dose regimen (1500mg) in 13 (18.3%) cases.

63 Overall, at the patients' last visit, clinical cure was observed in 54/72 patients, while failure  
64 was found in 14/72 patients.

65 First uses of dalbavancin in France were mostly off-label. Most of them were due to BJIs, and  
66 often as rescue therapy for severe infections. Even in off-label situations, dalbavancin seems  
67 safe and effective.

68 **Keywords:** dalbavancin; off-label; bone and joint infection; endocarditis; staphylococci

69        **1. Introduction**

70        Dalbavancin is a novel long-lasting glycopeptide approved for the treatment of skin and soft  
71        tissue infections (SSTIs) as an infusion in a single dose (1500 mg IV) or as 2 doses (1000 mg IV  
72        followed by 500 mg IV 7 days later) [1,2].

73        It has an excellent bactericidal activity against Gram-positive bacteria, especially  
74        *Staphylococcus aureus*, and a prolonged half-life of 14 to 15 days [3,4]. Its unique  
75        pharmacokinetic properties enable the treatment of serious infections as bone and joint  
76        infection (BJI) [5].

77        But few data on its current use is available since it has been marketed.

78        The objective of this study was to describe a national cohort comprising the first  
79        prescriptions of dalbavancin in the 18 months following access market in France.

80

81        **2. Material and methods**

82        We performed a national retrospective study of all adult patients who received at least one  
83        dose of dalbavancin from July 1<sup>st</sup>, 2017 to September 31<sup>st</sup>, 2018.

84        Standardized questionnaires were sent to the prescribers to collect patients' baseline  
85        characteristics, infection's type and management, identification of pathogens involved,  
86        reasons for dalbavancin use, doses and duration of dalbavancin treatment, adverse drug  
87        reactions (ADRs), and outcome.

88        No patient included in the study expressed opposition to the use of clinical data in this  
89        retrospective study. The research was conducted in accordance with the Declaration of  
90        Helsinki and national and institutional standards.

91 Immunosuppression was defined as: asplenia, neutropenia, agammaglobulinemia, organ  
92 transplant, hematologic malignancies, known HIV and CD4<400/mm<sup>3</sup>, or Child-Pugh class C  
93 cirrhosis.

94 Were considered as immunosuppressive treatment: corticosteroid if daily dose > 20mg of  
95 prednisolone equivalent, chemotherapy or immunosuppressive treatment, such as  
96 cyclophosphamide, azathioprine, and cyclosporine.

97 Liver failure was defined by a factor V ≤ 50% and/or hepatic encephalopathy.

98 Disseminated disease was considered when, at least, two different sites were infected.

99 Minimum inhibitory concentrations (MIC) of dalbavancin and vancomycin were obtained  
100 with the agar dilution susceptibility method or the broth microdilution procedure, according  
101 to local procedure. The breakpoints used were those defined by the French Committee for  
102 Antimicrobial Susceptibility Testing (CA-SFM) [6].

103 Outcome was evaluated by the investigators at the patients' latest visit after completion of  
104 their dalbavancin treatment. In case of suppressive treatment by dalbavancin, outcome was  
105 evaluated at the latest control visit.

106 Clinical cure was defined as the absence of clinical signs of infection and was confirmed by  
107 the physician on charge.

108 Failure was defined as a composite of the following criteria: persistent or reappearance of  
109 signs of infection with or without microbiological identification; and/or switch to suppressive  
110 antibiotic treatment; and/or death from infection.

111 Quantitative variables are presented as mean and standard deviation (SD), or median and  
112 interquartile range (IQR). Qualitative variables are presented as number of occurrences and  
113 relative frequencies. All analyses were performed using the SPSS 17.0 software (SPSS Inc,  
114 Chicago, IL, USA).

115 **3. Results**

116 Overall, 75 patients from 29 French hospitals were included in the study.

117 Demographic and baseline characteristics of the study population are shown in Table 1.

118 The main types of infection treated by dalbavancin were: bone and joint infections (BJI)  
119 (64.0%), endocarditis (25.3%), skin and soft tissue infections (SSTI) (17.3%). Concomitant  
120 bacteraemia to infections was reported in 38 patients (50.7%).

121 Of the 72 documented infections (Table 1), 25 (34.7%) were polymicrobial. The main Gram-  
122 positive pathogens identified were: *S. aureus* (n=37; 51.4%), including methicillin-resistant *S.*  
123 *aureus* (MRSA) (n=14; 19.4%); coagulase-negative staphylococci (CNS) (n=32; 44.4%).

124 The median minimum inhibitory concentrations (MIC) of dalbavancin depending on the  
125 bacteria were: 0.064 mg/L (IQR 0.051-0.064) for *S. aureus* and MRSA, 0.047 mg/L (IQR 0.047-  
126 0.064) for methicillin-susceptible *S. aureus* (MSSA), 0.047 mg/L (IQR 0.025-0.064) for *S.*  
127 *epidermidis*, and 0.032 mg/L (IQR 0.023-0.064) for methicillin-resistant *S. epidermidis*  
128 (MRSE).

129 The median MICs of vancomycin depending on the bacteria were: 1.0 mg/L (IQR 0.094-1.0)  
130 for *S. aureus*, 0.875 mg/L (IQR 0.173-1.375) for MRSA, 1.0 mg/L (IQR 0.297-1.0) for MSSA, 2.0  
131 mg/L (IQR 1.125-2.0) for *S. epidermidis*, and 2.0 mg/L (IQR 1.675-2.0) for MRSE.

132 Among our patients, 74 (98.7%) had received a prior antibiotic treatment, with a mean of 2.3  
133  $\pm$ 1.2 lines (range 1-8).

134 The most common antimicrobials prescribed were: rifampin (n=21; 28.4%), daptomycin  
135 (n=20; 27.0%), linezolid (n=19; 25.7%), fluoroquinolones (n=19; 25.7%), vancomycin (n=17;  
136 23.0%), clindamycin (n=16; 21.6%), and cefazolin (n=16; 21.6%).

137 Median duration of previous antibiotic therapy was 22.5 days (IQR 14.3-39.8).

138 Main reasons for switching to dalbavancin treatment are also described in Table 1.

139 Several dalbavancin treatment regimens were recorded and are presented in Table 2, with  
140 dosing regimens according to the site of infection.

141 Concomitant antibiotics were used with dalbavancin for 34 (45.3%) patients. The most  
142 frequently antibiotics used were rifampicin (n=12; 35.3%), sulfamethoxazole-trimethoprim  
143 (n=10, 29.4%), fluoroquinolones and tetracyclines (n=6; 17.6%, each).

144 Outcomes in total and according to type of infection are shown in Table 2. Overall, at the  
145 patients' last visit, with a mean follow-up duration of  $87.8 \pm 86.9$  days, clinical cure with  
146 dalbavancin was observed in 54/72 patients. Failure was found in 14/72 patients. Nine  
147 patients received an antibiotic suppressive treatment after the end of their dalbavancin  
148 treatment. Two patients died from their infections. Also, 2 microbiological failures were  
149 reported, and 1 clinical failure was not microbiologically documented (endocarditis). Finally,  
150 4 patients died from non-infectious causes, 1 patient was lost to follow-up, and 2 patients  
151 were initially misdiagnosed, and their antibiotic treatments were either altered or  
152 discontinued.

153 Main dalbavancin treatment regimens among cured patients were: two 1500 mg injections  
154 with a 7-day interval (n=26; 48.2%), or a 14-day interval (n=6; 11.1%); and a single 1500 mg  
155 injection (n=7; 13.0%).

156 After patient's discharge from the hospital, dalbavancin was administered in outpatient  
157 parenteral antimicrobial therapy (OPAT) setting (n=37; 49.3%).

158 Only 5 ADRs were reported, without any dalbavancin treatment discontinuation. Two ADRs  
159 concurred with hypersensitivity to dalbavancin (erythematous rash; chills and fever after the  
160 first infusion). One patient suffered from headaches. An increase in eosinophils level was  
161 also reported, which was self-resolving. Lastly, one patient had local inflammatory signs  
162 after a single infusion of 1500 mg dalbavancin.



163 **4. Discussion**

164 Dalbavancin is a novel antibiotic with a long half-life, which received its label for SSTI.

165 Few recent studies present the experience of dalbavancin in some specific indications, e.g.

166 osteomyelitis or endocarditis [5,7]. One study focused on real-life experience of dalbavancin,

167 but not with a national scale and not since the very beginning of market access [8].

168 The originality of this study is to describe the first use, since dalbavancin is available, in real

169 life, at a national level.

170 Our study results show a high off-label use, with only 4 (5.3%) patients receiving dalbavancin

171 as approved. They suggest that dalbavancin is a well-tolerated and effective treatment for

172 different Gram-positive infections, especially those with off-label indications. Global cure

173 rate was high (79.4%), despite dalbavancin being mostly used as salvage therapy.

174 A substantial proportion of our patients presented with BJIs.

175 Regarding BJIs, a randomized controlled trial recently compared dalbavancin *versus* standard

176 of care and reported a good efficacy with two 1500 mg IV injections of dalbavancin [5].

177 In literature, dalbavancin is associated with a high rate of clinical success (from 78% to 97%)

178 in this indication as in our study [5,8–12].

179 Our study also included 19 cases of endocarditis with a 73.2% cure rate.

180 A recent study shows high efficacy of dalbavancin in first line or as salvage therapy during

181 endocarditis [7].

182 However, it should be noted that most of these patients (88.9%) received dalbavancin as

183 salvage therapy.

184 Overall, the optimal scheme of administration is still under debate in literature [5,8–

185 12,7,13,14].

186 The most prescribed regimen in our study was 1500 mg on day 1 and day 8, but it seems that  
187 other regimens, such as 1500 mg twice with a 14-day interval or a single 1500 mg injection  
188 are also effective, whatever the indication.

189 These dosages (1500mg) are higher than those used in the pivotal trial which included only  
190 SSTI [15]. Indeed, data on 1500mg dosages at day 1 and 8 were supported by clinical studies  
191 on BJI [5]. Nonetheless, more data on optimal dosages are still warranted.

192 Also, in our study, dalbavancin was used in combination in 34 cases with low cure rate  
193 (66.7%), whereas the cure rate was 91.4% when it was used in monotherapy.

194 The need for combination during dalbavancin treatment is still discussed in the literature.

195 One previous study reported that > 35% of patients received combination treatment with a  
196 worst clinical course than in our study [8]. It could probably be due to the severity of the  
197 disease, thus physicians are more prone to prescribe combination therapy.

198 In a foreign-body infection experimental model with MRSA, the activity of dalbavancin, in  
199 combination with rifampicin, was superior to dalbavancin alone and prevented from  
200 emergence of rifampicin resistance [16]. So, the benefit of combination therapy with  
201 dalbavancin, according to indications and microorganism involved, needs to be further  
202 evaluated with interventional clinical studies.

203 Median MIC for staphylococci to vancomycin and dalbavancin ranged from 0.875 mg/L to 2.0  
204 mg/L, and 0.032 mg/L to 0.064 mg/L, respectively. This underlines its efficacy even in cases  
205 of resistant bacteria to vancomycin.

206 Lastly, the number of reported ADRs in this study was similar to what is found in literature  
207 [5,8–12,7,13,14]. Therefore, in our study, dalbavancin demonstrated an excellent safety  
208 profile, which is consistent with the results from a previous safety analysis [17].

209 There are several limitations of this study: the small number of patients and the  
210 retrospective nature of the analysis and absence of long-term follow-up.

211

212 **5. Conclusions**

213 In our experience, dalbavancin was used mainly in off-label indications, and often as rescue  
214 therapy for severe infections. Even in these situations, dalbavancin seems safe and effective.

215

216 **Acknowledgments:**

217 The authors acknowledge as co-authors all of the following Dalbavancin French study group  
218 members:

219 Chandra Adjodah (Montreuil-sur-mer), Nicolas Baclet (Lille), Odile Bouchard (Avignon),  
220 David Boutoille (Nantes), Guillaume Brunin (Boulogne-sur-Mer), Daniel Carbognani  
221 (Perpignan), Pierre Delobel (Toulouse), H el ene Ferrand (Libourne), Yves Imbert (Agen),  
222 Sophie Leautez-Nainville (La-Roche-sur-Yon), Vincent Le Moing (Montpellier), Bouchra Loutfi  
223 (Mont-de-Marsan), Natacha Mrozek (Clermont-Ferrand), Nicolas Rouzic (Lorient), Jean-  
224 Philippe Talarmin (Quimper), Pierre Tattevin (Rennes), Pierre Weyrich (Lille).

225

226 **Declarations**

227 **Funding:** No funding

228 **Competing Interests:** None

229 **Ethical Approval:** Not required

230

231

232 **References**

- 233 [1] Food and Drug Administration (FDA). DALVANCE highlights of prescribing information  
234 n.d. [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2014/021883s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/021883s000lbl.pdf)  
235 (accessed May 10, 2019).
- 236 [2] European Medicines Agency (EMA). Xydalba summary of product characteristics n.d.  
237 [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002840/WC500183869.pdf)  
238 [\\_Product\\_Information/human/002840/WC500183869.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002840/WC500183869.pdf) (accessed May 10, 2019).
- 239 [3] Candiani G, Abbondi M, Borgonovi M, Romanò G, Parenti F. In-vitro and in-vivo  
240 antibacterial activity of BI 397, a new semi-synthetic glycopeptide antibiotic. *J*  
241 *Antimicrob Chemother* 1999;44:179–92.
- 242 [4] Streit JM, Fritsche TR, Sader HS, Jones RN. Worldwide assessment of dalbavancin  
243 activity and spectrum against over 6,000 clinical isolates. *Diagn Microbiol Infect Dis*  
244 2004;48:137–43. doi:10.1016/j.diagmicrobio.2003.09.004.
- 245 [5] Rappo U, Puttagunta S, Shevchenko V, Shevchenko A, Jandourek A, Gonzalez PL, et al.  
246 Dalbavancin for the Treatment of Osteomyelitis in Adult Patients: A Randomized  
247 Clinical Trial of Efficacy and Safety. *Open Forum Infect Dis* 2019;6:ofy331.  
248 doi:10.1093/ofid/ofy331.
- 249 [6] Société Française de Microbiologie (SFM), The European Committee on Antimicrobial  
250 Susceptibility Testing (EUCAST). [Recommendations CASFM / EUCAST][In French] n.d.  
251 <https://www.sfm-microbiologie.org/2019/05/06/casfm-eucast-2019-v2/> (accessed  
252 May 9, 2019).
- 253 [7] Tobudic S, Forstner C, Burgmann H, Lagler H, Ramharter M, Steininger C, et al.  
254 Dalbavancin as Primary and Sequential Treatment for Gram-Positive Infective  
255 Endocarditis: 2-Year Experience at the General Hospital of Vienna. *Clin Infect Dis*

- 256 2018;67:795–8. doi:10.1093/cid/ciy279.
- 257 [8] Bouza E, Valerio M, Soriano A, Morata L, Carus EG, Rodríguez-González C, et al.  
258 Dalbavancin in the treatment of different gram-positive infections: a real-life  
259 experience. *Int J Antimicrob Agents* 2018;51:571–7.  
260 doi:10.1016/J.IJANTIMICAG.2017.11.008.
- 261 [9] Wunsch S, Krause R, Valentin T, Prattes J, Janata O, Lenger A, et al. Multicenter clinical  
262 experience of real life Dalbavancin use in gram-positive infections. *Int J Infect Dis*  
263 2019;81:210–4. doi:10.1016/j.ijid.2019.02.013.
- 264 [10] Bryson-Cahn C, Beielor AM, Chan JD, Harrington RD, Dhanireddy S. Dalbavancin as  
265 Secondary Therapy for Serious *Staphylococcus aureus* Infections in a Vulnerable  
266 Patient Population. *Open Forum Infect Dis* 2019;6:ofz028. doi:10.1093/ofid/ofz028.
- 267 [11] Morata L, Cobo J, Fernández-Sampedro M, Guisado Vasco P, Ruano E, Lora-Tamayo J,  
268 et al. Safety and Efficacy of Prolonged Use of Dalbavancin in Bone and Joint Infections.  
269 *Antimicrob Agents Chemother* 2019;63. doi:10.1128/AAC.02280-18.
- 270 [12] Almangour TA, Perry GK, Terriff CM, Alhifany AA, Kaye KS. Dalbavancin for the  
271 management of gram-positive osteomyelitis: Effectiveness and potential utility. *Diagn*  
272 *Microbiol Infect Dis* 2019;93:213–8. doi:10.1016/j.diagmicrobio.2018.10.007.
- 273 [13] Raad I, Darouiche R, Vazquez J, Lentnek A, Hachem R, Hanna H, et al. Efficacy and  
274 Safety of Weekly Dalbavancin Therapy for Catheter-Related Bloodstream Infection  
275 Caused by Gram-Positive Pathogens. *Clin Infect Dis* 2005;40:374–80.  
276 doi:10.1086/427283.
- 277 [14] Bork JT, Heil EL, Berry S, Lopes E, Davé R, Gilliam BL, et al. Dalbavancin Use in  
278 Vulnerable Patients Receiving Outpatient Parenteral Antibiotic Therapy for Invasive  
279 Gram-Positive Infections. *Infect Dis Ther* 2019. doi:10.1007/s40121-019-0247-0.

- 280 [15] Boucher HW, Wilcox M, Talbot GH, Puttagunta S, Das AF, Dunne MW. Once-Weekly  
281 Dalbavancin versus Daily Conventional Therapy for Skin Infection. *N Engl J Med*  
282 2014;370:2169–79. doi:10.1056/NEJMoa1310480.
- 283 [16] Baldoni D, Furustrand T, Aeppli S, Angevaere E, Oliva A, Haschke M, et al.  
284 Activity of dalbavancin, alone and in combination with rifampicin, against meticillin-  
285 resistant *Staphylococcus aureus* in a foreign-body infection model. *Int J Antimicrob*  
286 *Agents* 2013;42:220–5. doi:10.1016/j.ijantimicag.2013.05.019.
- 287 [17] Dunne MW, Talbot GH, Boucher HW, Wilcox M, Puttagunta S. Safety of Dalbavancin in  
288 the Treatment of Skin and Skin Structure Infections: A Pooled Analysis of Randomized,  
289 Comparative Studies. *Drug Saf* 2016;39:147–57. doi:10.1007/s40264-015-0374-9.
- 290
- 291

**Table 1:** Study patients' demography, baseline characteristics, and description of dalbavancin use

	<b>N = 75</b>
Age (years, mean, SD)	63.1 ± 17.0
Sex ratio (M/F)	2.26
<b>Hospitalization</b>	
Length of stay (d, mean, SD)	25.2 ± 25.8
Hospital ward (n, %)	
Intensive care unit (ICU)	6 (8.0)
Medecine	64 (85.3)
Surgery	7 (9.3)
Other	3 (4.0)
<b>Comorbidities (n, %)</b>	
Chronic respiratory failure	6 (8.0)
Heart failure	28 (37.3)
Chronic renal failure	10 (13.3)
Liver failure	7 (9.3)
Neurological disease	15 (20.0)
Immunosuppression	25 (33.3)
Blood disorder	3 (4.0)
Chemotherapy	4 (5.3)
Immunosuppressive treatment	5 (6.7)
Corticotherapy (> 20 mg/L per day)	2 (2.7)
Diabetes mellitus	19 (25.3)
Organ transplant	1 (1.3)
Renal clearance (mL/min, mean, SD)	90.8 ± 42.5
Allergy to antibiotics	9 (12.0)
<b>Before hospitalization (n, %)</b>	
Outpatient	56 (74.7)
Institutionalized	6 (8.0)
Other hospital	11 (14.7)
<b>Site of infection (n, %)</b>	
Disseminated disease	19 (25.3)
Bone and joint infection	48 (64.0)
Endocarditis	19 (25.3)
Native valve	9 (12.0)
Prosthetic valve	10 (13.3)
Skin and soft tissue infection	13 (17.3)
Vascular infection	5 (6.7)
Catheter-line infection	4 (5.3)
Bloodstream infection	3 (4.0)
Mediastinitis	2 (2.7)
<b>Severity (n, %)</b>	
Septic shock	6 (8.0)
ICU admission during episode	7 (9.3)
Mechanical ventilation	2 (2.7)



Vasopressor requirement	2 (2.7)
Volume expansion	5 (6.7)
<b>Before dalbavancin treatment</b>	
Biological analysis (mean, SD)	
White blood count (G/L)	9.4 ± 4.4
Hemoglobin (g/dL)	10.7 ± 1.9
Absolute neutrophil count (G/L)	6.6 ± 3.3
Eosinophil count (G/L)	0.3 ± 0.4
C-Reactive Protein (mg/L)	81.3 ± 81.9
Surgical treatment (n, %)	47 (62.7)
DAIR	12
Previous antibiotic treatments (n, %)	74 (98.7%)
Number of lines (mean, SD)	2.3 ± 1.2
Duration (d, median, IQR)	22.5 (14.3-39.8)
<b>Microbiology analysis (n, %)</b>	
Documented infections	72 (96.0)
Polymicrobial infections	25 (34.7)
<i>Staphylococcus</i> sp.	69 (95.8)
<i>S. aureus</i>	37 (51.4)
Methicillin-resistant <i>S. aureus</i>	14 (19.4)
Coagulase-negative staphylococci	32 (44.4)
<i>S. epidermidis</i>	24 (33.3)
Methicillin-resistant <i>S. epidermidis</i>	15 (20.8)
<i>Enterococcus faecalis</i>	5 (6.9)
<i>Corynebacterium</i> sp.	5 (6.9)
<b>Reason for Dalbavancin use (n, %)</b>	
Clinical failure of previous antibiotic treatment	16 (21.3)
Microbiological failure of previous antibiotic treatment	4 (5.3)
Adverse event of previous antibiotic treatment	26 (34.7)
Multidrug-resistant bacteria	17 (22.7)
Impossible venous access	18 (24.0)
Patient's autonomy	29 (38.7)
Early hospital discharge	26 (34.7)
Better compliance	21 (28.0)

---

Y: year; d: days; SD: standard deviation; M: male; F: female; DAIR: debridement, antibiotics and implant retention

**Table 2:** Dalbavancin dosing regimen and patients' outcome in total and according to site of infection

	TOTAL (n=75)	BJI (n=48)	Endocarditis (n=19)	SSTI (n=13)	Vascular infection (n=5)	CLI (n=4)	BSI (n=3)	Mediastinitis (n=2)
<b>Dalbavancin dosing regimen (n)</b>								
<b>1 dose</b>	<b>15</b>	<b>5</b>	<b>2</b>	<b>5</b>	<b>1</b>	<b>3</b>	<b>2</b>	<b>0</b>
1 g	2	1	0	1	0	1	0	0
1.5 g	13	4	2	4	1	2	2	0
<b>2 doses</b>	<b>44</b>	<b>34</b>	<b>11</b>	<b>7</b>	<b>2</b>	<b>1</b>	<b>1</b>	<b>1</b>
Unknown	2	0	2	0	0	0	0	0
<i>7-day interval</i>								
1 g - 0.5 g	1	0	0	0	1	0	0	0
1 g x2	1	1	0	0	0	0	0	0
1.5 g x2	31	29	5	5	0	0	1	1
<i>14-day interval</i>								
1.5 g - 1 g	1	1	1	0	0	0	0	0
1.5 g x2	7	2	3	2	1	1	0	0
<i>21-day interval</i>								
1.5 g - 0.5 g	1	1	0	0	0	0	0	0
<b>3 doses</b>	<b>2</b>	<b>1</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
<i>7-day interval</i>								
1.5 g - 0.5 g x2	1	0	1	0	0	0	0	0
1.5 g x3	1	1	0	0	0	0	0	0
<b>4 doses</b>	<b>4</b>	<b>3</b>	<b>1</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
<i>7-day interval</i>								
1.5 g x4	1*	0	0	0	0	0	0	0
<i>14-day interval</i>								
1 g - 0.5 g x3	2	2	0	0	0	0	0	0
1.5 g x4	1	1	1	1	0	0	0	0
<b>&gt; 4 doses (max 10)</b>	<b>5</b>	<b>3</b>	<b>1</b>	<b>0</b>	<b>2</b>	<b>0</b>	<b>0</b>	<b>0</b>
<i>7-day interval</i>								
1 g - 0.5 g xN	1	1	0	0	0	0	0	0
1.5 g - 0.5 g xN	1	1	0	0	0	0	0	0
<i>14-day interval</i>								
1 g - 0.5 g xN	2	1	1	0	1	0	0	0
1.5 g xN	1	0	0	0	1	0	0	0
<b>Suppressive</b>	<b>3</b>	<b>2</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>1</b>
<i>21-day interval</i>								
1.5 g - 0.5 g xN	1	1	0	0	0	0	0	0
1.5 g x3 - 0.5 g xN	1	1	0	0	0	0	0	0
1.5 g xN	1	0	1	0	0	0	0	1
<b>Outcome at last visit** (n, %)</b>								
Cure	54/68	35/46	13/18	9/11	5/5	2/2	1/1	1/2

	(79.4)	(76.1)	(72.2)	(81.8)	(100)	(100)	(100)	(50.0)
Failure	14/68 (20.6)	11/46 (23.9)	5/18 (27.8)	2/11 (18.2)	0 (0)	0 (0)	0 (0)	1/2 (50.0)
Delay since first dose (d, mean, SD)	87.8 ± 86.9	80.0 ± 73.9	97.9 ± 99.7	102.8 ± 96.6	88.0 ± 81.1	36.0 ± 26.9	82.5 ± 27.6	182

\*1 patient with other indication

\*\* Patients lost to follow-up, who died from non-infectious causes, or misdiagnosed are excluded.

BJI: Bone and joint infection; BSI: Bloodstream infection; CLI: Catheter-line infection; SSTI: Skin and soft tissue infection; d: Day; SD: Standard deviation