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Dalbavancin in Osteomyelitis and Joint Infections: An Analysis From an Observational, Multicenter, Retrospective Cohort Study of Real-World Use in Adult Patients

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CONCLUSIONS

In this real-world study of patients with staphylococcal osteomyelitis or joint infection, dalbavancin resulted in high rates of clinical and microbiological success

Most patients required either 1 or 2 IV doses of dalbavancin, and the majority were treated without admission to hospital

The rate of SAEs was low, consistent with the safety profile of dalbavancin; no new safety signals were identified

RESULTS

Study Population

- Data for 96 patients with osteomyelitis and 33 patients with joint infection (safety population) were entered into this subanalysis **(Table 1)**.

Table 1. Patient Baseline Demographics, Medical History, and Laboratory Parameters

	Safety Population		Evaluable Population	
Patient Characteristics	Osteomyelitis (n=96)	Joint Infection (n=33)	Osteomyelitis (n=78)	Joint Infection (n=32)
Demographics				
Age (median, range), years	58.0 (18–89)	59.0 (24–83)	58.0 (18–89)	59.0 (24–83)
Sex (M/F)	60/36 (62.5/37.5)	20/13 (60.6/39.4)	46/32 (59.0/41.0)	19/13 (59.4/40.6)
Ethnicity				
Hispanic or Latino	9 (9.4)	1 (3.0)	7 (9.0)	1 (3.1)
Not Hispanic or Latino	85 (88.5)	32 (97.0)	69 (88.5)	31 (96.9)
Not Reported	2 (2.1)	—	2 (2.6)	—
Race				
White	80 (88.3)	29 (87.9)	64 (82.1)	28 (87.5)
Black or African American	9 (9.4)	3 (9.1)	8 (10.3)	3 (9.4)
Asian	1 (1.0)	1 (3.0)	1 (1.3)	—
Not reported	5 (5.2)	1 (3.0)	4 (5.1)	1 (3.1)
Treatment history for this infection				
Home infusion treatment at onset of index infection	9 (9.9)	1 (3.0)	7 (9.5)	1 (3.1)
Hospitalization ≥2 days within 90 days before onset of index infection	40 (41.7)	9 (27.3)	30 (38.5)	8 (25.0)
Medical history				
Charlson Comorbidity Index, median (IQR)	3.0 (2.0, 5.0)	2.0 (1.0, 3.0)	3.0 (2.0, 5.0)	2.0 (0.5, 3.0)
Peripheral vascular disease	23 (24.0)	1 (3.0)	21 (26.9)	1 (3.1)
Cerebrovascular disease	2 (2.1)	0 (0.0)	0 (0.0)	0
Diabetes	55 (57.3)	7 (21.2)	46 (59.0)	7 (21.9)
With end-organ damage	44 (80.0)	4 (57.1)	37 (80.4)	4 (57.1)
Moderate to severe chronic kidney disease	15 (15.6)	5 (15.2)	14 (17.9)	4 (12.5)
GFR severity*				
30–59 (moderate)	11 (73.3)	3 (60.0)	10 (7.1)	2 (50.0)
15–29 (severe)	1 (6.7)	2 (40.0)	1 (7.1)	0
<15 or renal dialysis patient (very severe)	2 (13.3)	0 (0.0)	2 (14.3)	0
Hemodialysis	2 (100)*	—	2 (100.0)	—
Drug abuse (alcohol)	7 (7.3)	4 (12.1)	5 (6.4)	4 (12.5)
Drug abuse (non-alcohol)	12 (12.5)	6 (18.2)	10 (12.8)	6 (18.8)
Illicit needle use	11 (11.5)	5 (15.2)	9 (11.5)	5 (15.6)
Current or past smoker	29 (30.2)	17 (51.5)	21 (26.9)	16 (50.0)
Immunocompromised				
Leukemia	2 (2.1)	0 (0.0)	2 (2.6)	0 (0.0)
Malignant solid tumor	6 (6.3)	2 (6.1)	5 (6.4)	2 (6.3)
HIV (excluding AIDS)	0 (0.0)	1 (3.0)	0 (0.0)	1 (3.1)
Receiving steroid	0 (0.0)	2 (6.1)	0 (0.0)	2 (6.3)
Receiving TNF inhibitors	0 (0.0)	0 (0.0)	0 (0.0)	0
Receiving other immune-modulating medication (including biologics)	1 (1.0)	1 (3.0)	1 (1.3)	1 (3.1)
Receiving chemotherapy	3 (3.1)	0 (0.0)	3 (3.8)	0
Laboratory assessments				
Hemoglobin A1c, median (IQR), %	n=5 10.30 (6.90, 13.00)	n=1 6.80 (–, –)	n=5 10.30 (6.90, 13.00)	n=1 6.80 (–, –)
White blood cell count (× 10^3/L), median (IQR)	n=67 7.500 (6.550, 9.500)	n=28 8.450 (6.700, 10.500)	n=56 7.385 (6.475, 9.350)	n=27 8.300 (6.700, 10.500)
Serum creatinine (mg/dL), median (IQR)	n=68 1.000 (0.735, 1.345)	n=27 0.860 (0.750, 1.060)	n=56 1.000 (0.800, 1.345)	n=26 0.850 (0.750, 1.000)
C-reactive protein (mg/dL), median (IQR)	n=29 1.390 (0.900, 3.000)	n=8 10.600 (3.050, 32.700)	n=24 1.815 (0.950, 4.300)	n=7 10.800 (1.100, 54.200)

All data shown are n (%) unless otherwise noted.
*Denominator=number of patients with "yes" in parent question.
GFR=glomerular filtration rate; IQR=interquartile range; TNF=tumor necrosis factor.

Dalbavancin Use

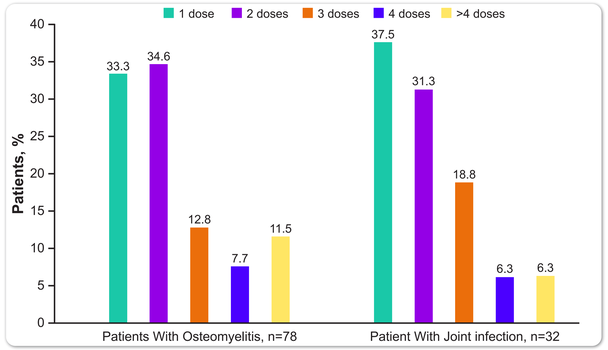
- The majority (80.4%–100%) of patients received dalbavancin as concurrent therapy **(Table 2)**
- Most patients received 1 or 2 IV dalbavancin doses total **(Figure 2)**
- For patients with osteomyelitis, mean (SD) total dalbavancin dose=2247.5 (1165.25) mg; median=2000 mg (interquartile range [IQR]: 1500.00, 3000.0 mg)
- For patients with joint infection, mean (SD) total dalbavancin dose=2101.6 (941.56) mg; median=2000 mg (IQR: 1500.00, 3000.0 mg)

Table 2. Final Diagnosis and Clinical Outcome by Dalbavancin Used as Monotherapy or Concurrent Therapy (Evaluable Population)

		Dalbavancin Use, n (%)			
Final Diagnosis	Clinical Success (n/N, %) [95% CI]*	Monotherapy	Concurrent Therapy	Clinical Success With Monotherapy [95% CI]*	Clinical Success With Concurrent Therapy [95% CI]*
Osteomyelitis					
All patients (n=78)	63/78 (80.8) [70.3–88.8]	11/78 (14.1)	67/78 (85.9)	9/11 (81.8) [48.2–97.7]	54/67 (80.6) [69.1–89.2]
Osteomyelitis of the foot (n=51)	43/63 (84.3) [71.4 to 93.0]	10/51 (19.6)	41/51 (80.4)	8/10 (80.0) [44.4–97.5]	35/41 (85.4) [70.8–94.4]
Osteomyelitis of upper body sites† (n=17)	11/17 (64.7)	0/17 (0.0)	17/17 (100.0)	0 (0.0)	11/17 (64.7)
Osteomyelitis of lower body sites† (n=10)	9/10 (90.0)	1/10 (10.0)	8/10 (80.0)	1/1 (100.0)	7/8 (87.5)
Joint infection					
All patients (n=32)	28/32 (87.5) [71.0–96.5]	4/32 (12.5)	28/32 (87.5)	4/4 (100.0)	24/28 (85.7) [67.3–96.0]
Knee (n=10)	8/10 (80.0) [44.4–97.5]	1/10 (10.0)	9/10 (90.0)	1/1 (100.0)	7/9 (77.8) [40.0–97.2]

*Where available.
†Upper body=skull, spine, thorax/ribs, hand, forearm, arm, shoulder; lower body=leg, thigh, hip, pelvis.

Figure 2. Number of Intravenous Dalbavancin Doses Received (Evaluable Population)



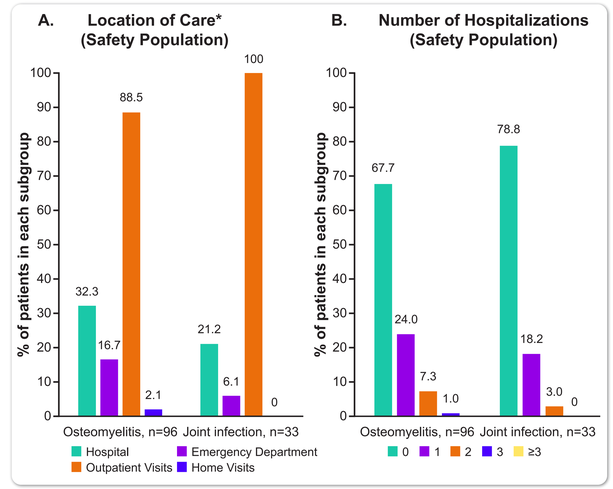
Clinical Outcome

- Clinical success, defined qualitatively, was achieved in 64.7%–87.5% of patients **(Table 2)**

Location of Care, Hospitalization and Discharge Destination

- The majority of patients with osteomyelitis were treated as hospital outpatients (88.5%); 32.3% were treated as hospital inpatients
- All patients with joint infections were treated at least once as hospital outpatients; 21.2% were hospitalized at some time during treatment **(Figure 3A)**
- A higher proportion of patients with joint infection (78.8%) were treated without the need for hospitalization, compared with osteomyelitis patients (67.7%), and a lower proportion required >1 hospitalization **(Figure 3B)**

Figure 3. Location of Care and Number of Hospitalizations (Safety Population)



*Any visits, patients may appear in >1 category.

- Mean (SD) length of hospital stay among patients with osteomyelitis who were hospitalized (n=31) was 7.2 (8.7) days
  - One patient (3.2%) was admitted to the intensive care unit, for 2 days
- Among 7 patients with joint infection who were hospitalized, mean (SD) length of stay was 2.9 (2.7) days
  - No patient with joint infection was admitted in the intensive care unit
- The majority of patients, 77.4% of patients with osteomyelitis and 100% of patients with joint infection, were discharged home following their hospital stay; the remaining osteomyelitis patients were discharged to a long-term-care facility

Microbiology

- The most frequently isolated organism at baseline was Staphylococcus spp.
- At 60 days post-dalbavancin treatment, numbers of Staphylococcus spp. isolated from both patient subgroups had decreased **(Table 3)**

Table 3. Isolation of *Staphylococcus* spp at Baseline and During and After Dalbavancin Treatment (Evaluable Population)

	Baseline	Dalbavancin Treatment Period	60 Days After End of IV Dalbavancin Treatment
Osteomyelitis, n (%)			
All patients (n=78)			
Specimen collected	35/78 (44.9)	14/78 (17.9)	13/78 (16.7)
Isolates grown from the specimen	29/35 (82.9)	8/14 (57.1)	7/13 (53.8)
Staphylococcus	20/29 (69.0)	6/8 (75.0)	2/7 (28.6)
Resistant to oxacillin	11/18 tested (61.1)	0 /4 tested (0.0)	1/1 tested (100.0)
Osteomyelitis of the foot (n=51), n (%)			
Specimen collected	24/51 (47.1)	10/51 (19.6)	9/51 (17.6)
Isolates grown from the specimen	21/24 (87.5)	6/10 (60.0)	5/9 (55.6)
Staphylococcus	14/21 (66.7)	5/6 (83.3)	1/5 (20.0)
Resistant to oxacillin	8/13 tested (61.5)	0/3 tested (0.0)	1/1 tested (100.0)
Joint infection (n=32), n (%)			
Specimen collected	19/32 (59.4)	3/32 (9.4)	2/32 (6.3)
Isolates grown from the specimen	15/19 (78.9)	2/3 (66.7)	2/2 (100.0)
Staphylococcus	15/15 (100.0)	2/2 (100.0)	2/2 (100.0)
Resistant to oxacillin	5/14 tested (35.7)	0/1 tested (50.0)	1/2 tested (50.0)

IV=intravenous.

Safety

- The rate of SAEs was low (16 events in 7 [7.3%] patients with osteomyelitis; 2 events in 2 [6.1%] patients with joint infection) and consistent with the safety profile of dalbavancin **(Table 4)**

Table 4. Serious Adverse Events Occurring in >2% of Patients (Safety Population)

	Osteomyelitis (n=96)		Joint Infection (n=33)	
	Patients, n (%)	Events (n)	Patients, n (%)	Events (n)
Any serious adverse event	7 (7.3)	16	2 (6.1)	2
Infection/infestation	6 (6.3)	10	1 (3.0)	1
Osteomyelitis	2 (2.1)	3	1 (3.0)	1

INTRODUCTION

- Dalvance® (dalbavancin; Allergan, Madison, NJ) is approved by the US Food and Drug Administration and the European Medicines Agency for the treatment of acute bacterial skin and skin structure infections (ABSSSIs) caused by susceptible isolates of designated Gram-positive microorganisms (including methicillin-susceptible and -resistant *Staphylococcus aureus*)[1,2]
  - Dalbavancin may be administered in either a 2-dose intravenous (IV) regimen (2 weekly doses on days 1 and 8) or as a single-dose regimen, for the same total dose of 1500 mg
- Bone and joint infections are challenging to treat, typically requiring 4–6 weeks of daily parenteral therapy, either by IV infusion or a peripherally inserted central catheter line
- A 2-dose regimen (1500 mg IV on days 1 and 8) of dalbavancin was effective and well tolerated in the treatment of adult patients with osteomyelitis[3]
- Dalvance Utilization Registry Investigating Value and Efficacy (DRIVE™) is a multicenter, retrospective cohort study designed to capture information about clinical use of dalbavancin in adult patients with ABSSSI and non-ABSSSI in the United States

Objectives

- To describe clinical features, use, efficacy, and safety of dalbavancin in 129 patients with osteomyelitis or joint infection in the real-world setting

METHODS

Patients and Study Design (Figure 1)

- DRIVE is a phase 4 observational, multicenter, retrospective cohort study designed to characterize the real-world use of dalbavancin in adult patients (≥18 years) across the United States
- Data were abstracted from medical records of eligible patients who had received ≥1 dose of dalbavancin, from the date of infectious disease diagnosis until 60 days after the last IV dose of dalbavancin
  - Data collection period: March 25, 2017, to November 27, 2018; 34 sites participated

Data Collection

- Collected data included demographic information, pathogen characteristics, systemic antibiotic use administration, adverse events (AEs) and serious AEs (SAEs) (Medical Dictionary for Regulatory Activities, version 20.0 or later)

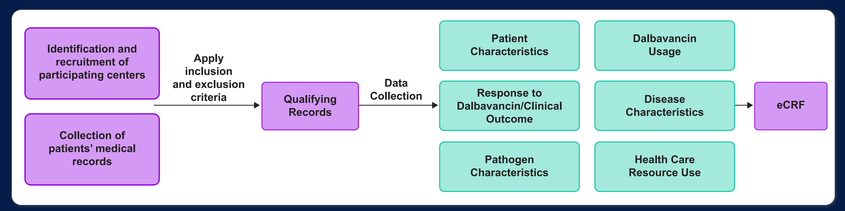
Clinical Outcome of Dalbavancin Treatment

- Success: dalbavancin discontinued due to no further need for dalbavancin, switch to oral antibiotic, or clinical improvement at time of discontinuation/patient discharge
- Failure: dalbavancin discontinued due to AE, insufficient therapeutic effect, or lack of clinical improvement at time of discontinuation/patient discharge
- Indeterminate: insufficient evidence to support clear categorization as success or failure

Statistical Analysis

- Subanalyses were performed using SAS® software version 9.4 or later (SAS Institute Inc., Cary, NC, USA)
- Safety population: all patients meeting all inclusion criteria and no exclusion criteria
- Evaluable population: all patients in the safety population with clear clinical success or failure

Figure 1. DRIVE Trial Design



eCRF=electronic case report form.

DISCLOSURES

This study was supported by Allergan (Dublin, Ireland; prior to its acquisition by AbbVie). Allergan (prior to its acquisition by AbbVie) was involved in the design and decision to present these results. Jennifer S. McGregor, John Lock, and Pedro L. Gonzalez are employees of AbbVie and may have stock. Ananthakrishnan Ramani has served as a speaker for Allergan plc and has received speakers honoraria from Allergan. Julia Garcia-Diaz and Yoav Golan have no disclosures.

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