Dalbavancina e oritavancina

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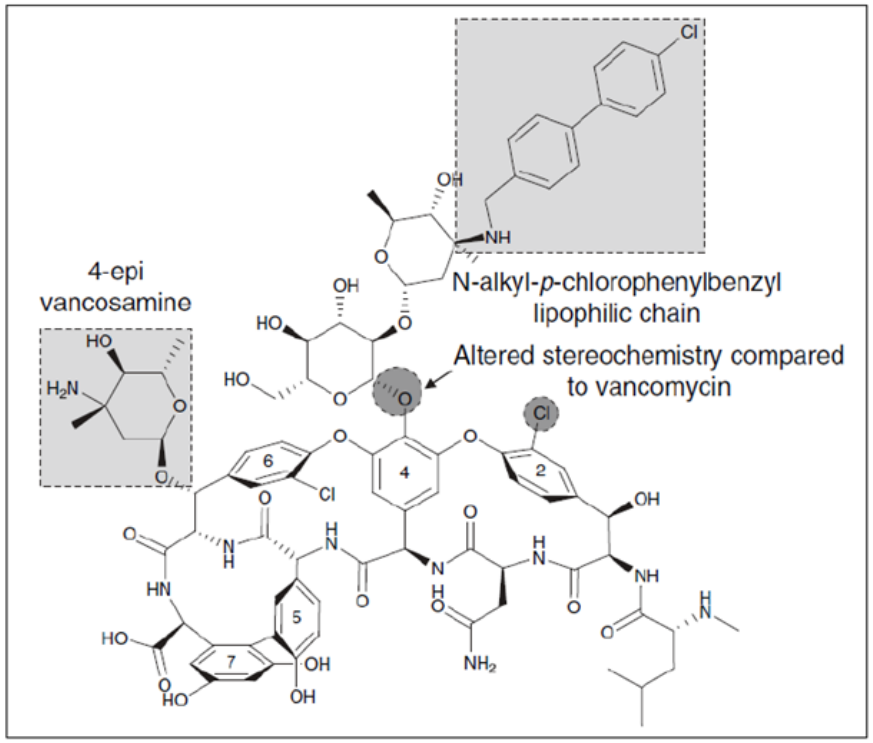
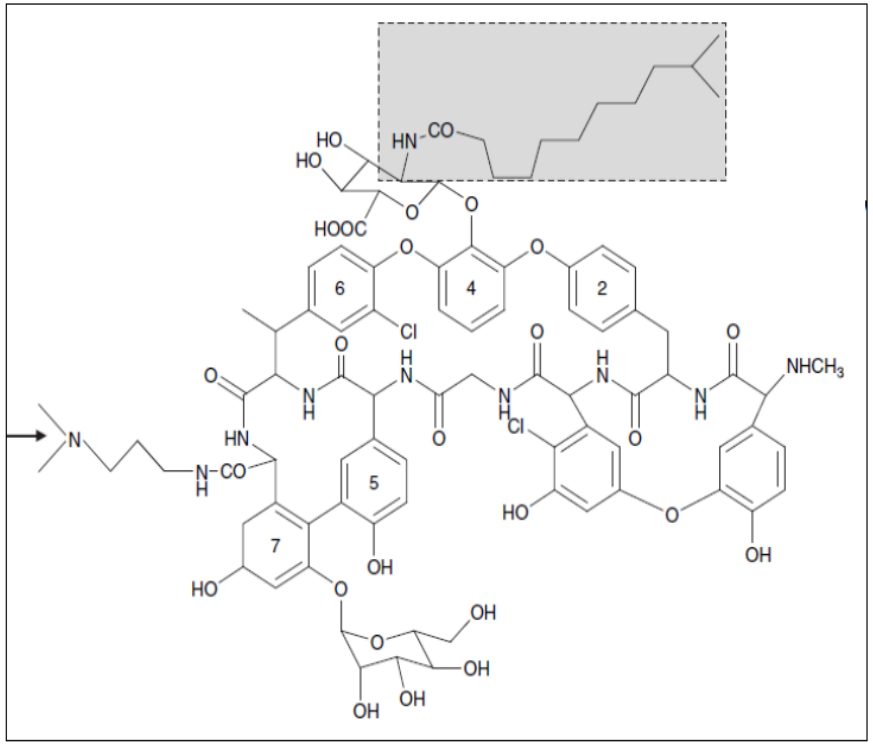
Dalbavancina e Oritavancina

- **Lypoglicopeptides**
- Concentration-dependent bactericidal activity.
- Interfere with peptidoglycan transglycosylation and transpeptidation and so inhibit cell wall synthesis.
- The presence of a lipophilic side chain in molecule prolongs the half-life of the drug and permits 1-time dosing.





- Compared to vancomycin and teicoplanin, these **lipoglycopeptides** have greater potency and less potential for development of resistant organisms.
- Currently FDA approved only for the treatment of skin and soft tissue infections.
- They have potential use in the treatment of other infections (case reports and randomized clinical trials have demonstrated success in treating more deep-seated or morbid infections, such as osteomyelitis, and endovascular infections, which typically require extended antibiotic durations).
- Long terminal half-lives wich may allow for infrequent dosing.

Table 1. Administration Considerations for Dalbavancin and Oritavancin

DRUG	DALBAVANCIN (DALVANCE)	ORITAVANCIN (ORBACTIV)
Half-life dosing	147-258 hours	393 hours
Dosing	Single dose: 1500 mg IV x 1 Two doses: 1000 mg IV x 1 initially, followed by 500 mg IV x 1, 1 week later	Single dose: 1200 mg IV x 1
Dose adjustment for renal impairment	If CrCl <30 mL/min: Single dose: 1225 mg IV x 1 Two doses: 750 mg IV x 1, followed by 375 mg IV x 1, 1 week later ESRD on iHD: No dose adjustment necessary; administer without regard to timing of hemodialysis	No dose adjustment for renal impairment Not studied for CrCl <30 mL/min Not removed by hemodialysis
Dose adjustment for hepatic impairment	No dose adjustment for mild hepatic impairment Not studied in moderate to severe hepatic impairment	No dose adjustment for Child-Pugh class A or B Not studied in Child-Pugh class C
Contraindications	Hypersensitivity	Hypersensitivity Use of IV unfractionated heparin should not occur for 120 hours (5 days) after oritavancin administration
Warnings/Precautions	Hypersensitivity Infusion reactions: Red man syndrome Superinfection: CDAD or pseudomembranous colitis Hepatic effects: Patients may have ALT elevation >3x ULN during therapy	Hypersensitivity Infusion reactions: Red man syndrome Superinfection: CDAD or pseudomembranous colitis Osteomyelitis
Common adverse drug events	Headache, pyrexia, nausea, vomiting, diarrhea, constipation	Phlebitis at injection site, fever, nausea, vomiting, diarrhea
Administration	Infuse over 30 minutes*	Infuse over 3 hours*

Once-Weekly Dalbavancin versus Standard-of-Care Antimicrobial Regimens for Treatment of Skin and Soft-Tissue Infections

Elyse Seltzer, Mary Beth Dorr, Beth P. Goldstein, Marc Perry, James A. Dowell

Table 2. Standard-of-care (comparator) antimicrobials used for treatment of skin and soft-tissue infections.

Antimicrobial	No. of patients receiving drug
Ceftriaxone alone or in combination	6
Cefazolin alone or in combination	4
Piperacillin and tazobactam in combination	3
Clindamycin alone	2
Vancomycin alone or in combination	4
Linezolid alone	1
Cephalexin alone	1

Table 3. Gram-positive pathogens isolated from samples obtained at baseline from patients with skin and soft-tissue infections (microbiological intent-to-treat population).

Pathogen	No. of patients with pathogen[a] in indicated treatment group		
	1-Dose dalbavancin (n = 14)	2-Dose dalbavancin (n = 13)	Comparator (n = 14)
Staphylococcus aureus	13	11	10
Methicillin-resistant *S. aureus*	6	5	2
Group B streptococcus	0	2	2
Streptococcus pyogenes	0	1	1
Miscellaneous *Streptococcus* and other species[b]	3	2	4

[a] More than 1 pathogen was detected in some patients at baseline.
[b] Includes β-hemolytic (nontypeable), group C, group G, and viridans streptococci and *Peptostreptococcus*.

Dalbavancin, a novel glycopeptide with a long elimination half-life (~9–12 days), was compared to standard antimicrobial therapy for skin and soft-tissue infections (SSTIs). In a randomized, controlled, open-label, phase 2 proof-of-concept trial, adults received 1100 mg of dalbavancin (as a single intravenous infusion), 1000 mg of dalbavancin intravenously and then 500 mg intravenously 1 week later, or a prospectively defined standard-of-care regimen. A gram-positive pathogen was isolated from samples obtained from 41 (66%) of 62 patients at baseline; *Staphylococcus aureus* was the most prevalent species (83% of pathogens). Clinical success rates at a follow-up visit (test of cure) were 94.1% among patients treated with 2 doses of dalbavancin, 61.5% among patients treated with 1 dose of dalbavancin, and 76.2% among patients treated with a standard-of-care regimen. All treatment regimens were well tolerated; drug-related adverse reaction rates were similar across the 3 groups. These findings suggest that a regimen of 2 doses of dalbavancin administered 1 week apart is effective in the treatment of complicated, gram-positive bacterial SSTIs and warrants further study.

Clinical Infectious Diseases 2003; 37:1298–1303

The NEW ENGLAND JOURNAL of MEDICINE

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Once-Weekly Dalbavancin versus Daily Conventional Therapy for Skin Infection

Helen W. Boucher, M.D., Mark Wilcox, M.D., George H. Talbot, M.D., Sailaja Puttagunta, M.D., Anita F. Das, Ph.D., and Michael W. Dunne, M.D.

- Pooled analysis of 2 phase 3, double-blind, double-dummy, international, multicenter, randomized trials (DISCOVER 1 and DISCOVER 2)
- Acute bacterial skin and skin-structure infection
- Dalbavancin 1000 mg d1, 500 mg d8 (659 pts) vs. Vancomycin iv for ≥3 days, then oral linezolid 600 mg bid to complete 10-14d (653 pts)
- Primary end point: early clinical response (cessation of spread of erythema and absence of fever at 48 to 72 hours).

Table 2. Primary and Secondary Efficacy End Points.*

End Point	Dalbavancin	Vancomycin–Linezolid	Absolute Difference (95% CI)
	number/total number (percent)		*percentage points*
Primary end point			
DISCOVER 1	240/288 (83.3)	233/285 (81.8)	1.5 (–4.6 to 7.9)
DISCOVER 2	285/371 (76.8)	288/368 (78.3)	–1.5 (–7.4 to 4.6)
Both trials	525/659 (79.7)	521/653 (79.8)	–0.1 (–4.5 to 4.2)
Sensitivity analysis			
DISCOVER 1	259/288 (89.9)	259/285 (90.9)	–1.0 (–5.7 to 4.0)
DISCOVER 2	325/371 (87.6)	316/368 (85.9)	1.7 (–3.2 to 6.7)
Both trials	584/659 (88.6)	575/653 (88.1)	0.6 (–2.9 to 4.1)
Secondary end point			
Clinical status	517/570 (90.7)	502/545 (92.1)	–1.5 (–4.8 to 1.9)
Sensitivity analysis of clinical status†	533/570 (93.5)	517/545 (94.9)	–1.4 (–4.2 to 1.4)
Investigator's assessment of outcome	547/570 (96.0)	527/545 (96.7)	–0.7 (–3.0 to 1.5)

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Table 4. Adverse Events.

Variable	Dalbavancin (N=652)	Vancomycin–Linezolid (N=651)	P Value*
Any adverse event			
Any event — no. of patients (%)	214 (32.8)	247 (37.9)	0.05
Total no. of events	540	645	0.05
Treatment-related adverse event†			
Any event — no. of patients (%)	80 (12.3)	89 (13.7)	0.45
Total no. of events	139	183	0.02
Serious adverse event — no. of patients (%)			
Any event	17 (2.6)	26 (4.0)	0.16
Treatment-related event†	2 (0.3)	4 (0.6)	0.41
Death — no. (%)‡	1 (0.2)	7 (1.1)	0.03
Treatment-limiting adverse event — no. of patients (%)§	14 (2.1)	13 (2.0)	0.85
Most common treatment-related adverse event — no. of patients (%)¶			
Nausea	16 (2.5)	19 (2.9)	0.62
Diarrhea	5 (0.8)	16 (2.5)	0.02
Pruritus	4 (0.6)	15 (2.3)	0.01

Adverse events and study days with an adverse event were less frequent in the dalbavancin group than in the vancomycin–linezolid group. The most common treatment-related adverse events in either group were nausea, diarrhea, and pruritus.

Clinical Infectious Diseases

MAJOR ARTICLE

A Randomized Clinical Trial of Single-Dose Versus Weekly Dalbavancin for Treatment of Acute Bacterial Skin and Skin Structure Infection

Michael W. Dunne,[1] Sailaja Puttagunta,[1] Philip Giordano,[2] Dainis Krievins,[3] Michael Zelasky,[1] and James Baldassarre[4]

Table 2. Clinical Response at Early and Late Timepoints

	Dalbavancin Treatment Group		
Timepoint	Single-Dose, no./No. (%)	2-Dose, no./No. (%)	Difference[a] (95% CI)
48–72 h			
Treatment response (ITT)	284/349 (81.4)	294/349 (84.2)	−2.9 (−8.5, 2.8)
Treatment nonresponder or indeterminate	65/349 (18.6)	55/349 (15.8)	
Death	0	1/55 (1.8)	
Antibacterial therapy for ABSSSI	4 /65 (6.2)	4/55 (7.3)	
Decrease of <20% in lesion area	41/65 (63.1)	34/55 (61.8)	
Missing lesion data	22/65 (33.8)	18/55 (32.7)	
Lesion area data outside window	15/65 (23.1)	11/55 (20.0)	
Treatment response (mITT)	284/349 (81.4)	294/346 (85.0)	−3.6 (−9.2, 2.0)
Treatment response at 36–75 hours (ITT)	293/349 (84.0)	298/349 (85.4)	−1.4 (−6.8, 4.0)
Day 14			
Clinical success (ITT)	293/349 (84.0)	296/349 (84.8)	−0.9 (−6.3, 4.6)
Clinical success (CE)	267/302 (88.4)	270/302 (89.4)	−1.0 (−6.1, 4.1)
Day 28			
Clinical success (ITT)	295/349 (84.5)	297/349 (85.1)	−0.6 (−6.0, 4.8)
Clinical success (CE)	250/271 (92.3)	247/267 (92.5)	−0.3 (−4.9, 4.4)
Investigator assessment of cure			
Clinical response, day 14 (CE)	292/302 (96.7)	292/301 (97.0)	−0.3 (−3.4, 2.7)
Clinical response, day 28 (CE)	263/271 (97.0)	258/266 (97.0)	0.1 (−3.1, 3.2)

- Randomized, double-blind trial
- N=698 adults
- Acute bacterial SSTI

- Dalbavancin 1500 mg either as a single intravenous infusion
- Dalbavancin 1000 mg IV on day 1 followed 1 week later by 500 mg IV.

Conclusions: A single 1500-mg infusion of dalbavancin is non-inferior to a 2-dose regimen, has a similar safety profile, and removes logistical constraints related to delivery of the second dose.

The NEW ENGLAND JOURNAL of MEDICINE

Single-Dose Oritavancin in the Treatment of Acute Bacterial Skin Infections

2014

G. Ralph Corey, M.D., Heidi Kabler, M.D., Purvi Mehra, M.D., Sandeep Gupta, M.D., J. Scott Overcash, M.D., Ashwin Porwal, M.D., Philip Giordano, M.D., Christopher Lucasti, M.D., Antonio Perez, M.D., Samantha Good, Ph.D., Hai Jiang, Ph.D., Greg Moeck, Ph.D., and William O'Riordan, M.D., for the SOLO I Investigators*

- Phase 3, randomized, double-blind trial
- Acute bacterial skin and skin-structure infections
- Primary composite end point: cessation of spreading or reduction in lesion size, absence of fever, and no need for administration of a rescue antibiotic 48 to 72

- Oritavancin 1200 mg a single intravenous dose (475 pts - mITT) vs. Vancomycin iv twice daily 7-10 days (479 pts - mITT)

Subgroup	Oritavancin	Vancomycin	Percentage-Point Difference (95% CI)
	no. of events/total no. (%)		
Modified intention-to-treat population			
Primary efficacy outcome at ECE	391/475 (82.3)	378/479 (78.9)	3.4 (−1.6 to 8.4)
Investigator-assessed clinical cure at PTE	378/475 (79.6)	383/479 (80.0)	−0.4 (−5.5 to 4.7)
Lesion size reduction ≥20% at ECE	413/475 (86.9)	397/479 (82.9)	4.1 (−0.5 to 8.6)
CE population			
Primary efficacy outcome at ECE	344/394 (87.3)	342/397 (86.1)	1.2 (−3.6 to 5.9)
Investigator-assessed clinical cure at PTE	357/394 (90.6)	352/397 (88.7)	1.9 (−2.3 to 6.2)
Lesion size reduction ≥20% at ECE	362/394 (91.9)	370/397 (93.2)	−1.3 (−5.0 to 2.3)
Patients infected with MRSA in intention-to-treat population with microbiologic evaluation			
Primary efficacy outcome at ECE	84/104 (80.8)	80/100 (80.0)	0.8 (−10.1 to 11.7)
Investigator-assessed clinical cure at PTE	86/104 (82.7)	83/100 (83.0)	−0.3 (−10.7 to 10.0)
Lesion size reduction ≥20% at ECE	94/104 (90.4)	84/100 (84.0)	6.4 (−2.8 to 15.5)
Patients infected with MSSA in intention-to-treat population with microbiologic evaluation			
Primary efficacy outcome at ECE	96/116 (82.8)	92/110 (83.6)	−0.9 (−10.6 to 8.9)
Investigator-assessed clinical cure at PTE	89/116 (76.7)	88/110 (80.0)	−3.3 (−14.0 to 7.4)
Lesion size reduction ≥20% at ECE	98/116 (84.5)	94/110 (85.5)	−1.0 (−10.3 to 8.3)

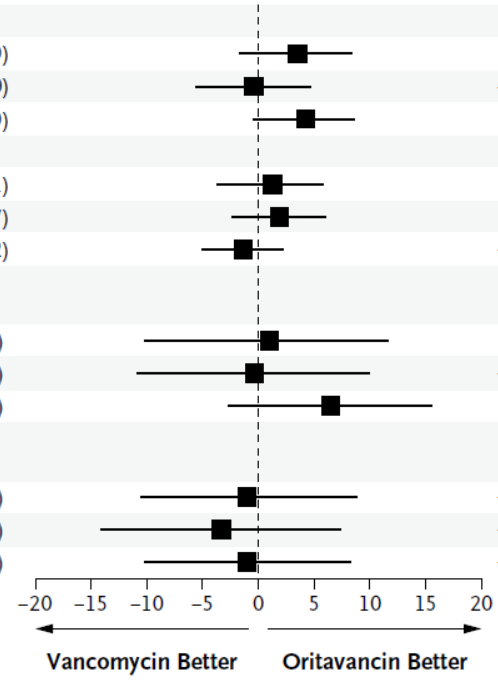

Figure 2. Primary and Secondary Efficacy End Points According to Analysis Population and MRSA Subgroup.

The NEW ENGLAND JOURNAL of MEDICINE

Single-Dose Oritavancin in the Treatment of Acute Bacterial Skin Infections

2014

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Table 3. Patients with Adverse Events (Safety Population).*

Adverse Event	Oritavancin (N=473)	Vancomycin (N=481)
	no. of patients (%)	
At least 1 adverse event that developed during treatment	284 (60.0)	307 (63.8)
Related to study drug	108 (22.8)	151 (31.4)
Leading to discontinuation of study drug	18 (3.8)	28 (5.8)
Serious adverse event†	35 (7.4)	35 (7.3)
Related to study drug	3 (0.6)	3 (0.6)
Leading to discontinuation of study drug	11 (2.3)	13 (2.7)
Death	1 (0.2)	2 (0.4)
Most frequently reported adverse events‡		
Nausea	52 (11.0)	43 (8.9)
Headache	34 (7.2)	38 (7.9)
Pruritus	16 (3.4)	44 (9.1)
Infusion-site reaction	19 (4.0)	34 (7.1)
Infusion-site extravasation	18 (3.8)	23 (4.8)
Vomiting	23 (4.9)	18 (3.7)
Constipation	19 (4.0)	21 (4.4)
Diarrhea	23 (4.9)	17 (3.5)
Cellulitis	20 (4.2)	17 (3.5)
Pyrexia	15 (3.2)	20 (4.2)
Dizziness	15 (3.2)	15 (3.1)
Insomnia	14 (3.0)	13 (2.7)
Chills	10 (2.1)	12 (2.5)
Urticaria	7 (1.5)	15 (3.1)
Pruritus, generalized	11 (2.3)	9 (1.9)
Subcutaneous abscess	9 (1.9)	11 (2.3)
Abscess on limb	13 (2.7)	5 (1.0)
Infusion-site phlebitis	8 (1.7)	10 (2.1)
Alanine aminotransferase elevation	11 (2.3)	5 (1.0)
Fatigue	10 (2.1)	6 (1.2)

Single-Dose Oritavancin Versus 7–10 Days of Vancomycin in the Treatment of Gram-Positive Acute Bacterial Skin and Skin Structure Infections: The SOLO II Noninferiority Study

Clinical Infectious Diseases® 2015;60(2):254–62

G. Ralph Corey,[1] Samantha Good,[2] Hai Jiang,[2] Greg Moeck,[2] Matthew Wikler,[2] Sinikka Green,[3] Paul Manos,[4]

- Phase 3, randomized, double-blind trial
- Acute bacterial skin and skin-structure infections
- Primary composite end point: cessation of spreading or reduction in lesion size, absence of fever, and no need for administration of a rescue antibiotic 48 to 72

- Oritavancin 1200 mg a single intravenous dose (503 pts - mITT) vs. Vancomycin iv twice daily 7-10 days (502 pts - mITT)

Efficacy and safety conclusions from the SOLO II study were generally consistent with those of the SOLO I

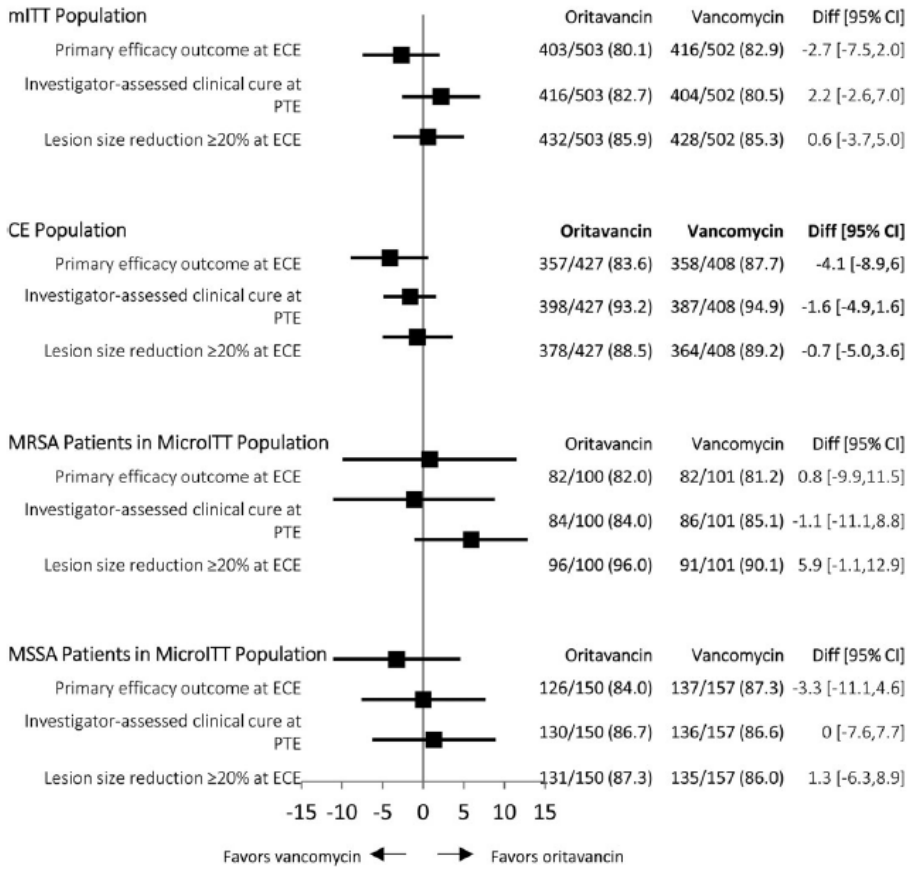


Figure 2. Results of the primary and secondary efficacy endpoints by analysis population and subgroup.

Open Forum Infectious Diseases
MAJOR ARTICLE
2018

A Real-world Patient Registry for Oritavancin Demonstrates Efficacy and Safety Consistent With the Phase 3 SOLO Program

Mark Redell,[1] Greg Moeck,[2] Christopher Lucasti,[3] Stephanie Durso

Results from the first phase of the CHROME registry, a multicenter, multiyear, retrospective observational study to characterize the population of adult patients who have received oritavancin

Table 1. Demographics and Baseline Characteristics for Oritavancin-Treated Patients in the CHROME Registry and SOLO Clinical Program

Characteristic[a]	CHROME (n = 112 patients)	Pooled SOLO[b] (n = 978)
Age, y		
Mean (SD)	58.6 (17.0)	45.6 (13.8)
Median	60.0	46.0
Range	18 – 96	18 – 89
No. (%) age ≥65 y	44 (39.3)	86 (8.8)
Body mass index (n = 109), kg/m^2		
Mean (SD)	33.0 (9.6)	27.7 (7.6)
Median	31.6	26.2
Range	16–65	15–74
Meets SIRS criteria, No. (%)[c]	4/112 (3.6)	169 (17.3)
Temperature ≥38°C	0/104 (0)	186/978 (19.0)
WBC count >12 000 mm^3	11/52 (21.2)	216/887 (24.4)
Patients receiving antibiotics prior to oritavancin, % (n/N)	70.5 (79/112)[f]	19.6 (192/978)[f]
Concomitant medical conditions, %		
Vascular disorders	55.4	
Hypertension	44.6	
Diabetes	37.5	14.2
Intravenous drug use	ND	29.2
Hyperlipidemia	25.1	
Neoplastic disease	17.9	
Infection type, No. (%)		
Cellulitis	67.0 (75)	39.6 (387)
Cutaneous abscess	21.4 (24)	31.5 (288)
Wound infection	4.5 (5)	28.9 (283)
Other[i]	7.1 (8)	NA

Table 2. Clinical and Microbiologic Outcomes for Oritavancin-Treated Patients in the CHROME Registry and SOLO Clinical Program

Outcome	CHROME (n = 112), % (n/N)	Pooled SOLO (n = 978), % (n/N)
Clinical success[a]	92.8 (103/111)	92.6 (760/821)[b]
Clinical failure	7.2 (8/111)	7.4 (61/821)
Post-therapy microbiologic assessment in 30 patients[c]		Not available; clinical response by pathogen at defined end points
Microbiologic eradication	90.0 (27/30)	
Microbiologic persistence	10.0 (3/30)	

Conclusions: Clinical and microbiologic outcomes and safety of single-dose oritavancin 1200 mg were similar in this older patient population with multiple comorbid conditions to those observed in the phase 3 SOLO trials.

Table I. *In vitro* activity of dalbavancin, oritavancin, telavancin and vancomycin against Gram-positive organisms[2,24,28-48]

Bacteria	Dalbavancin			Oritavancin			Telavancin			Vancomycin		
	MIC_{50}	MIC_{90}	range	MIC_{50}	MIC_{90}	range	MIC_{50}	MIC_{90}	range	MIC_{50}	MIC_{90}	range
Staphylococcus aureus (MS)	0.06	0.06	≤0.008–0.5	0.06	0.12	≤0.004–2	0.25	0.5	≤0.015–2	1	1	0.25–2
S. aureus (MR)	0.06	0.06	≤0.008–0.5	0.06	0.25	≤0.004–4	0.25	0.5	≤0.06–2	1	2	0.25–2
Staphylococcus epidermidis (MS)	≤0.03	0.06	0.015–0.25	0.25	0.5	0.008–1	0.25	1	0.12–1	2	2	1–2
S. epidermidis (MR)	0.06	0.06	0.015–1	0.5	0.5	≤0.004–4	0.5	1	0.25–2	2	4	1–4
Streptococcus pyogenes (group A)	0.015	0.03	≤0.002–0.06	0.12	0.25	0.008–0.5	0.03	0.06	0.03–0.12	0.5	1	0.5–1
Streptococcus agalactiae (group B)	0.06	0.12	0.008–0.25	N/A	0.12	0.03–0.5	0.06	0.06	0.002–0.25	0.25	0.5	0.25–0.5
Other β-haemolytic *Streptococcus* spp.	≤0.008	0.06	≤0.002–0.25	N/A	0.5	0.001–1	0.03	0.06	0.002–0.25	0.25	0.5	0.25–1
Streptococcus pneumoniae (PS)	0.015	0.03	≤0.008–0.06	0.002	0.004	≤0.0005–0.25	0.015	0.03	0.008–0.06	0.25	0.5	0.06–1
S. pneumoniae (PI)	0.015	0.03	≤0.008–0.06	0.004	0.008	≤0.0005–0.5	0.015	0.03	0.008–0.12	0.5	1	0.25–1
S. pneumoniae (PR)	0.015	0.03	≤0.008–0.25	0.004	0.008	≤0.0005–0.015	0.015	0.03	0.008–0.12	0.25	0.5	0.06–2
Enterococcus faecalis (VS)	0.03	0.06	0.015–4	0.03	0.06	≤0.0005–0.5	0.25	0.5	≤0.015–4	1	2	0.5–4
E. faecalis (VR)	4	32	0.015–>32	0.5	1	0.015–4	8	8	0.25–32	512	512	8 to >512
Enterococcus faecium (VS)	0.06	0.12	≤0.015–4	0.015	0.015	≤0.0005–0.06	0.12	0.25	≤0.015–2	0.5	1	0.5–2
E. faecium (VR)	8	32	0.03–>32	0.06	0.25	≤0.0005–4	2	4	0.5–16	512	512	8 to >512
E. faecium (VanA)	16	32	0.03–>32	N/A	0.25	0.004–2	4	8	≤0.015–16	512	512	64 to >512
E. faecium (VanB)	0.03	0.12	0.03–0.12	N/A	0.03	0.004–0.06	0.5	2	0.06–4	32	64	4 to >512
Clostridium spp.	0.03	2	≤0.015–8	0.25	1	0.06–1	0.25	0.25	0.12–0.5	0.5	1	0.25–8

MIC_{50} = minimum concentration to inhibit growth of 50% of isolates; **MIC_{90}** = minimum concentration to inhibit growth of 90% of isolates; **MR** = meticillin resistant; **MS** = meticillin susceptible; **N/A** = not available; **PI** = penicillin intermediate (MIC 0.12–1 mg/L); **PR** = penicillin resistant (MIC ≥2 mg/L); **PS** = penicillin susceptible (MIC ≤0.06 mg/L); **VR** = vancomycin resistant (MIC ≥32 mg/L); **VS** = vancomycin susceptible (MIC ≤4 mg/L).

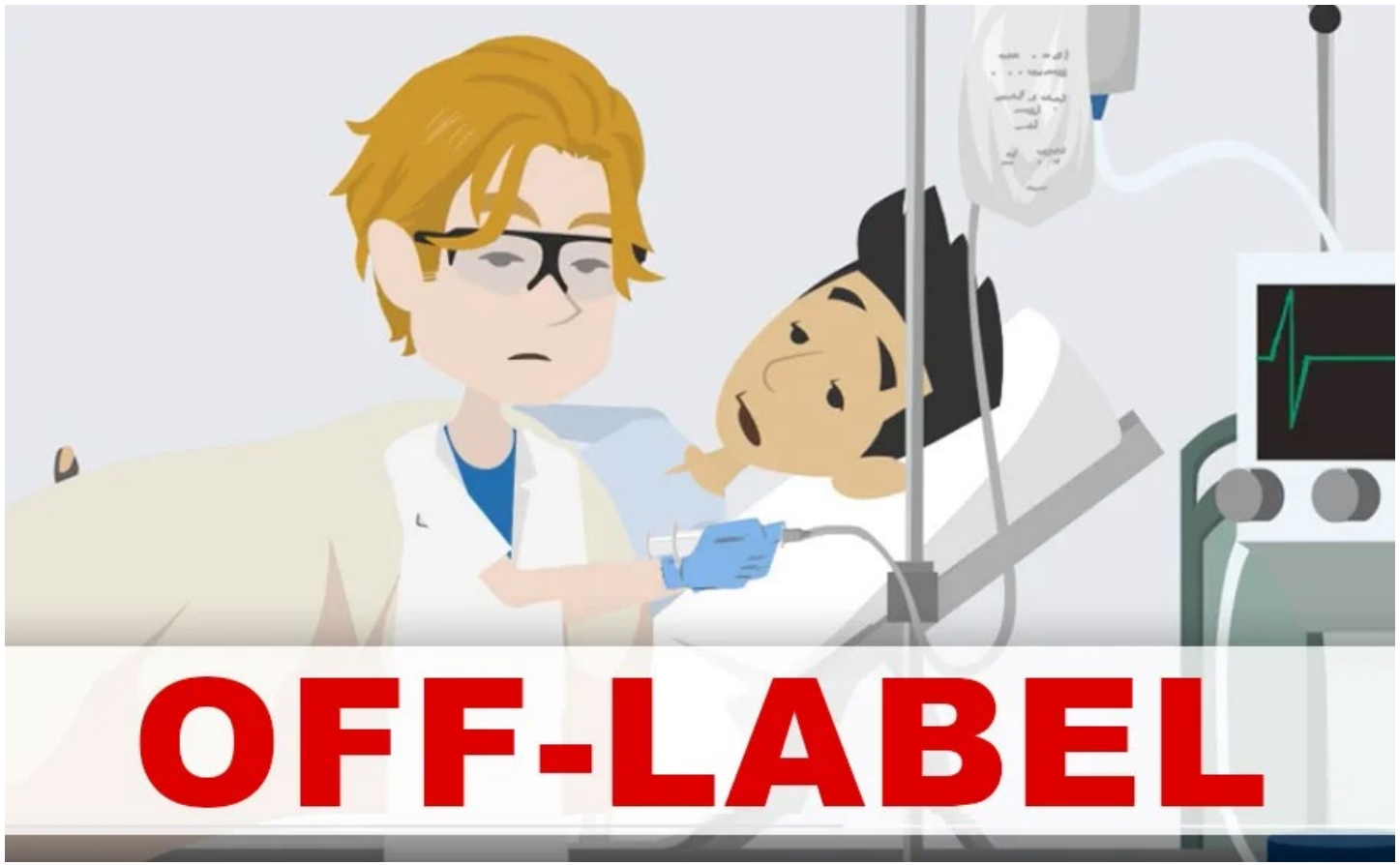
Dalbavancin:

- MSSA, MRSA, MSSE, MRSE
- VISA but poor activity versus VRSA
- Enterococci (and VRE **only VanB**)
- *Streptococcus pneumoniae*
- *Clostridium* spp

Oritavancin:

- MSSA, MRSA, MSSE, MRSE
- VISA and VRSA
- Enterococci (VRE **VanA and VanB**)
- *Streptococcus pneumoniae*
- *Clostridium* spp

Drugs 2010; 70 (7): 859-886
0012-6667/10/0007-0859/$55.55/0


OFF-LABEL

J Antimicrob Chemother 2019; **74**: 2405–2416
doi:10.1093/jac/dkz162 Advance Access publication 23 April 2019

Journal of Antimicrobial Chemotherapy

On- and off-label utilization of dalbavancin and oritavancin for Gram-positive infections

Taylor Morrisette [1,2], Matthew A. Miller[2], Brian T. Montague[3,4], Gerard R. Barber[2], R. Brett McQueen[5] and Martin Krsak [3,4]*

Table 1. Baseline characteristics; *N*=56

Age (years), mean ± SD	46.7 ± 15.4
Weight (kg), mean ± SD	82.3 ± 20.4
Height (cm), mean ± SD	173.2 ± 11.1
Male	33 (59)
Caucasian	46 (82)
IDU/PSA	17 (30)
Concomitant diseases	
diabetes mellitus	14 (25)
cardiovascular disease	5 (9)
chronic kidney disease	7 (13)
hepatic disease	8 (14)
oncological disease	8 (14)
Charlson comorbidity index, median (IQR)	2 (1–4)
ICU admission	13 (23)
ID consultation	49 (88)
Non-OPAT candidate	29 (52)

56 patients were included dalbavancin, 71%; oritavancin, 25%; both, 4%.

Indications for laLGP: ABSSSIs 36%, osteomyelitis 27%, endocarditis 9%, catheter-associated bacteraemia and pneumonia 4%, various other infections 21%.

Clinical success was found in 85% cases with adequate follow-up.

Mild adverse effects occurred in 11% of patients.

15 cases of osteomyelitis treated with laLGPs with a 92% success rate

5 cases of endocarditis with a 100% success rate.

Projected reduction in hospital LOS: 514 days (9.18 days/person average)

Projected reduction in hospital costs: $963456.72 ($17204.58/person average)

International Journal of Infectious Diseases 81 (2019) 210–214

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journal homepage: www.elsevier.com/locate/ijid

Multicenter clinical experience of real life Dalbavancin use in gram-positive infections

S. Wunsch[a], R. Krause[a], T. Valentin[a], J. Prattes[a], O. Janata[b], A. Lenger[b], R. Bellmann-Weiler[c], G. Weiss[c], I. Zollner-Schwetz[a,*]

- **A total of 101 patients included.**
- **The treated infections were PJI (31%), osteomyelitis (29%), endocarditis (25%) and acute bacterial skin and soft tissue infections (12%).**
- **Concomitant use of other antimicrobial substances was common (63%).**
- **Clinical success rate was 89%.**
- **Side effects occurred in 3/101 patients.**

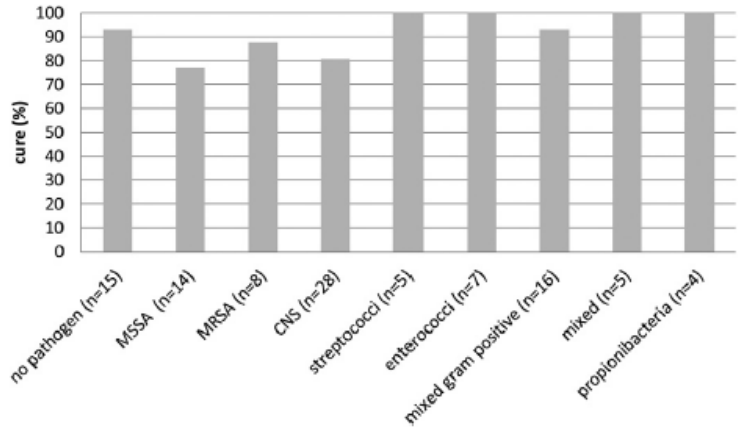


Figure 2. Etiology of infections and percentage of patients cured with dalbavancin.

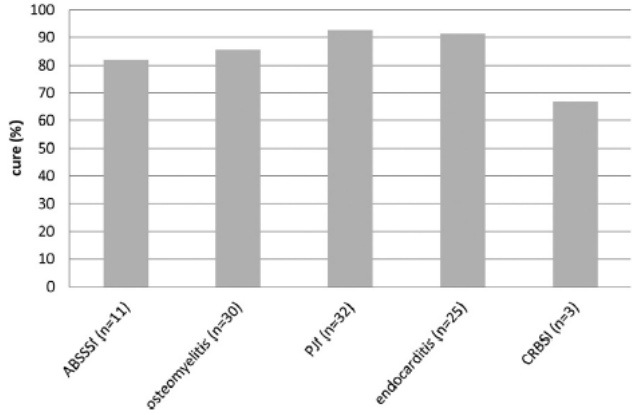


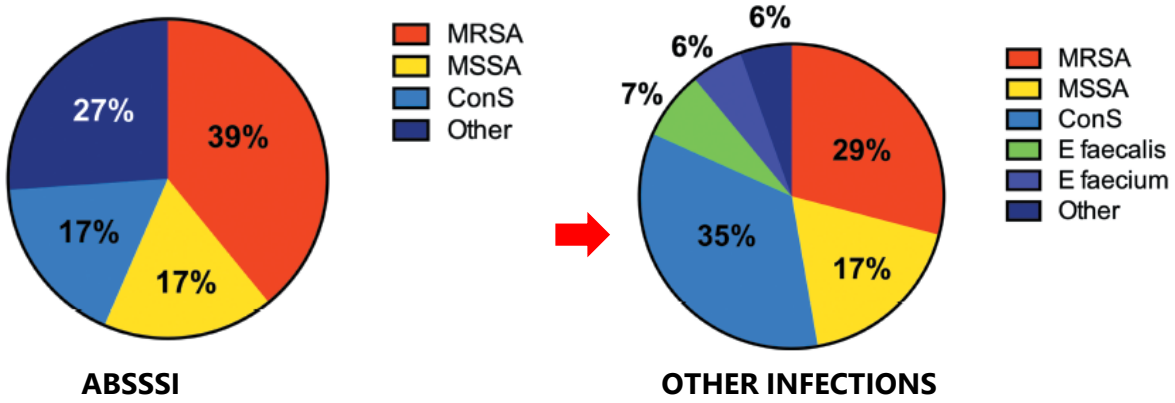
Figure 1. Percentage of cured patients in different indications for dalbavancin use.

"We therefore speculate that treatment failure may have been caused by inadequate source control"

Efficacy and safety of dalbavancin in the treatment of acute bacterial skin and skin structure infections (ABSSSIs) and other infections in a real-life setting: data from an Italian observational multicentric study (DALBITA study)

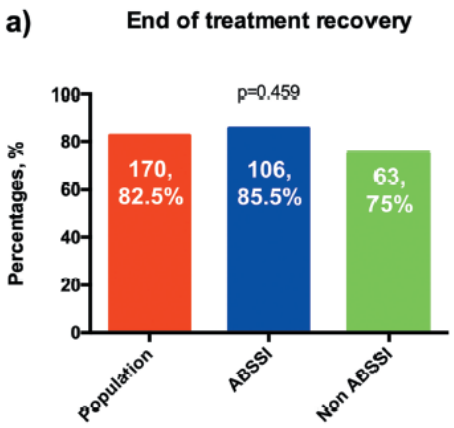
Francesca Bai[a], Chiara Aldieri[a], AnnaMaria Cattelan[b], Francesca Raumer[b], Eugenia Di Meco[b], Maria Cristina Moioli[c]

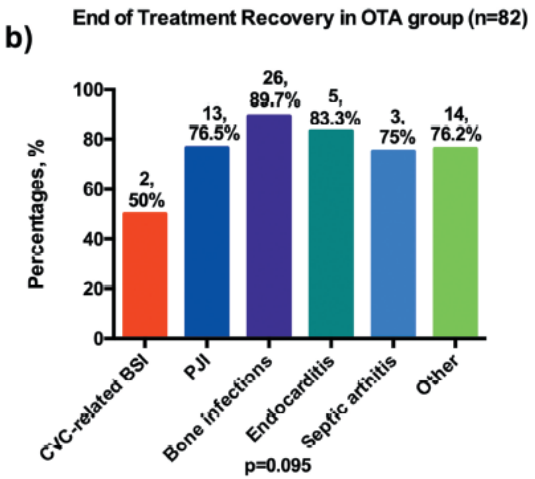
EXPERT REVIEW OF ANTI-INFECTIVE THERAPY



ABSSSI **OTHER INFECTIONS**

- Retrospective observational study in 11 Italian hospitals
- 206 patients treated with ≥1 dose of dalbavancin: 124 (60.2%) ABSSSI, 82 (39.8%) OTA
- No difference in clinical relapse rate between ABSSSI and OTA
- At the follow-up visit (~80 days) **81.3% patients recovered**





	Population	ABSSSI	Other sites' infections (OTA)	
N = 206	*N* = 124	*N* = 82		*p* Values
Outcome (EOT)				0.459
Recovery	170 (82.5%)	106 (85.5%)	63 (75%)	
Failure	25 (12.2%)	13 (10.5%)	12 (14.2%)	
Unknown	11 (5.3%)	5 (4%)	9 (10.8%)	
Relapse				0.907
No	128 (62.1%)	82 (66.2%)	45 (53.6%)	
<7 days	12 (5.8%)	7 (5.6%)	5 (5.9%)	
≥7 days	27 (13.1%)	17 (13.7%)	10 (11.9%)	
Unknown	39 (18.9%)	18 (14.5%)	24 (28.6%)	
Outcome (follow-up)				0.305
Recovery	126 (61.2%)	83 (66.9%)	43 (52.5%)	
Relapse with new hospitalization	12 (5.8%)	5 (4%)	7 (8.5%)	
Relapse without hospitalization	17 (8.3%)	12 (10%)	5 (6.1%)	
Unknown	51 (24.7%)	24 (19.3%)	27 (32.9%)	
AE				0.258
No	155 (75.7%)	101 (81.5%)	54 (64.3%)	
Nonserious	10 (4.9%)	5 (4%)	5 (5.9%)	
Serious	1 (0.5%)	0	1 (1.2%)	
Unknown	40 (18.9%)	18 (14.5%)	22 (28.6%)	
Type of AE				0.369
Dermatologic	5 (2.4%)	2 (1.6%)	3 (3.7%)	
Gastrointestinal	3 (1.4%)	1 (0.8%)	2 (2.5%)	
Liver toxicity	1 (0.4%)	0	1 (1.2%)	

J Antimicrob Chemother 2020; **75**: 2717–2722
doi:10.1093/jac/dkaa188 Advance Access publication 26 May 2020

Journal of Antimicrobial Chemotherapy

Dalbavancin for the management of osteomyelitis: a major step forward?

Thamer A. Almangour[1] and Abdullah A. Alhifany[2]*

Bone penetration

Preclinical and Phase I bone penetration studies indicated that dalbavancin concentrations were maintained above the MIC range for Gram-positive pathogens (0.03–0.25mg/L) for up to 14 days post-dose. Dalbavancin mean non-infected cortical bone to plasma AUC **penetration ratio** has been reported to be **13.1%**. This is higher than the mean ratio of vancomycin, previously reported at 7%.

Limited published real-life clinical experience assessing the effectiveness and tolerability of dalbavancin in the treatment of osteomyelitis.

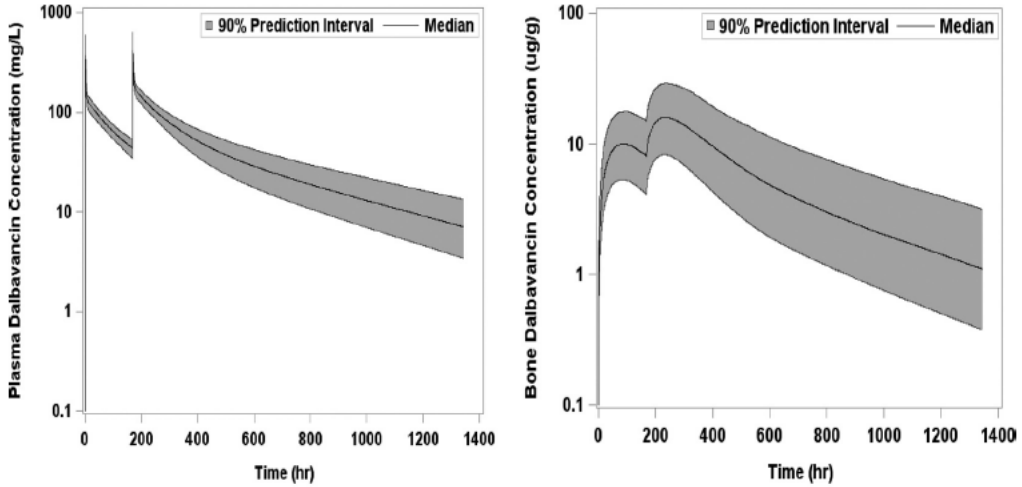
Table 1. Summary of published real-life experience with dalbavancin in the treatment of osteomyelitis in adult patients

Citation (year)	Study design	Country; no. of sites	No. of patients	Dosage regimen	Clinical success	Adverse events
Almangour *et al.*[27] (2017)	CR	USA; 1	1	1000 mg × 2 then 500 mg weekly for 6 weeks	yes, at the end of treatment	none
Bouza *et al.*[18] (2018)	RCS	Spain; 29	overall = 69, OM = 12	variable; median of 4 doses (range 1–9) and duration of 3 weeks (range 1–24)	11/12 (92%) up to 1 month after end of treatment	9/69 mild–moderate (rash, tachycardia and impaired renal function)
Wunsch *et al.*[28] (2019)	RCS	Austria; 3	overall = 101, OM = 30	variable; median of 3 doses (range 1–32)	89% up to 3 months after the end of therapy	3/101 (dyspnoea, fatigue, vertigo, arterial hypertension and reversible increase in creatinine); 1 required treatment discontinuation
Bryson-Cahn *et al.*[26] (2019)	RCS	USA; 1	overall = 32, OM = 7	variable; median of 1 dose (range 1–5)	5/7 (71%) at 1 year follow-up	none
Morata *et al.*[29] (2019)	RCS	Spain; 30	overall = 64, OM = 19	variable; median of 5 doses (IQR 3–8)	17/19 (90%) at latest medical visit (median of 6 months)	7/64 (gastrointestinal distress, rash, phlebitis, asthenia and increased serum creatinine)
Almangour *et al.*[4] (2019)	RCS	USA; 3	31	variable; median of 3 doses (range 1–14)	28/31 (90%) at 3 months after end of treatment	none
Bork *et al.*[6] (2019)	RCS	USA; 2	overall = 21, OM = 11	variable; median of 3 doses (IQR 4.5)	6/11 (55%) at 1 month after end of therapy	3/21 (rash and renal impairment)
Rappo *et al.*[24] (2019)	RCT	Ukraine; 1	dalbavancin = 70, SOC = 10	1500 mg on Days 1 and 8	at 1 year: dalbavancin, 96%; SOC, 88%	no serious adverse events were considered to be related to dalbavancin
Morrisette *et al.*[20] (2019)	RCS	USA; 1	overall = 56, OM = 15, dalbavancin = 40, oritavancin = 14, combination = 2	variable; median of 1 dose (IQR 1–2)	14/15 (93%) at median follow-up of 6.1 months after treatment	6/56 [infusion reactions (itching and rash), nausea, chest tightness, line infiltration with oedema, acute kidney injury or headache]
Tobudic *et al.*[30] (2019)	RCS	Austria; 1	overall = 72, OM = 34	variable; median duration of 8 weeks (range 4–32)	26/34 (76%) at 6 months after the end of treatment	4/72 (nausea, exanthema and hyperglycaemia)
Streifel *et al.*[21] (2019)	RCS	USA; 1	overall = 37, OM = 11	variable; mean duration of 2.7 weeks	28/37 (76%) at 1 month after the end of treatment	3/37 (thrombophlebitis, pruritus, chest pain and increase in serum creatinine)
Almangour *et al.*[31] (2020)	RMCS	USA; 1	dalbavancin = 11, SOC = 11	variable; median of 2 doses	11/11 (100%) at 3 months after the end of treatment	none

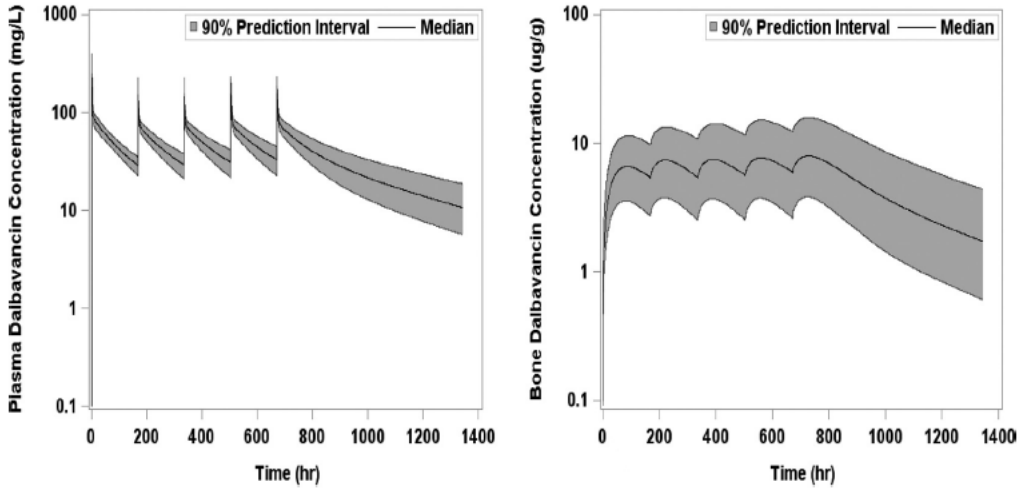
Extended-Duration Dosing and Distribution of Dalbavancin into Bone and Articular Tissue

Michael W. Dunne,[a] Sailaja Puttagunta,[a] Craig R. Sprenger,[c*] Chris Rubino,[b] Scott Van Wart,[b] James Baldassarre[a]

1500 mg, day 1 then day 8



1000 mg, day 1 then 500 mg weekly for seven additional weeks



The MIC_{90} of dalbavancin for S. aureus is 0.06 µg/ml, with 99.9% of organisms inhibited at a concentration of 0.12 µg/ml.

Evidence that dalbavancin distributes in the bone, skin, and articular tissue at concentrations that are expected to exceed the MIC for *S. aureus* for extended periods of time (6- to 8-weeks) after a significantly shortened dosing regimen.

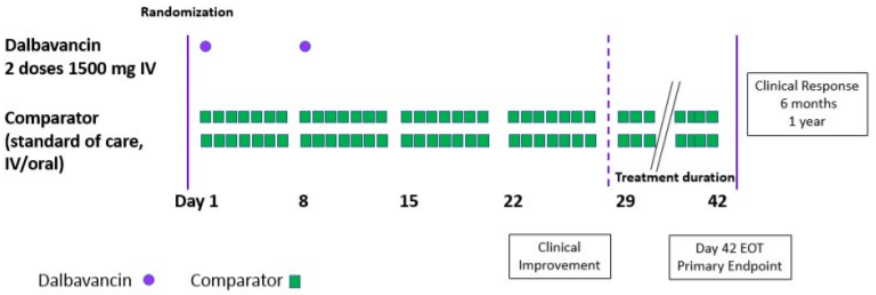
Antimicrob Agents Chemother 59:1849–1855.
doi:10.1128/AAC.04550-14.

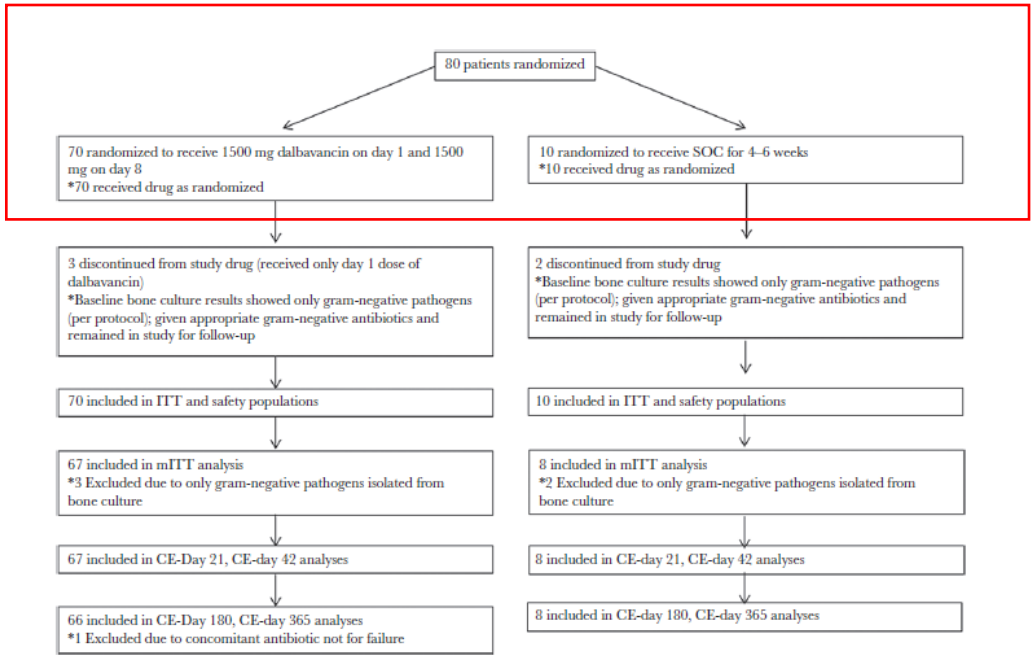
Dalbavancin for the Treatment of Osteomyelitis in Adult Patients: A Randomized Clinical Trial of Efficacy and Safety

2018.

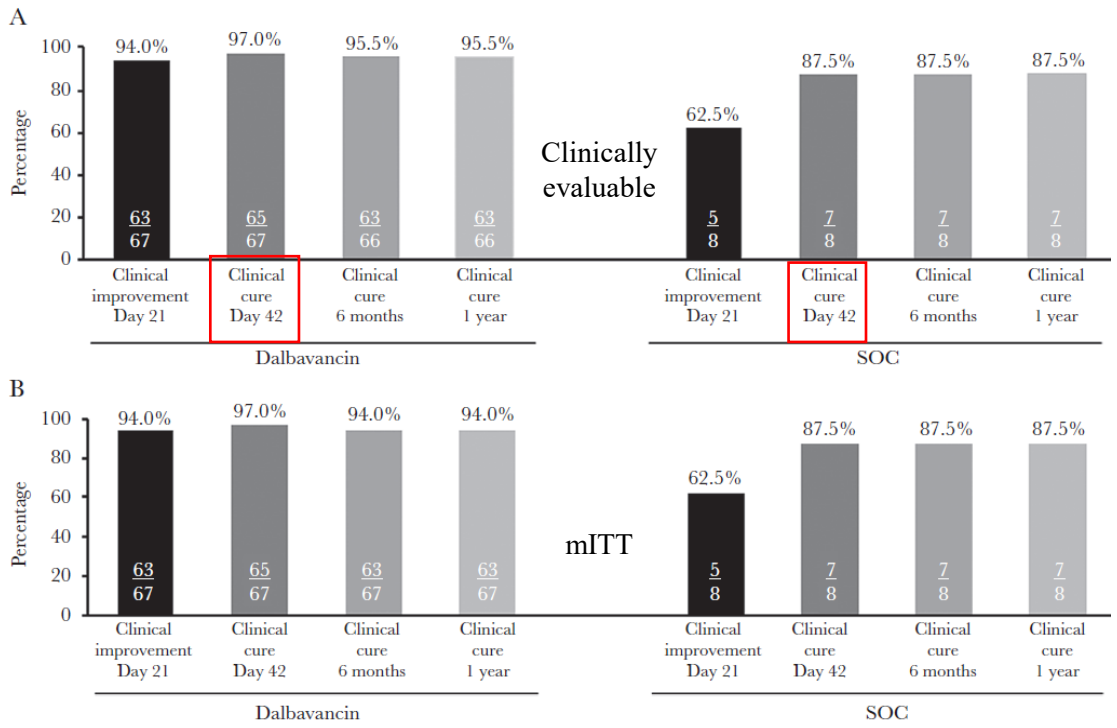
Urania Rappo,[1,*] Sailaja Puttagunta,[1,a,*] Vadym Shevchenko,[2] Alena Shevchenko,[2]

Open Forum Infectious Diseases
MAJOR ARTICLE





Primary endpoint: clinical response at day 42



The clinical response was similar in the dalbavancin group at Day 21 (94%), 6 months and 1 year (96%), so a **two-dose regimen of weekly dalbavancin** (3 g overall) **is effective for the treatment of the first episode of osteomyelitis in adults**.

Dalbavancin was well tolerated in this study; no patient discontinued treatment due to an adverse event, and no serious adverse events were considered related to dalbavancin.

Treatment of Acute Osteomyelitis with Once-Weekly Oritavancin: A Two-Year, Multicenter, Retrospective Study

Drugs - Real World Outcomes (2020) 7 (Suppl 1):S41–S45
https://doi.org/10.1007/s40801-020-00195-7

ORIGINAL RESEARCH ARTICLE

Nicholas W. Van Hise[1] · Vishnu Chundi[1] · Vishal Didwania[1] · Michael Anderson[1] · David McKinsey[2] · Ingrid Roig[3] · Akhilesh Sharma[4] · Russell M. Petrak[1]

- 134 patients were treated with oritavancin for acute osteomyelitis.
- Oritavancin was administered an initial treatment of 1200 mg and then 800 mg weekly for a total number of doses of four or five.
- Relapse or persistent infection was diagnosed in 9.7% of patients.
- Adverse events were reported in 3.7% of patients (hypoglycemia-related symptoms, tachycardia and tachycardia with chest pain).
- Clinical success was observed in 118 (88.1%) of 134 patients at ETE

None of these patients were hospitalized due to adverse events, and all patients eventually finished their treatment regimens.

Culture and pathogen by unique patient	*n/N* (%)
Positive cultures with ≥ 1 GP result	119/134 (88.8)
Staphylococcus aureus, monomicrobial	
MRSA	92
MSSA	25
S. aureus, mixed	
MRSA + ≥ 1 other GP pathogen[a]	16
MSSA + ≥ 1 other GP pathogen[a]	10
Vancomycin-resistant enterococci[b]	7
Vancomycin-intermediate *S. aureus*[b]	2
VRE with daptomycin MIC ≥ 4 mg/L	2

	No. of patients, *n* (%)	Clinical cure, *n* (%)
Clinical success ETE	134	118 (88.1)
Clinical success PTE	130	104 (80.0)
Subgroups evaluated at ETE		
Four-dose regimen	118 (88.1)	107 (90.7)
Five-dose regimen	16 (11.9)	11 (68.8)
MRI-proven infection	128 (95.5)	113 (90.4)
Diabetes	51 (38.1)	43 (84.3)
Prosthetic device	24 (17.9)	20 (88.3)
Heart failure	25 (18.7)	21 (84)
Previous antibiotic therapy	18 (13.4)	14 (77.8)
Malignancy on immunosuppression	12 (9)	11 (91.7)

ETE end of the last dose, *MRI* magnetic resonance imaging, *PTE* post-treatment

Open Forum Infectious Diseases
MAJOR ARTICLE

Oritavancin vs Standard of Care for Treatment of Nonendovascular Gram-Positive Bloodstream Infections

Ryan P. Moenster,[1] Ashleigh Wallace-Lacey,[2] Hannah Western,[3] Seth Tiefenaur,[3] Anosha Abdulbasir,[3] Justin Alberts,[3] Jonathan Doty,[3] Hartley Abner,[3]

- Two hundred-forty patients were identified for screening with 96 meeting criteria (27 in ORT and 69 in SOC groups).
- The pathogen most prevalent was methicillin susceptible *Staphylococcus aureus* (MSSA) (ORT 33.3% (9/27) vs SOC 46.4% (32/69)).
- In the full cohort of patients 7.4% (2/27) in the ORT group and 18.8% (13/69) in the SOC group had the primary outcome of clinical failure (P = .336).
- In the cohort of patients being treated for *S. aureus* (n = 64), 13.3% (2/15) in the ORT group vs 20.4% (10/49) in the SOC group had clinical failure
- Patients treated with ORT for some of the most common non–deep-seated gram-positive BSIs had outcomes similar to patients treated with SOC.

Covariate	Clinical Failure	No Clinical Failure	*P* Value
Received oritavancin therapy	2	25	.227
Received >1 dose of oritavancin	2	6	.392
MRSA isolated from the blood	**7**	**16**	**.019**
Enterococcus isolated from the blood	0	7	.976
Received daptomycin	2	0	.976
Received vancomycin	5	18	.271
BMI ≥30	**4**	**39**	**.195**
Received >96 h of prior antibiotics	**2**	**26**	**.200**
Other cultures positive	3	28	.353

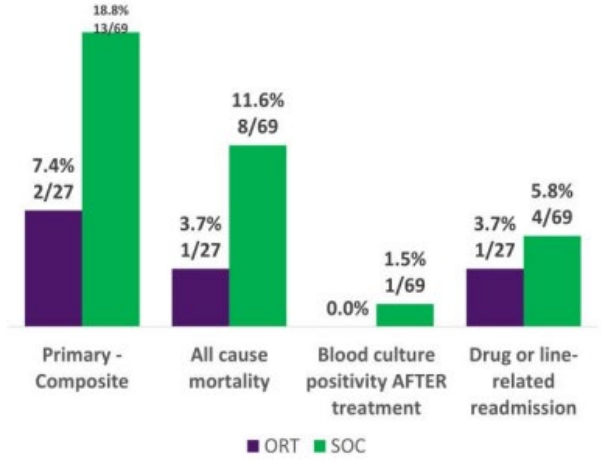


Figure 1. Primary outcome: full cohort. ORT, oritavancin; SOC, standard of care.

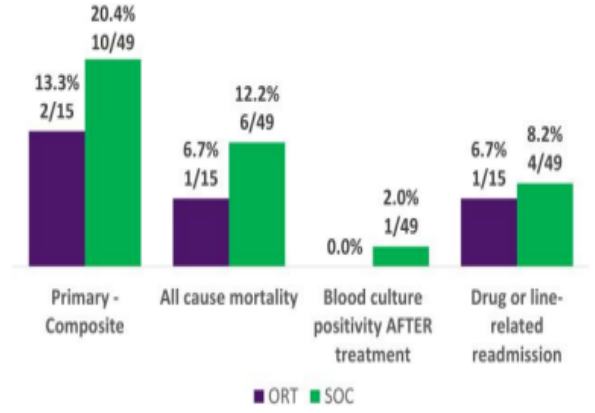


Figure 3. Primary outcomes: cohort treated for *Staphylococcus aureus*. ORT, oritavancin; SOC, standard of care.

RESEARCH Open Access

DALBACEN cohort: dalbavancin as consolidation therapy in patients with endocarditis and/or bloodstream infection produced by gram-positive cocci

Carmen Hidalgo-Tenorio[1*], David Vinuesa[2], Antonio Plata[3]

Annals of Clinical Microbiology and Antimicrobials
Hidalgo-Tenorio *et al.*
Ann Clin Microbiol Antimicrob (2019) 18:30
https://doi.org/10.1186/s12941-019-0329-6

- Eighty-three patients with median age of 73 years who received at least one dose of DBV were enrolled.
- 59.04% had BSI and 49.04% IE (44.04% prosthetic valve IE, 32.4% native IE, 23.5% pacemaker lead).
- The most frequently isolated microorganism was *Staphylococcus aureus* in BSI (49%) and coagulase-negative staphylococci in IE (44.1%).
- All patients with IE were clinically cured in hospital; at 12 months, there was 2.9% loss to follow-up, 8.8% mortality unrelated to IE, and 2.9% therapeutic failure rate. The percentage effectiveness of DBV to treat IE was 96.7%.
- The clinical cure rate for BSI was 100% during hospital stay and at 3 months.
- There were no recurrences or deaths during the follow-up.

Table 1 Characteristics of patients with infective endocarditis

	N = 34
Patient received prior antibiotic therapy, n (%)	34 (100)
Days of previous antibiotic treatment, median (IQR)	28 (17–35)
Prior antibiotic therapy, n (%)	
Daptomycin	24 (68.6)
Ceftriaxone	10 (28.6)
Linezolid	3 (8.6)
Vancomycin	8 (22.9)
Surgery, n (%)	12 (34.3)
Surgery before administering DBV	11 (91.6)
Reason for DBV administration, n (%)	
Facilitate discharge	30 (88.6)
Prior treatment failure	3 (8.6)
DBV dose, n (%)	
1000 mg (1 day), 500 mg (8 days)	10 (29.4)
1000 mg 1 day	5 (14.7)
1500 mg (1 day)	12 (35.3)
1000 mg (1 day), 500 mg (8 days), 500 mg (15 days)	1 (2.9)
1500 mg (1 day), 1000 mg (15 days)	3 (.8)
1500 mg (1 day), 1000 mg (15 days, 30 days, 45 days)	1 (2.9)
1000 mg (1 days), 500 mg every week/9 weeks	1 (2.9)
1500 mg (1 days), 1000 mg every 2 weeks/10 weeks	1 (2.9)
DBV-covered days, median (IQR)	14 (14–21)
Clinical cure, n (%)	34 (100)
Microbiological cure, n (%)	33 (97.1)
Follow-up blood cultures:	17 (48.6)
Negative follow-up blood cultures	17 (100)
IE-related death, n (%)	
During hospitalisation	0
At 12 months	0
Relapse, n (%)	0
Median reduction in hospital stay (IQR)	14 (7–17)
Total reduction, days	557

Table 2 Bloodstream infection characteristics

	N = 49
Days of prior AB therapy, median (IQR)	8 (0–15)
Prior antibiotic therapy, n (%)	46 (93.9)
Daptomycin	22 (44.9)
Ceftriaxone	10 (20.4)
Linezolid	9 (18.4)
Vancomycin	11 (22.4)
Reason for DBV administration, n (%)	
Facilitate discharge	38 (77.6)
Prior treatment failure	1 (2)
Toxicity	2 (4)
DBV dose, n (%)	
1000 mg (1 day), 500 mg (8 days)	14 (28.6)
1000 mg 1 day	11 (22.4)
1500 mg 1 day	21 (42.9)
Other	3 (6.1)
DBV-covered treatment days (IQR)	14 (14)
Clinical cure, n (%)	49 (100)
Microbiological cure	
Follow-up blood cultures, n (%)	36 (73.5)
Negative follow-up blood cultures	35 (97.2)
Death related to bloodstream infection, n (%)	0
Relapse, n (%)	0
Readmission for different reason	1 (2)
Reduction in days of hospital stay (IQR)	14 (7–14)
Total reduction, days	636

International Journal of Antimicrobial Agents
Volume 62, Issue 3, September 2023, 106918

EN-DALBACEN 2.0 Cohort: real-life study of dalbavancin as sequential/consolidation therapy in patients with infective endocarditis due to Gram-positive cocci

Carmen Hidalgo-Tenorio [a], Svetlana Sadyrbaeva-Dolgova [a], Andrés Enríquez-Gómez [b],

- 124 patients with median age of 67.4 years who received at least one dose of DBV.
- IE was native in 46.8%, late prosthetic in 24.2%, early prosthetic in 19.4%, on pacemaker lead in 8.9%, and on pacemaker lead and valve in 0.8%.
- The aortic valve was the most frequently involved (56.6%), followed by mitral (31.9%), tricuspid (9.7%), and pulmonary (1.8%) valves.
- Isolated microorganisms included coagulase-negative staphylococci (38.7%), *Staphylococcus aureus* (22.6%), *Enterococcus faecalis* (19.4%), *Streptococcus* spp. (9.7%).
- The total DBV dose administered to treat IE was 1500 mg (IQR 1500–2093.7) for a median of about 2 weeks.
- Clinical success at 12 months was 95.2% when the patient lost to the follow-up was included, and 95.9% when only patients completing the 1-year follow-up were considered. The clinical cure rate for BSI was 100%

Table 1
Infective endocarditis characteristics.

	N = 124
Age (years), mean (SD)	67.4 (15.4)
Male, n (%)	87 (70.2)
Charlson index, median (IQR)	4 (2.5–6)
Chronic kidney failure (clearance <60 mL/min), n (%)	33 (26.6)
Haemodialysis, n (%)	2 (1.6)
Peritoneal dialysis, n (%)	1 (0.8)
Diabetes mellitus, n (%)	38 (30.6)
Neurological disease, n (%)	18 (14.5)
HIV infection, n (%)	2 (1.6)
Solid organ transplantation, n (%)	2(1.6)
Active neoplasm, n (%)	9 (7.3)
Chronic liver disease, n (%)	6 (4.8)
Corticoids/other immunosuppressive drugs in previous month, n (%)	10 (8.1)
Type of infection, n (%)	
Definite IE	113 (91.1)
Probable IE	11 (8.9)
Type of endocarditis, n (%)	
Native	58 (46.8)
Late prosthetic	30 (24.2)
Early prosthetic	24 (19.4)
Pacemaker lead endocarditis	11 (8.9)
Pacemaker lead and valve	1 (0.8)
Valve affected, n (%)	
Aortic	64 (56.6)
Mitral	36 (31.9)
Tricuspid	11 (9.7)
Pulmonary	2 (1.8)
Causative organism, n (%)	
CNS	48 (38.7)
MSSA	28 (22.6)
E. faecalis	24 (19.4)
Streptococcus Spp.	18 (9.7)
E. faecium	3 (2.4)
MRSA	1 (0.8)
Abiatrophia defectiva	1 (0.8
Enterococo caseliflavus	1 (0.8)

CNS, coagulase-negative *staphylococci*; HIV, human immunodeficiency virus; IE, infective endocarditis; IQR, interquartile range; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.

Table 3
Outcomes.

	N = 124
Clinical success, n (%)	
- Effectiveness including loss of follow-up (one IE-related death, four relapse, one loss)	118 (95.2)
- Effectiveness including subjects who completed follow-up (one IE-related death, four relapse)	119 (95.9)
Microbiological healing, n (%)	
- Blood cultures performed after DBV	99 (79.8)
- Negative blood cultures after DBV	99 (100)
Hospital stay reduction (d), median (IQR)	14 (14-25)
IE relapse and readmission within 12 months after DBV treatment, n (%)	4 (3.2)
Loss to follow-up, n (%)	1 (0.81)
Death, n (%)	
- IE-related death	1 (0.8)
- Non-related death	5 (9.7)
Aortic valve pseudoaneurysm	1 (20)
Sepsis related to kidney transplant	1 (20)
Advanced heart disease with cardiorespiratory insufficiency	1 (20)
Advanced oncological disease	1 (20)
Underlying haematological disease	1(20)
- Median (IQR) months after DBV treatment of IE non-related deaths	6 (4.8–8.9)
- Days after DBV treatment of IE-related deaths	67

DBV, dalbavancin; IE, infective endocarditis; IQR, interquartile range.

Comparison of Dalbavancin with standard of care in the management of infective endocarditis: efficacy, safety, and cost analysis

M Suárez , A Pérez-Landeiro , A Sanjurjo , O. Lima , A. Sousa , A. López , L. Martínez-Lamas , X. Cabrera , M Rubianes , MT Pérez-Rodríguez

Table 3: Outcome of patients

	Dalbavancin (n = 22)	Standard of care (n = 47)	P
Clinical efficacy, n (%)	19 (86)	45 (96)	0.318
Clinical cure, n (%)	20 (91)	46 (98)	0.375
12-month recurrence, n (%)	1 (5)	1 (2)	0.538
12-month mortality, n (%)	4 (18)	5 (11)	0.452
Hospital stays, days (IQR)	22 (16-34)	37 (23-49)	**0.001**
Overall costs, € (IQR)	12,206 (8,998-17,283)	16,249 (11,496-22,367)	**0.032**
- Hospital assistance, € (IQR)	9,847 (7,210-13,536)	15,044 (11,260-22,216)	**0.003**
- Antibiotic costs, € (IQR)	2,065 (1,805-2,398,2)	197 (49-400)	**<0.001**
Adverse events, n (%)	0	7 (15)	0.087

Note: IQR, interquartile range.

Retrospective multicentre cohort study of adult patients with Gram-positive cocci definite IE. Dalbavancin was used as a sequential therapy before discharge. Efficacy was a combined variable of clinical cure and absence of recurrence in 12-month follow-up. Length of hospital stay, and the associated costs were analysed in both groups of treatment.

RESULTS: Twenty-two patients received dalbavancin and 47 SOC. The efficacy was similar between the groups (dalbavancin 18 vs. SOC 44. Hospital stay was shorter in the dalbavancin group especially in those with E. faecalis IE (dalbavancin 30 days vs. SOC 65 days, p <0.001). A reduction of cost was observed between both groups.

CONCLUSION: Dalbavancin could be a safe and effective option in the sequential treatment of patients with IE. Also, a cost reduction was detected, due to a significant shortness of hospital stay.

Dalbavancin reduces biofilms of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *Staphylococcus epidermidis* (MRSE)

Eur J Clin Microbiol Infect Dis (2017) 36:677–680
DOI 10.1007/s10096-016-2845-z

ORIGINAL ARTICLE

D. Knafl[1] · S. Tobudic[1] · S. C. Cheng[2] · D. R. Bellamy[3] · F. Thalhammer[1]

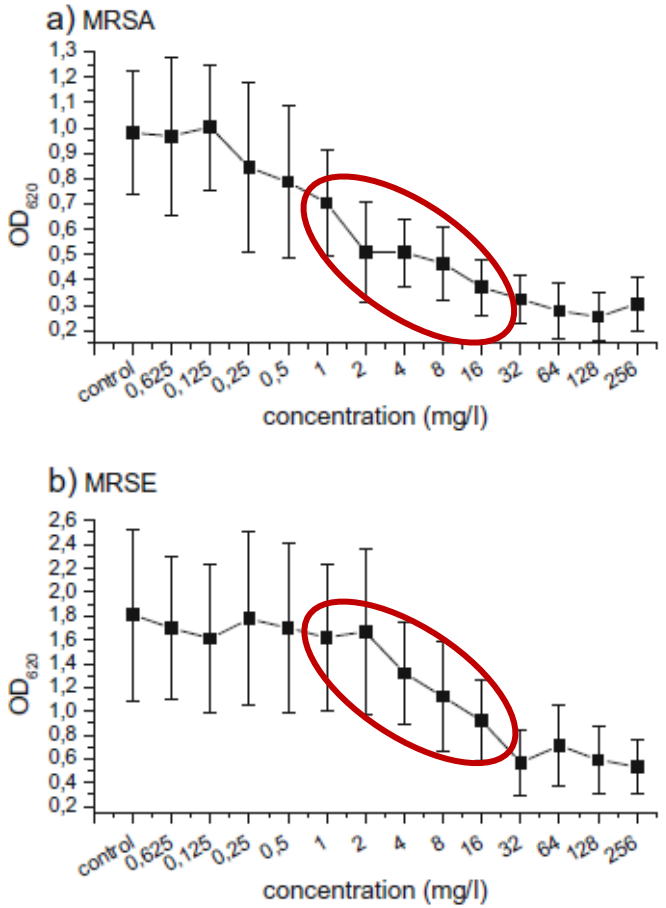


Fig. 1 Mean OD_{620} for MRSA ($\mu_{OD620} = 0.579$; $SD_{OD620} = \pm 0.186$) and MRSE ($\mu_{OD620} = 0.952$; $SD_{OD620} = \pm 0.318$) in biofilms incubated with dalbavancin and TSB in decreasing concentrations measured with BEPII-Photometer

For planktonic cells, the MIC of dalbavancin ranged from 0.032 mg/l to 0.064 mg/l for MRSA and from 0.023 mg/l to 0.0625 mg/l for MRSE. **For MRSA biofilms, the microbicidal biofilm concentrations (MBC) of dalbavancin ranged from 1 mg/l to 4 mg/l, and from 2 mg/l to 16 mg/l for MRSE.**

From the results of this study, dalbavancin shows **in-vitro activity against biofilms with MRSA and MRSE in concentrations between 1 and 16 mg/l**, which are concentrations easily reached in vivo, as **mean plasma concentrations have been shown to be > 35 mg/l for 7 days after one dose of 1000 mg**

MBC, defined as the concentration of dalbavancin leading to a 50% reduction of biofilm

Dalbavancin is active *in vitro* against biofilms formed by dalbavancin-susceptible enterococci

Katharina Neudorfer, Suzannah M. Schmidt-Malan, Robin Patel

Table 2
Cumulative minimum biofilm inhibitory concentration (MBIC) of enterococcal isolates in this study (number of isolates and percentage).
VSE = vancomycin-susceptible enterococci, VRE = vancomycin-resistant enterococci.

			MBIC (μg/mL)													MBIC$_{50}$	MBIC$_{90}$
			≤0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	>16			
Dalbavancin	*E. faecalis*		11 (19)	10 (36.2)	12 (56.9)	12 (77.6)	7 (89.7)	0 (89.7)	0 (89.7)	0 (89.7)	0 (89.7)	0 (89.7)	0 (89.7)	6 (100)		0.06	0.25
		VSE	11 (21.2)	10 (40.4)	12 (63.5)	12 (86.5)	7 (100)									0.06	0.25
		VRE												6 (100)			
															vanA 3 (100)		
															vanB1 1 (100)		
															vanB2/3 2 (100)		
	E. faecium		1 (4)	0 (4)	2 (12)	1 (16)	0 (16)	0 (16)	0 (16)	0 (16)	0 (16)	0 (16)	0 (16)	21 (100)		>16	>16
		VSE	1 (25)	0 (25)	2 (75)	1 (100)											
		VRE												21 (100)		>16	>16
															vanA 17 (100)	>16	>16
															vanB1 1 (100)		
															vanB2/3 3 (100)		

Table 3
Cumulative minimum biofilm bactericidal (MBBC) of enterococcal isolates in this study (number of isolates and percentage).
VSE = vancomycin-susceptible enterococci, VRE = vancomycin-resistant enterococci.

			MBBC (μg/mL)													MBBC$_{50}$	MBBC$_{90}$
			≤0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	>16			
Dalbavancin	*E. faecalis*		3 (5.2)	1 (6.9)	4 (13.8)	3 (19)	10 (36.2)	11 (55.2)	18 (86.2)	1 (87.9)	1 (89.7)	0 (89.7)	0 (89.7)	6 (100)		0.5	4
		VSE	3 (5.8)	1 (7.7)	4 (15.4)	3 (21.2)	10 (40.4)	11 (61.5)	18 (96.2)	1 (98.1)	1 (100)					0.5	1
		VRE												6 (100)			
															vanA 3 (100)		
															vanB1 1 (100)		
															vanB2/3 2 (100)		
	E. faecium		1 (4)	1 (8)	0 (8)	0 (8)	0 (8)	0 (8)	0 (8)	2 (16)	0 (16)	0 (16)	0 (16)	21 (100)		>16	>16
		VSE	1 (25)	1 (50)	0 (50)	0 (50)	0 (50)	0 (50)	0 (50)	2 (100)							
		VRE												21 (100)		>16	>16
															vanA 17 (100)	>16	>16
															vanB1 1 (100)		
															vanB2/3 3 (100)		

- Dalbavancin showed in vitro activity against VS enterococcal biofilms but not against VR enterococcal biofilms.
- It inhibited biofilm formation at low concentrations.
- These values were lower than those observed for other agents such as vancomycin and daptomycin.

Diagnostic Microbiology and Infectious Disease (2017),
doi:10.1016/j.diagmicrobio.2017.09.015

Int J Antimicrob Agents. 2022 Oct;60(4):106664. doi: 10.1016/j.ijantimicag.2022.106664.
Epub 2022 Aug 21.

Comparative efficacy of dalbavancin alone and with rifampicin against in vitro biofilms in a pharmacodynamic model with methicillin-resistant Staphylococcus aureus

Cristina El Haj [1], Eva Benavent [1], Yanik Sierra [2], Laura Soldevila [1], Raul Rigo-Bonnin [3], Benjamin Torrejón [4], Joan Gomez-Junyent [1], Irantzu Rosselló [5], Oscar Murillo [6]

The anti-biofilm efficacy of DAL was improved significantly by adding RIF. Although DAL resistance did not occur, RIF resistance appeared in all combination therapies and decreased their efficacy over time. DAL-RIF in vitro treatment appears to be a promising anti-biofilm therapy, but further studies are needed to evaluate the efficacy and risk of resistance in vivo.

Role of dalbavancin as combination therapy: evidence from the literature and clinical scenarios

Is monotherapy or combination therapy indicated in patients with ABSSSI?

Based on available studies, there are no data supporting the use of dalbavancin in combination with other antibiotics in patients with ABSSSI. Indeed, dalbavancin mono-therapy is an efficacious treatment option in these patients and combination regimens should be avoided unless highly suspected or documented polymicrobial infections.

Is monotherapy or combination therapy indicated in patients with infections other than ABSSSI?

- Patients with bone and prosthetic joint infections
- Subacute/chronic infective endocarditis or intravascular device (that cannot be removed).

Cacopardo et al, ERAT 2022

Evaluation of dalbavancin alone and in combination with β-lactam antibiotics against resistant phenotypes of *Staphylococcus aureus*

Journal of Antimicrobial Chemotherapy

Xhilda Xhemali[1], Jordan R. Smith[2], Razieh Kebriaei[1], Seth A. Rice[1], Kyle C. Stamper[1], Matthew Compton[1], Nivedita B. Singh[1], Seyedehameneh Jahanbakhsh[1] and Michael J. Rybak[1,3]*

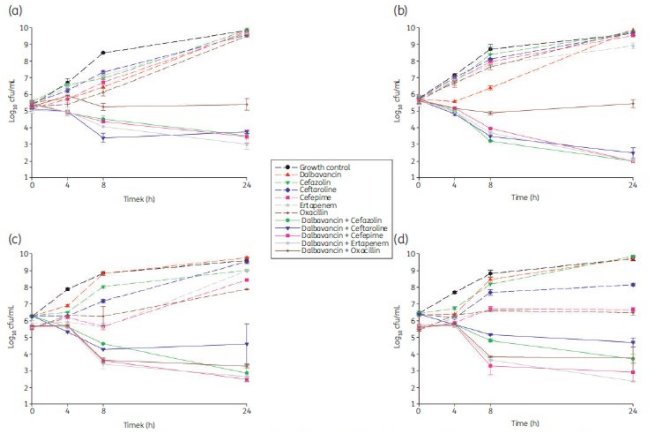


Figure 1. Twenty-four-hour time–kill curves against strains (a) MRSA R4932, (b) MRSA R5013, (c) MRSA R7400 and (d) MRSA R7528. This figure appears in colour in the online version of *JAC* and in black and white in the print version of *JAC*.

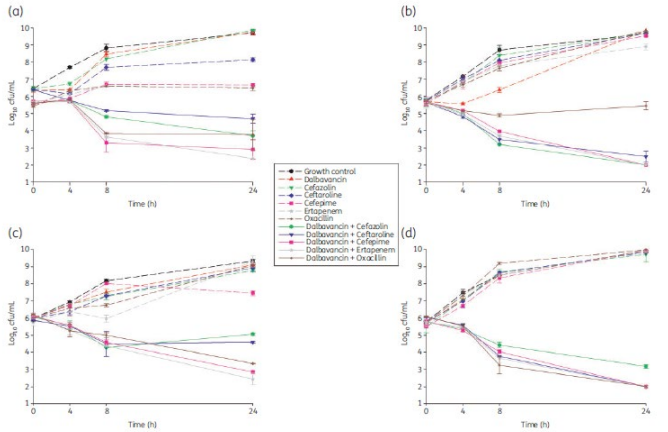


Figure 2. Twenty-four hour time–kill curves against strains (a) hVISA R5459, (b) DNS hVISA R5483, (c) DNS VISA R6913 and (d) DNS VISA D712. This figure appears in colour in the online version of *JAC* and in black and white in the print version of *JAC*.

Dalbavancin MICs decreased in combination testing against all isolates.

Table S1. Dalbavancin MIC ranges alone and in combination against *S. aureus*

DAL MIC Values Alone and in Combination with the Various β-lactams						
Phenotype (# of strains)	DAL Range (mg/L)	DAL+ CFZ Range (mg/L)	DAL + FEP Range (mg/L)	DAL+ CPT Range (mg/L)	DAL+ ERT Range (mg/L)	DAL+ OXA Range (mg/L)
MRSA (15)	0.031 – 0.125	<0.002 – 0.002	<0.002	<0.002 – 0.004	<0.002	<0.002 – 0.031
hVISA (10)	0.063 – 0.25	<0.002 – 0.031	<0.002 – 0.008	<0.002 – 0.008	<0.002 – 0.002	<0.002 – 0.063
VISA (5)	0.063 – 0.5	<0.002 – 0.13	<0.002 – 0.25	<0.002 – 0.125	<0.002 – 0.125	<0.002 – 0.063
DNS (10)	0.016 – 0.25	<0.002 – 0.002	<0.002	<0.002 – 0.016	<0.002 – 0.002	<0.002 – 0.016
LZR (10)	0.016 – 0.063	<0.002 – 0.002	<0.002	<0.002 – 0.008	<0.002 – 0.031	<0.002 – 0.016

DAL, dalbavancin; CFZ, cefazolin; FEP, cefepime; CPT, ceftaroline; ERT, ertapenem; OXA, oxacillin; MRSA, methicillin-resistant *Staphylococcus aureus*; hVISA, heteroresistant VISA; VISA, vancomycin-intermediate *S. aureus*; DNS, daptomycin-nonsusceptible; LZR, linezolid-resistant

The combinations of dalbavancin with cefazolin, cefepime and ertapenem were synergistic against all strains tested. The combination of dalbavancin and ceftaroline was synergistic against all strains except MRSA R7400. The combination of dalbavancin and oxacillin was synergistic against five of eight strains

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Original article

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

B.J. Werth [1], R. Jain [1], A. Hahn [2], L. Cummings [3], T. Weaver [3], A. Waalkes [3], D. Sengupta [3]

Here we explore a case of MRSA central line associated bloodstream infection in which dalbavancin, and vancomycin non-susceptibility emerged in a urine isolate collected after the patient was treated with vancomycin and dalbavancin sequentially.

The blood isolate was subjected to successive passage in vitro **in the presence of escalating dalbavancin concentrations** and the emergent isolate was subjected to repeat susceptibility testing: **vancomycin and dalbavancin non-susceptibility isolates emerged**.

Antimicrobial	S72982 (blood)	F34968 (urine)	S7-D2(*in vitro*)
	MIC (μg/mL)	MIC (μg/mL)	MIC (μg/mL)
Dalbavancin	0.015	0.5	1
Daptomycin	0.25	1	0.5
Levofloxacin	>4	>4	>4
Moxifloxacin	2	2	2
Nafcillin	16	128	16
Telavancin	0.064	0.25	0.38
Trimethoprim/sulfamethoxazole	>2/38	>2/38	>2/38
Vancomycin	1	4	4

This change in vancomycin and dalbavancin MICs was concomitant with **fourfold increases in daptomycin and telavancin MICs despite a lack of exposure to those drugs**.

Conclusions: This is the first case in which VISA has emerged in the context of a dalbavancin-containing regimen. The selection for cross-resistance to vancomycin *in vitro* by dalbavancin exposure alone is troubling. Clinicians should be aware of the possibility for emergence of dalbavancin non-susceptibility and glycopeptide cross-resistance arising following therapy.

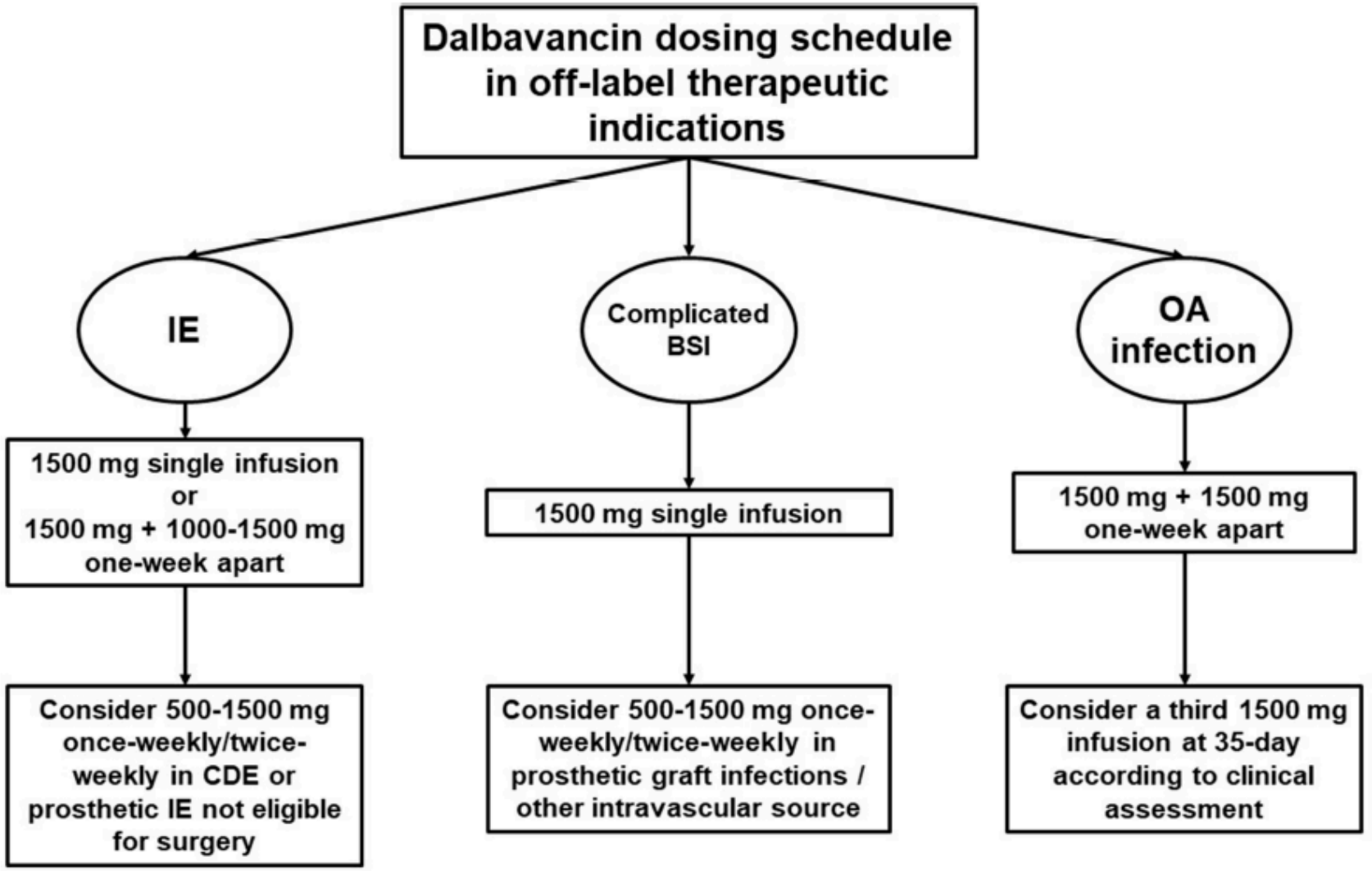

Figure 1 A proposal of algorithm for dalbavancin dosing schedule in off-label therapeutic indications.
Abbreviations: BSI, bloodstream infection; CDE, cardiac device-associated endocarditis; IE, infective endocarditis; OA, osteoarticular infection.

Gatti et al, DDDT 2021

Key points

- Ottima efficacia in vitro nei confronti dei batteri Gram-positivi (anche con profili MDR), anche in forma sessile (in biofilm)
- Evidenza di ottimi dati di efficacia clinica nel trattamento di infezioni batteriche di cute e tessuti molli
- Ottimo profilo di *safety*
- Considerevole risparmio della spesa sanitaria
- Dati insufficienti per numero e qualità per indicazioni *off-label* anche relativamente al corretto dosaggio da utilizzare
- Scarse evidenze su eventuale vantaggio di utilizzo in regimi di combinazione, soprattutto per indicazioni *off-label*