UWTASP tele-antimicrobial stewardship program | echo

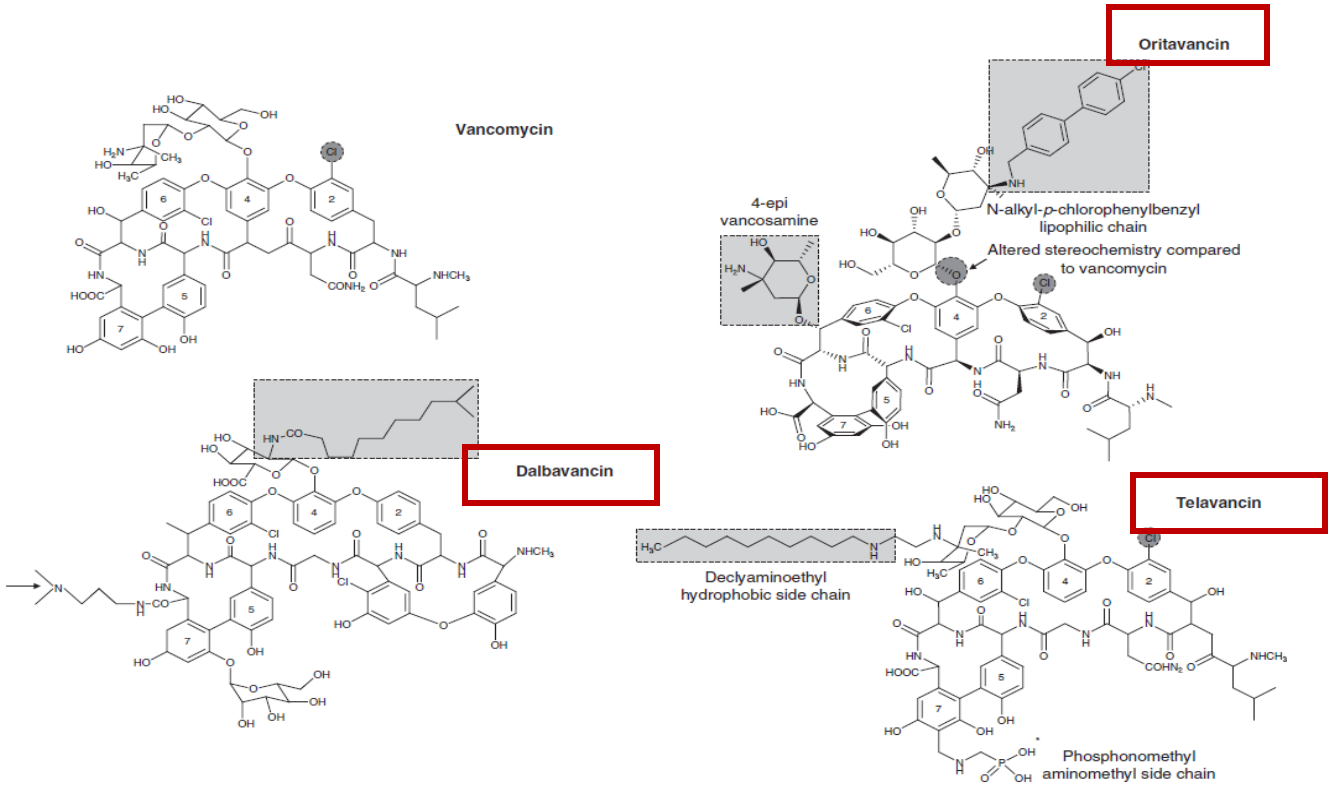
July 26, 2022

Agenda

- Speaker:
  - *Long-Acting Lipoglycopeptides*
- Case Discussions
- Open Discussion

Chemical Structure

- Inhibition of cell wall peptidoglycan cross linking
- Structural modification enhances binding affinity to the cell membrane and prolongs its half-life



Zhanel GG, et al. New Lipoglycopeptides. Drugs 2010

Comparison

	Dalbavancin	Oritavancin
Spectrum	• MRSA, MSSA, Streptococcus spp, and Enterococcus spp • VRE variable activity depends on VanA vs VanB	
VRE	Limited	Some
Half life	8.5 days (1000mg)	10.2 days
Bone	Detectable levels in bone matrix and synovial fluid	
FDA indication	Skin and soft tissue infections	
Potentials	Osteomyelitis, Bacteremia, facilitate discharge in vulnerable population requiring prolonged IV therapy and non-adherent to orals	

Lexi-Drugs. Hudson, OH: Lexicomp, 2021; Dunne MW et al. Antimicrob Agents Chemother. 2015 Apr; 59(4): 1849–1855; Lehoux D et al. Antimicrob Agents Chemother . 2015 Oct;59(10):6501-5.; Schroeder CP et al. Int J Antimicrob Agents . 2017 Jul;50(1):93-96.

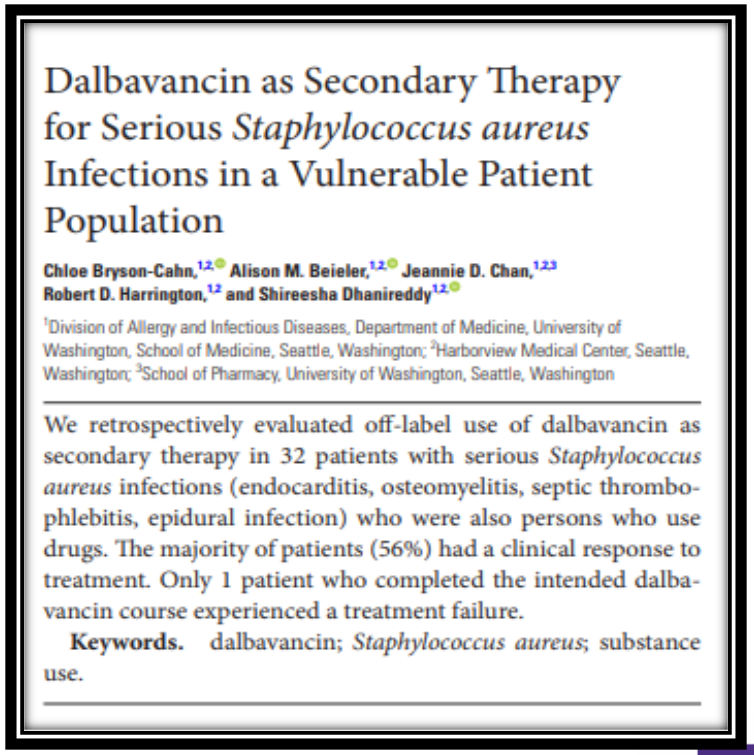
Comparison

	Dalbavancin	Oritavancin
Dosing	<u>Osteomyelitis:</u> 1500mg x1, followed by 1500mg on Day 8 <u>Endocarditis/deep seated:</u> 1000 mg x1, followed by 500 mg once weekly OR 1500 mg x1, followed by 1000 mg every 2 weeks	1200mg x1 OR 1200mg x 1, followed by 800mg qweekly
Administration	Infused over 30 mins	Orbactiv (2014): infused over 3h Kimyrsa (2021): infused over 1h
Cost	Comparable; depends on formulation and contract pricing	

Lexi-Drugs. Hudson, OH: Lexicomp, 2021; Dunne MW et al. Antimicrob Agents Chemother. 2015 Apr; 59(4): 1849–1855; Lehoux D et al. Antimicrob Agents Chemother . 2015 Oct;59(10):6501-5.; Schroeder CP et al. Int J Antimicrob Agents . 2017 Jul;50(1):93-96.

Dalbavancin at UW Medicine

- Case by case basis with ID approval
- ID Attending, Fellow, OPAT, and PharmD
- Severe infections (off-label)
  - bacteremia
  - septic arthritis
  - osteomyelitis
  - endocarditis



Dalbavancin as Secondary Therapy for Serious *Staphylococcus aureus* Infections in a Vulnerable Patient Population

Chloe Bryson-Cahn,[1,2] Alison M. Beieler,[1,2] Jeannie D. Chan,[1,2,3] Robert D. Harrington,[1,2] and Shireesha Dhanireddy[1,2]

[1]Division of Allergy and Infectious Diseases, Department of Medicine, University of Washington, School of Medicine, Seattle, Washington; [2]Harborview Medical Center, Seattle, Washington; [3]School of Pharmacy, University of Washington, Seattle, Washington

We retrospectively evaluated off-label use of dalbavancin as secondary therapy in 32 patients with serious *Staphylococcus aureus* infections (endocarditis, osteomyelitis, septic thrombophlebitis, epidural infection) who were also persons who use drugs. The majority of patients (56%) had a clinical response to treatment. Only 1 patient who completed the intended dalbavancin course experienced a treatment failure.

Keywords. dalbavancin; *Staphylococcus aureus*; substance use.

Bryson-Cahn, et al. Dalbavancin as Secondary Therapy for Serious Staphylococcus aureus Infections in a Vulnerable Patient Population. Open Forum Infectious Diseases, Volume 6, Issue 2, February 2019, ofz028.

Early Data in 2005

Efficacy and Safety of Weekly Dalbavancin Therapy for Catheter-Related Bloodstream Infection Caused by Gram-Positive Pathogens

Issam Raad,[1] Rabih Darouiche,[2] Jose Vazquez,[3] Arnold Lentnek,[4] Ray Hachem,[1] Hend Hanna,[1] Beth Goldstein,[5] Tim Henkel,[5] and Elyse Seltzer[5]

[1]The M. D. Anderson Cancer Center and [2]Veterans Affairs Medical Center, Houston, Texas; [3]Harper University Hospital, Detroit, Michigan; [4]Wellstar/Kennestone Hospital, Marietta, Georgia; and [5]Vicuron Pharmaceuticals, King of Prussia, Pennsylvania

- Open label trial, 75 patients randomized to dalbavancin (1000mg x1, 500mg one week later) or vancomycin x 2 wks
- Overall success rate was 87% (dalbavancin) vs. 50% (vancomycin), $p<0.05$
- Catheter removal: 93% (dalbavancin) vs. 56% (vancomycin)

Osteomyelitis - 2019

Open Forum Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

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

Urania Rappo,[1,*] Sailaja Puttagunta,[1,a,*] Vadym Shevchenko,[2] Alena Shevchenko,[2] Alena Jandourek,[1,b] Pedro L. Gonzalez,[3] Amy Suen,[1] Veronica Mas Casullo,[1] David Melnick,[1,c] Rosa Miceli,[1] Milan Kovacevic,[1] Gertjan De Bock,[1,d] and Michael W. Dunne[1,a]

[1]Clinical Development, Allergan plc, Madison, New Jersey; [2]Orthopedic and Trauma Department, Cherkasy Regional Hospital, Cherkasy, Ukraine; [3]Medical Affairs, Allergan plc, Jersey City, New Jersey

Study Population:

- Open label RCT
- Dalbavancin (n=70) vs. Standard of Care [SOC] (n=10) with first episode OM, 60% *S. aureus*

Intervention:

- Dalbavancin 1500mg x1 on Day 1 and repeat on Day 8

Primary Outcome:

- Clinical cure at Day 42: Dalba - 97% vs. SOC - 88%

Adverse Events:

- Reported in 10 Dalbavancin patients; no discontinuation of therapy

Real World Experiences – Dalbavancin

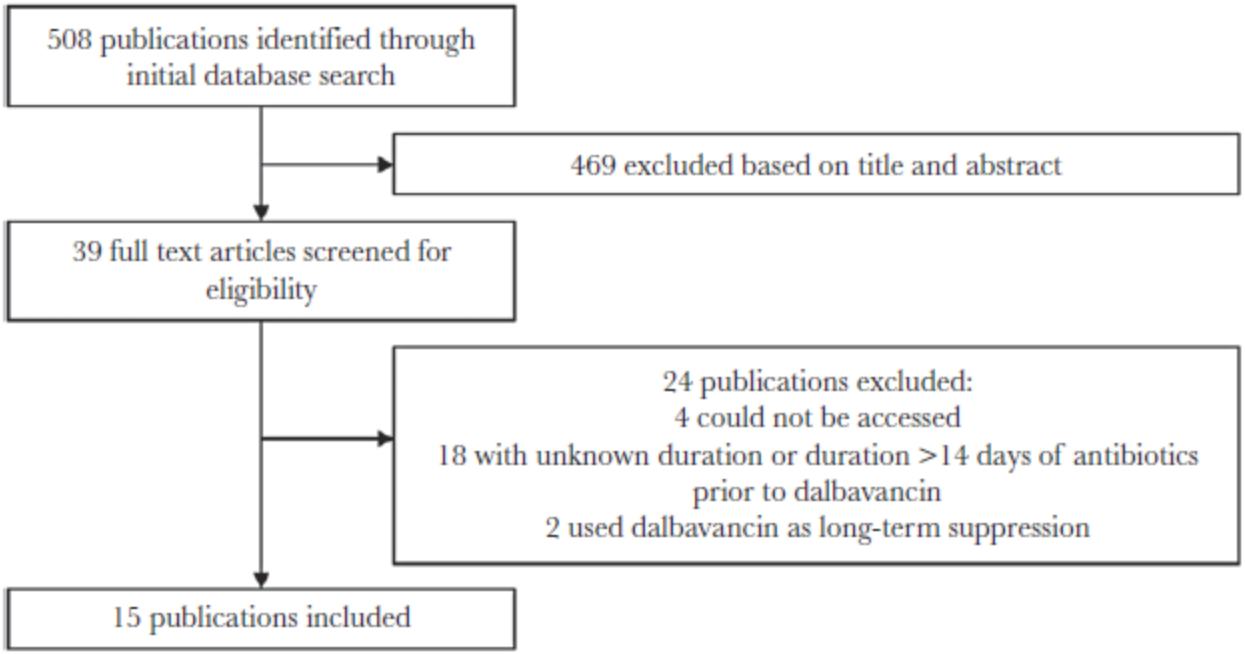
Open Forum Infectious Diseases

REVIEW ARTICLE

Multiple-Dose Dalbavancin Regimens as the Predominant Treatment of Deep-Seated or Endovascular Infections: A Scoping Review

Margaret M. Cooper,[1] Candice R. Preslaski,[1] Katherine C. Shihadeh,[1] Kellie L. Hawkins,[2,3] and Timothy C. Jenkins[2,3]

[1]Pharmacy Department, Denver Health Medical Center, Denver, Colorado, USA, [2]Division of Infectious Diseases, Department of Medicine, Denver Health Medical Center, Denver, Colorado, USA; and [3]Division of Infectious Diseases, Department of Medicine, University of Colorado School of Medicine, Aurora, Colorado, USA



Results

Various dosing regimen used

Table 3. Dalbavancin Dosing by Indication

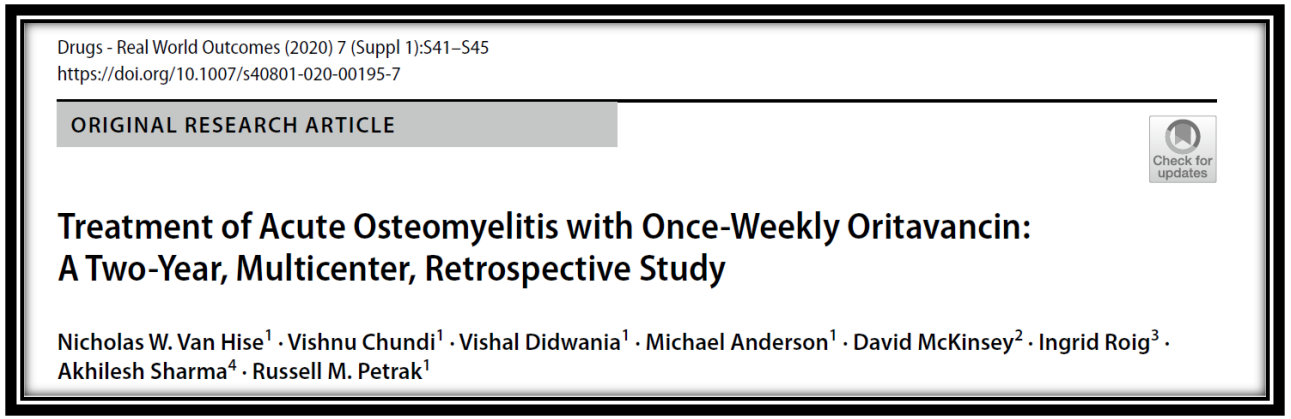
Indication	No. of Doses, Median (Range)	Total Dalbavancin Dose, g, Median (Range)
Bone or joint infection (n = 94)	2 (2–14)	3 (1.5–7.5)
Catheter-related bloodstream infection (n = 24)	2 (2–2)	1.5 (1.5–3)
Infective endocarditis (n = 19)	3 (2–6)	3.5 (1.5–4)
Complicated bacteremia (n = 7)	2 (2–3)	2.5 (1.5–4.5)

Lack of standardized clinical outcomes

Table 4. Clinical Outcomes by Indication

Indication	Clinical Success	Treatment Failure	Loss to Follow-up[a]
Bone or joint infection (n = 94)	89 (94.7)	2 (2.1)	3 (3.2)
Catheter-related bloodstream infection (n = 24)	22 (91.7)	2 (8.3)	0
Infective endocarditis (n = 19)	18 (95)	0	1 (5)
Complicated bacteremia (n = 7)	4 (57.1)	2 (28.6)	1 (14.3)

Oritavancin – Osteomyelitis



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

ORIGINAL RESEARCH ARTICLE

Check for updates

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

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]

- Retrospective review of 134 patients with acute OM (72% MRSA) across 20 ID infusion centers in 6 states
- Oritavancin 1200mg, followed by 800mg qweekly x 4-5 wks
- Clinical cure: 80%
- Adverse events: 4% without discontinuation of therapy

Dalbavancin - facilitate discharge

Open Forum Infectious Diseases

BRIEF REPORT

Use of a Standardized Dalbavancin Approach to Facilitate Earlier Hospital Discharge for Vulnerable Patients Receiving Prolonged Inpatient Antibiotic Therapy

Axel A. Vazquez Deida,[1] Katherine C. Shihadeh,[1] Candice R. Preslaski,[1] Heather L. Young,[2,3] David L. Wyles,[2,3] and Timothy C. Jenkins[2,3]

[1]Pharmacy Department, Denver Health Medical Center, Denver, Colorado, USA, [2]Division of Infectious Diseases, Department of Medicine, Denver Health Medical Center, Denver, Colorado, USA, and [3]Division of Infectious Diseases, Department of Medicine, University of Colorado School of Medicine, Aurora, Colorado, USA

Twenty-seven patients receiving prolonged inpatient antibiotic therapy for a serious bacterial infection received a single dose of dalbavancin 7–10 days before the planned end date to facilitate earlier hospital discharge. Eighty-one percent met criteria for clinical success, 7% experienced a potential adverse event, and 182 hospital days were averted.

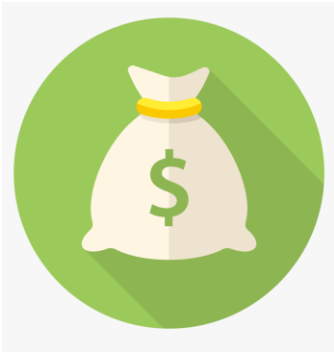
Table 1. Baseline and Clinical Characteristics (n = 27)

Age, median (IQR), y	49 (40–54)
Male	17 (63)
White/Caucasian	25 (93)
Experiencing homelessness	15 (56)
Substance use disorder[a]	
People who inject drugs	18 (67)
Noninjection drug use	7 (26)
Alcohol use disorder	6 (22)
Concomitant diseases	
Hepatitis C virus infection	13 (48)
HIV infection	4 (15)
Diabetes mellitus	2 (7)
Cirrhosis	1 (4)
Chronic kidney disease	0
Bacteremia	25 (93)
Infection	
Documented bacteremia	
Uncomplicated bacteremia	7 (26)
Complicated bacteremia	4 (15)
Right-sided infective endocarditis	7 (26)
Bone or joint infection with bacteremia	4 (15)
Pneumonia with bacteremia	2 (7)
Left-sided infective endocarditis	1 (4)

Safe and effective

Days of antibiotic therapy before dalbavancin administration, median (IQR)	21 (8.5–35)
Hospital length of stay, actual, median (IQR)	26 (10–34.5)
Hospital days averted per patient, median (IQR)	7 (6–7)
90-d inpatient re-admission, all-cause	4 (15)
90-d inpatient re-admission due to initial infection	1 (4)
90-d re-presentation to the emergency department/urgent care, all-cause	10 (37)
90-d re-presentation to the emergency department/urgent care due to initial infection	0
Follow-up appointment with either ID clinic, primary care provider, or other outpatient clinic to assess infection	13/25 (52)
Loss to follow-up	4 (15)
Potential dalbavancin-related adverse events	2 (7)
90-d mortality, all-cause	0
90-d mortality due to initial infection	0
Clinical success	22 (81)

- High clinical success
- Low rate of readmission
- Estimated cost avoidance **$9600 per patient**



STUDY PROTOCOL Open Access

Dalbavancin as an option for treatment of *S. aureus* bacteremia (DOTS): study protocol for a phase 2b, multicenter, randomized, open-label clinical trial

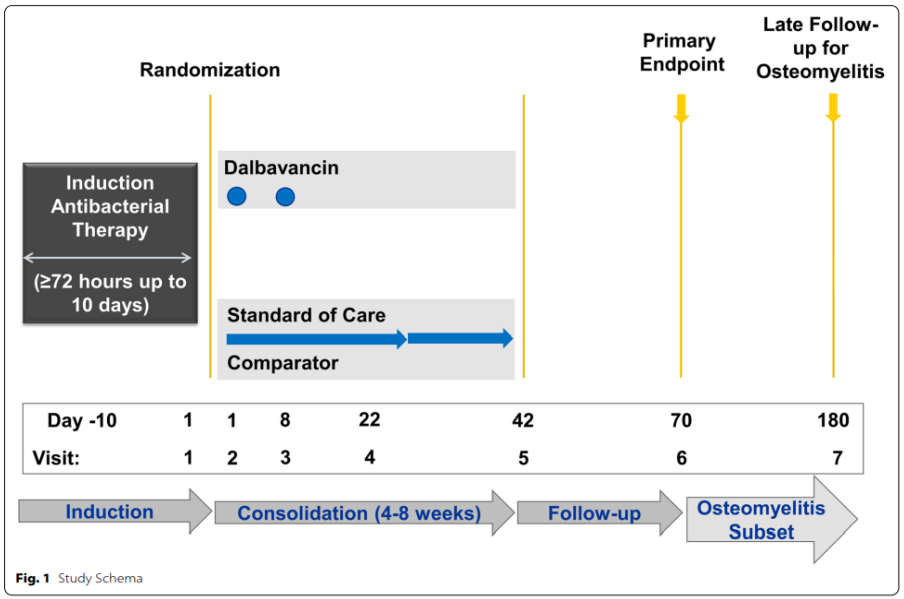


Fig. 1 Study Schema

- 200 patients with SAB (including endocarditis) treated with effective therapy for at least 3-10 days with documented clearance of bacteremia
- **Primary Outcome:** clinical success, adverse events, or complication
- **Secondary Outcome:** Quality of life and PK

Summary

- Long acting lipoglycopeptides may be an alternative as a secondary therapy for deep seated infections such as osteomyelitis, bacteremia and endocarditis

- Potential to facilitate discharge in vulnerable population with social barriers to prolonged IV therapy and non-adherent to orals as harm reduction strategy

- Clinical data are limited to observational studies but ongoing clinical trial will inform best practices