DOTS

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What’s dalbavancin

- Long-acting, lipoglycopeptide
- Mechanism: similar to vancomycin (targets cell wall cross-linking)
- Prolonged half-life 8-14 days
- FDA approved for ABSSSI

Appealing for Off-Label Use

- 32 PWUD treated with dalba for serious Staph aureus infections
- Average 13 days of standard therapy prior to transition
- 56% clinical success, 13% clinical failure

Bryson-Cahn et al. OFID 2019

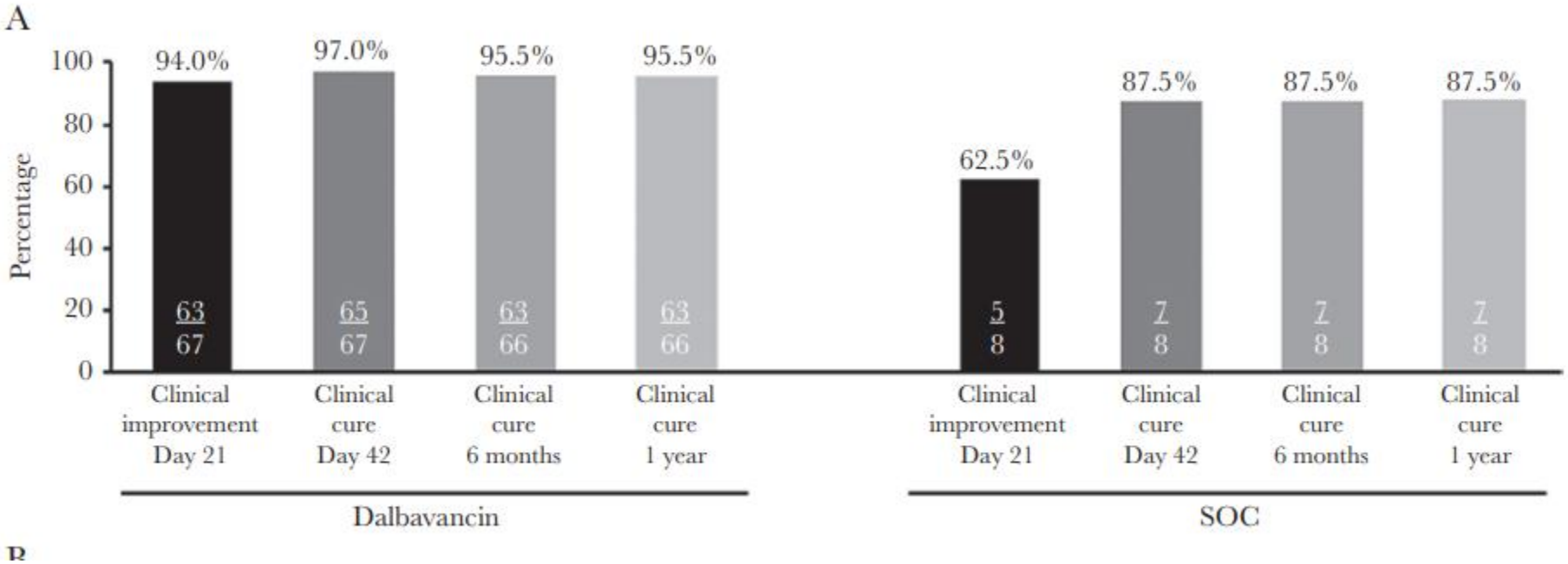
Appealing for Off-Label Use

Duration of Dalbavancin Therapy, wk		Weekly Dalbavancin Doses, mg	Successful Completion of Total Course	Type of Infection	Inpatient Antibiotics Used	No. of Days of Prior Antibiotic	Clinical Response
Planned	Actual						
5	5	1500, 1000, 500, 500, 500	Yes	Osteomyelitis, extremity	Vancomycin, TMP-SMX	10	Yes
3	3	1500, 1000, 1000	Yes	Bacteremia with infected thrombophlebitis	Vancomycin	6	Yes
2	2	1000, 500	Yes	Osteomyelitis, extremity	Vancomycin	1	Yes
3	2	1000, 500	No	Endocarditis	Ceftaroline	4	Yes
2	2	1000, 500	No	Osteomyelitis, extremity	Vancomycin, doxycycline	17	Yes
2	2	1000, 500	No	Endocarditis	Vancomycin	8	Yes
1	1	1000	No	Bacteremia, flexor tenosynovitis	Vancomycin	10	Yes
1	1	1000	Yes	Septic arthritis	Vancomycin	8	Yes
1	1	1000	No	Endocarditis	Cefazolin	24	Yes
1	1	1000	No	Osteomyelitis, spine	Vancomycin	3	Yes

Bryson-Cahn et al. OFID 2019

RCT for Osteomyelitis – 81 patients

- Phase 2, single-center, randomized, open-label RCT
- 7:1 dalba 1500mg IV day 1 and day 8 vs. IV 4-6 wks



Rappo, et al. OFID 2018

Original Investigation

Dalbavancin for Treatment of *Staphylococcus aureus* Bacteremia
The DOTS Randomized Clinical Trial

Nicholas A. Turner, MD, MHSc[1]; Toshimitsu Hamasaki, PhD[2]; Sarah B. Doernberg, MD, MAS[3] ; et al

- Is dalbavancin superior for complicated SAB compared with standard care?

- Open-label, assessor-masked, randomized, superiority trial
- 23 medical centers (US & Canada)

DOTS, JAMA. 2025;334;(10):866-877. doi:10.1001/jama.2025.12543 2025.

Major Inclusion/Exclusion Criteria

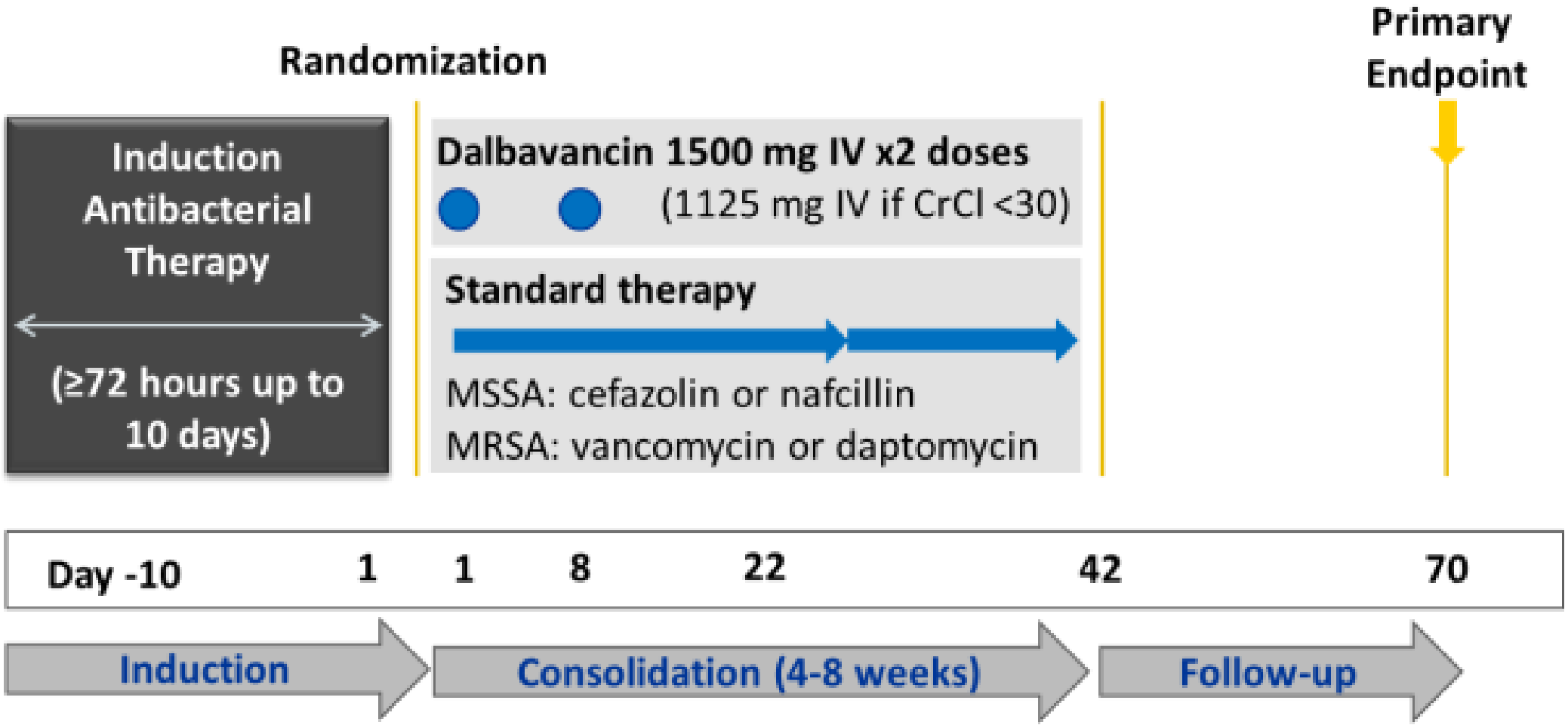
Inclusion

- Hospitalized
- >18 years
- Complicated SAB, but afebrile with culture clearance
- 3-10 days of initial antibiotics

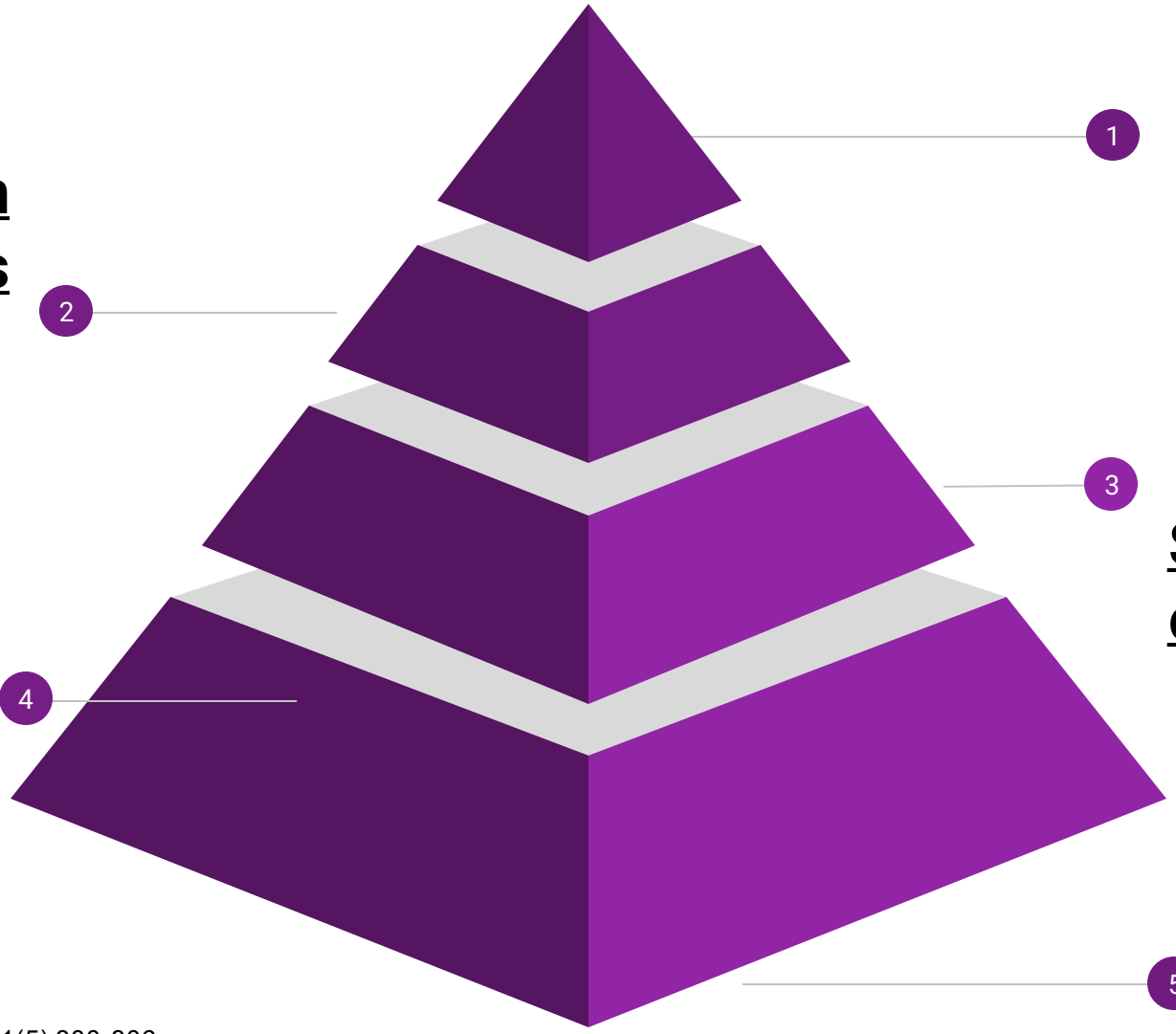
Exclusion

- CNS infection
- Left-sided IE, perivalvular abscess
- Planned R valve replacement
- Infected, unremoved hw
- Severe immunosuppression
- Vanco non-susceptible isolate

Protocol


Randomization
Primary Endpoint
Induction Antibacterial Therapy
(≥72 hours up to 10 days)
Dalbavancin 1500 mg IV x2 doses
(1125 mg IV if CrCl <30)
Standard therapy
MSSA: cefazolin or nafcillin
MRSA: vancomycin or daptomycin
Day -10
1
1
8
22
42
70
Induction
Consolidation (4-8 weeks)
Follow-up

DOOR analysis



1. **Clinical benefit without AEs**
2. **Clinical benefit with some AEs**
3. **Survival without clinical benefit or AEs**
4. **Survival without clinical benefit, AEs**
5. **Death**

Slide Credit: Joanne Huang, PharmD

Evans S, et al. Clinical Infectious Diseases. 2015;61(5):800-806.

Primary Outcome

- Desirability of outcome ranking (DOOR) at day 70

Table 1: Primary Outcome – Desirability of Outcome Ranking (DOOR) Endpoint Scoring

Rank	**Alive**	**How many of:** **1) Clinical failure** **2) Infectious complication** **3) Serious adverse event or adverse event leading to study drug discontinuation**	**Health-related Quality of Life**
1	Yes	0 of 3	Tiebreaker based on net change in health-related quality of life score from baseline
2	Yes	1 of 3	
3	Yes	2 of 3	
4	Yes	3 of 3	
5	No (Death)	Any	

Secondary Outcomes

- Clinical efficacy: composite of lack of failure, infectious complications or mortality
- Safety (serious AEs or AE leading to drug discontinuation)

Statistical Analysis

- Powered to eval for dalba superiority by DOOR
- Prespecified 20% noninferiority margin (Primary and Secondary)

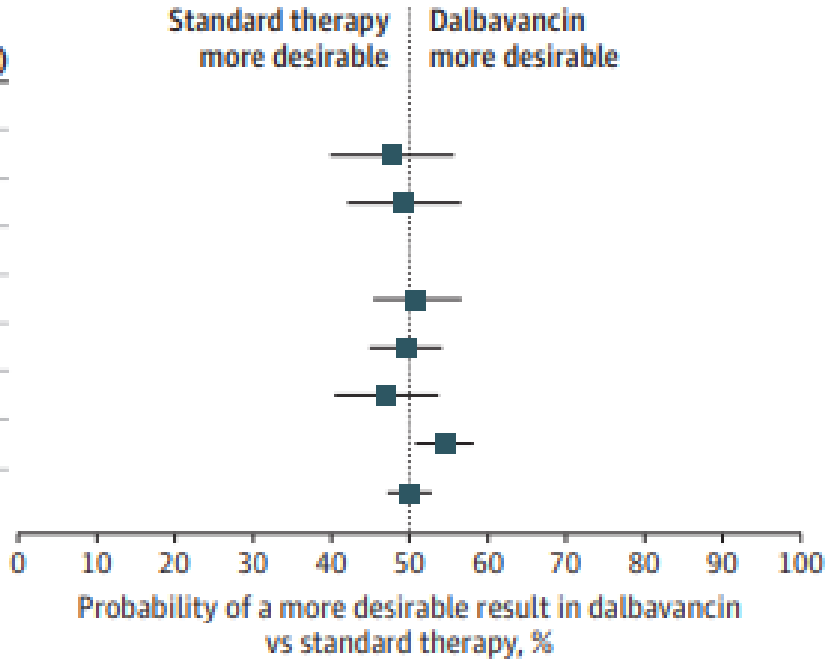
Table 1 Highlights

	Dalba (n = 100)	Standard (n=100)
PWID	16	13
Comorbidities		
Diabetes	44	48
Immunosuppressed	35	26
CKD/Dialysis	20/12	30/13
Implanted prosthetic material	12	4
MRSA	34	32
Site of infection		
SSTI	40	30
Osteo (non-vertebral)	17	19
Right-sided endocarditis	6	4
Deep-seated infection	54	51
Days of bacteremia >4	2	10
Duration pre-randomiz, median (IQR), d	8 (6-9)	7 (6-9)

Figure 2. Primary Outcome (As-Randomized Population)

A Desirability of outcome ranking and components by treatment group

Source	Participants, No. (%)		Desirability of outcome ranking probability, % (95% CI)
	Dalbavancin (n = 100)	Standard therapy (n = 100)	
Desirability of outcome ranking			
With quality-of-life tiebreak (primary)			47.7 (39.8-55.7)
Without quality-of-life tiebreak			49.3 (42.0-56.6)
Desirability of outcome ranking components			
Clinical failure	20 (20.0)	22 (22.0)	51.0 (45.3-56.7)
Infectious complications	13 (13.0)	12 (12.0)	49.5 (44.8-54.2)
Nonfatal serious adverse events	40 (40.0)	34 (34.0)	47.0 (40.4-53.7)
Adverse events leading to discontinuation	3 (3.0)	12 (12.0)	54.5 (50.8-58.2)
Death	4 (4.0)	4 (4.0)	50.0 (47.1-52.9)



Dalbavancin did not demonstrate superiority compared to standard therapy (probability of better DOOR with dalbavancin was 47%)

Table 2. Secondary and Exploratory Efficacy Analyses (As-Randomized Population)

Outcomes	No. (%)		
	Dalbavancin (n = 100)	Standard therapy (n = 100)	Difference in proportions (95% CI)
Secondary outcome			
Clinical efficacy at day 70	73 (73)	72 (72)	1.0 (−11.5 to 13.5)[a,b]

Dalbavancin was noninferiority relative to standard therapy for clinical efficacy

Subgroup analyses were all consistent for DOOR and clinical efficacy across pathogen, all categories of infection, bacteremia duration, PWID, immunosuppression

Adverse Events though Day 70

	Dalba (n = 100)	Standard (n=100)
Serious Adverse Events	40	34
AEs leading to study drug discontinuation	3	12
Catheter-associated thrombosis	0	3
Central-line associated infection	1	2
Treatment-emergent resistance	**1**	**1**

Conclusions

- Dalbavancin was not superior to standard IV therapy by DOOR for cleared, complicated SAB
- But it is non-inferior for clinical efficacy!
- Important exclusions: Left-sided IE, retained infected hardware
- Important inclusions: MSSA

Planned future analyses:

- Economic analysis
- Drug optimization