Clinical Outcomes and Cost Savings of Dalbavancin Use in OPAT: Focus on Complicated *Staphylococcus aureus* Infections

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INTRO / BACKGROUND

The practical and financial benefits of long-acting glycopeptides are increasingly recognized, and their efficacy is becoming better established for a variety of indications. One area of continuous focus for institutions is facilitating timely discharge from the inpatient setting, and thoughtful use of dalbavancin for discharge facilitation as early as clinically appropriate has been an effective way to minimize unnecessary inpatient days and maximize cost savings.

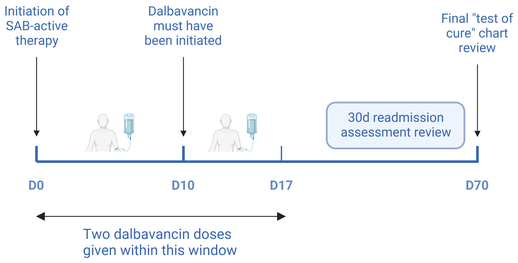
Dalbavancin use as primary therapy (initiation within the first 10 days of active therapy) for complicated *Staphylococcus aureus* (cSA) infections, however, has only been described in small case series to this point. In nearly all these cSA descriptions, dalbavancin was utilized exclusively as consolidation therapy following significant lead-in with other antimicrobials, and a recent manuscript highlighted the significant variability in approach to the use of multiple dose dalbavancin regimens in the literature.[1] The presently enrolling Dalbavancin as an Option for Treatment of *Staphylococcus aureus* Bacteremia study (DOTS; NCT04775953) is anticipated to provide controlled data evaluating a standardized approach, however, we aimed to retrospectively evaluate a subset of dalbavancin patients at our institution that had been treated under similar conditions.

METHODS

This retrospective review identified patients prescribed dalbavancin for any indication and followed by the Nebraska Medicine OPAT team since program implementation (4/1/2019 - 4/30/2022). A cohort of recent inpatients with similar lengths-of-stay, ID clinical indications, and lack of major inpatient complications was identified and used to calculate an average institutional cost per inpatient day for cost savings calculations ($2200/day).

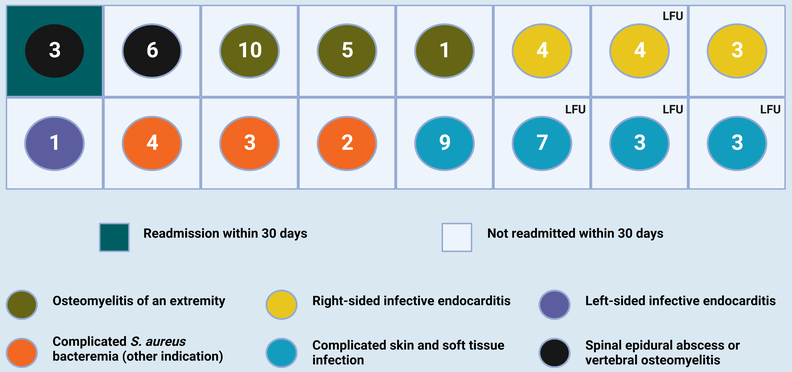
Patients in the cSA infection subgroup were defined by need for >2 weeks of treatment for *Staphylococcus aureus* infection involving bacteremia. Dalbavancin as primary therapy for cSA was defined as initiation of dalbavancin within the first 10 days of antibiotic therapy and continued to the end of treatment; patients must have received all prescribed doses to be included. The primary clinical outcome was 30-day readmission rate (both infection-related and not infection-related). Patients were also evaluated via chart review for "test-of-cure" at 70 days (clinical success, without complications or adverse events) following therapy initiation to assess longer-term treatment success.

Dalbavancin for cSA Subgroup Timeline



OPAT use of dalbavancin was associated with low readmission rates. Retrospective analysis of multiple-dose dalbavancin for primary therapy of complicated *Staphylococcus aureus* infections demonstrated favorable clinical outcomes.

FIGURE 1: Characteristics of the sixteen patients who received dalbavancin for cSA infections



Numbers within circles represent days from calculated therapy start date to dalbavancin initiation

A "LFU" in the upper right corner of the square indicates patients where 70-day clinical cure couldn't be assessed

Initiative	CY19 Savings	CY20 Savings	FY22 Savings	Total Documented Savings - Initial 3 Program Years:
Complex Ortho ID patients decreased time from OR to discharge	$435,600	$699,600	$621,600	
Decreased LOS secondary to utilization of dalbavancin in appropriate patients	$943,000	$1,034,000	$1,168,200	
Readmissions avoided due to preemptive outpatient OPAT interventions	$100,000	$460,000	$420,000	
Estimated Total Annual Contribution	**$1,478,600**	**$2,193,600**	**$2,209,800**	**$5,882,000**

FIGURE 2: OPAT Program Cost Savings Summary

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RESULTS

A total of 66 patients were prescribed dalbavancin for treatment of any infection during the study period (Table 1). **The all-cause 30-day readmission rate was 13.6% (9 of 66 patients), and the infection-related 30-day readmission rate was 3% (2 of 66).**

Table 1: Characteristics of the Overall Dalbavancin Cohort

Characteristic	(n=66)
Indication for dalbavancin (no. / %)	
Osteomyelitis	21 (32%)
Epidural abscess	3 (5%)
Septic arthritis	7 (11%)
Skin/soft tissue infection	11 (17%)
Endocarditis	12 (18%)
Catheter-related infection	2 (3%)
Other	10 (15%)
Organism identified (no. / %)	
S. aureus	46 (70%)
Coagulase-negative staphylococci	4 (6%)
Streptococci	2 (3%)
Polymicrobial	7 (11%)
Other	3 (5%)
Culture negative	4 (6%)
Dalbavancin regimen utilized (no. / %)	
1500mg once	21 (32%)
1500mg x2 doses, one week apart	39 (59%)
1500mg once, then 500mg weekly	6 (9%)

- Of 45 patients that were prescribed a multiple-dose dalbavancin regimen, 39 (86.7%) completed their regimen as planned (within 24 hours of schedule):
  - Three patients never returned for repeat dosing
  - One patient experienced itching, flushing, and tinnitis post-infusion and was switched to oral antibiotics to complete therapy
  - Two patients eventually completed therapy after OPAT team intervention (second doses were given 4 and 7 days late)
- Most common factors leading to patients being judged as preferential dalbavancin candidates:
  - Lack of financial resources or insurance (10 cases)
  - Active IV drug use (35 cases)
  - Inadequate social support or unstable housing (22 cases)
  - Avoid line placement or other medical indication (13 cases)
  - Facilitate discharge to decompress census during COVID-19 surge (2 cases)

In subgroup analysis, dalbavancin was utilized for primary therapy of cSA infections in 16 patients (Figure 1). Only one patient (6.3%) had a 30-day readmission, which was due to progression of cSA-associated vertebral osteomyelitis-discitis.

- In assessment of 70-day test-of-cure, 11 of 12 patients were evaluated as a clinical success (91.7%), with 4 patients lost to long-term follow-up with no chart documentation available at or beyond 70 days
- Patients were initiated on dalbavancin after a mean of 4 days following calculated therapy initiation date

Yearly institutional cost savings calculations for inpatient days of therapy avoided for the complete dalbavancin cohort were **$943,800** (CY2019); **$1,034,000** (CY2020); and **$1,168,200** (FY2022). Use of dalbavancin avoided a median of 25 days of inpatient stay per episode and 506 mean days per year in these patients where discharge was judged to have been suboptimal or impossible. These data are presented within **Figure 2** as a portion of overall cost savings and return-on-investment financial metrics for our OPAT program (including for other non-study-related initiatives) since inception.

CONCLUSIONS

Treatment success and readmission outcomes with the use of dalbavancin generally were consistent with those of our OPAT program overall, despite the complex infections and challenging circumstances characteristic of outpatient therapy in this cohort

Retrospective evaluation of a subset of patients treated for cSA infections involving bacteremia utilizing a similar methodology to the ongoing DOTS clinical trial demonstrated equally encouraging clinical outcomes. This study is the largest to-date evaluating dalbavancin as primary therapy for cSA infections and extends the work of other groups by demonstrating efficacy in a sizable cohort with an early shift from initial therapy to dalbavancin. Although we did not evaluate a paired standard-of-care cohort, DOTS will soon provide randomized controlled data evaluating this approach.

Significant cost savings was associated with OPAT interventions related to dalbavancin discharge facilitation, and when combined with other assessments of OPAT program return-on-investment, have more than justified OPAT service creation and subsequent approval of additional nursing and pharmacy resources

REFERENCES

1. Cooper MM, et al. Open Forum Inf Dis. 2021 Oct 27.