Real World Experience with Daptomycin (DAP) and Ceftaroline (CPT) Combination Therapy for Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia

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BACKGROUND

- MRSA bacteremia is associated with significant mortality rates up to 30%. Guideline-recommended first-line therapy includes monotherapy with either vancomycin or DAP.
- Alternative regimens are recommended for persistent MRSA bacteremia of ≥ 7 days or earlier if evident clinical deterioration.
- The combination of DAP plus CPT has been investigated as salvage therapy due to its synergistic mechanism potential.
- There are limited studies evaluating the clinical outcomes of MRSA bacteremia in patients treated with DAP plus CPT combination therapy.

OBJECTIVE

- Evaluate the efficacy of DAP plus CPT combination therapy for the treatment of MRSA bacteremia and identify independent predictors of 30-day mortality.

METHODS

Study Design
- Single center, retrospective chart review conducted from January 1, 2014 to August 31, 2019

Inclusion Criteria
- Age ≥ 18 years old
- Patients with ≥ 1 blood culture with MRSA and hospitalized for at least 24 hours

Exclusion Criteria
- Polymicrobial bacteremia

Primary Endpoint
- Independent predictors of 30-day mortality

Secondary Endpoints
- Duration of bacteremia
- Time to combination therapy
- Source control
- Rate of bacteremia reoccurrence

Statistical Analysis
- Univariate and multivariable analyses were performed to identify independent predictors of 30-day mortality
- Continuous data were compared by the Student's t test or Mann–Whitney U test

RESULTS

Table 1. Cohort Characteristics

Covariate	(n = 65)
Age, mean (±SD), y	61.1 (13.3)
Male, no. (%)	42 (67.7)
CCI, median (IQR)	3 (3-4)
Immunocompromised, no. (%)	15 (23.1)
Concomitant statin, no. (%)	18 (27.7)
Vancomycin MIC >1, no. (%)	11 (16.9)
Daptomycin dose (mg/kg), median (IQR)	8.9 (7.9-9.9)
Reason for combination therapy, no. (%)	
Persistent bacteremia	52 (80)
Physician preference	10 (15.4)
Endovascular source	3 (4.6)
Renal function, no. (%)	
CrCl ≥ 50 (no RRT)	31 (47.7)
CrCl <50 (no RRT)	11 (16.9)
HD	15 (23.1)
CRRT/SLED	8 (12.3)
Source, no. (%)	
Endovascular	20 (30.8)
Catheter	14 (21.5)
Secondary	31 (47.7)
ICU LOS, median (IQR)	6 (0-13)
Hospital LOS, median (IQR)	20 (16-32)
Days to combination therapy, median (IQR)	7 (5-9)
Combination within 72 hrs., no. (%)	11 (16.9)
Source control, no. (%)	31 (47.7)
Bacteremia cleared, no. (%)	59 (90.8)
Reoccurrence, no (%)	8 (12.3)
30-day mortality, no (%)	10 (15.4)

Table 2. Adverse events

Covariate	(n = 65)
Thrombocytopenia, no. (%)	8 (12.3)
Rhabdomyolysis, no. (%)	6 (9.2)
Daptomycin discontinued	4 (6.1)

RESULTS

Table 3. Analysis of 30-day mortality

Covariate	Univariate Analysis OR (95% CI)	p-value	Multivariable Analysis OR (95% CI)	p-value
Age	1.01 (0.96-1.06)	0.80	-	
Male	0.79 (0.20-3.15)	0.74	-	
CCI	0.99 (0.97-1.00)	0.25	-	
IVDU	6.00 (0.34-104.79)	0.22	-	
Immunocompromised	0.81 (0.15-4.29)	0.80	-	
Endovascular source	0.96 (0.22-4.16)	0.95	-	
Catheter source	2.67 (0.64-11.11)	0.18	2.76 (0.63-12.11)	0.18
Secondary source	0.51 (0.13-4.49)	0.58	-	
Source control	0.41 (0.10-1.77)	0.23	-	
Vancomycin MIC > 1	1.28 (0.23-7.04)	0.78	-	
CrCl ≥ 50 (no RRT)	0.57 (0.06-5.05)	0.61	-	
CrCl < 50 (no RRT)	0.22 (0.04-1.15)	0.07	0.26 (0.38-1.17)	0.08
HD	1.54 (0.34-6.86)	0.57	-	
CRRT/SLED	4.29 (0.84-21.99)	0.08	4.43 (0.83-23.74)	0.08
Any RRT	3.35 (0.84-13.44)	0.09	3.48 (0.84-14.25)	0.12

Table 4. Bacteremia duration relative to time of combination therapy

Covariate	DAP-CPT within 72 hours of index culture (n = 10)	DAP-CPT after 72 hours of index culture (n = 49)	p-value
Days to clearance after combination, median (IQR)	2 (1-5)	3 (1-6)	0.526
Days to clearance, median (IQR)	4 (2-6)	11 (8-15)	0.018

Table 5. Bacteremia duration relative to renal function

Covariate	RRT (n = 21)	No RRT (n = 38)	p-value
Days to clearance after combination, median (IQR)	5 (2-8)	2 (1-5)	0.04

CONCLUSIONS

- There were no significant independent predictors of 30-day mortality.
- Time to bacteremia clearance for patients switched to DAP-CPT within 72 hours versus after 72 hours did not differ.
- DAP-CPT combination therapy resulted in clearance of persistent bacteremia and may serve as an effective salvage therapy.

DISCLOSURES

Authors have no conflicts of interests regarding personal or financial relationships with commercial entities that may have influenced the content or subject matter of this presentation.

REFERENCES

A complete reference list will be made available upon request

Abbreviations: Charlson Comorbidity Index (CCI), length of stay (LOS), renal replacement therapy (RRT), continuous renal replacement therapy (CRRT), sustained low efficiency dialysis (SLED), hemodialysis (HD), intravenous drug use (IVDU)