Characterization of Ceftaroline or Daptomycin Escalation for Methicillin-Resistant Staphylococcus Aureus Bacteremia

Natalie Klein, PharmD; Katie Rocawich, PharmD, BCPS, BCCCP
VCU Health System Department of Pharmacy Services
Richmond, Virginia

Background/Purpose: Methicillin-resistant Staphylococcus aureus (MRSA) bacteremia is a serious infection associated with high morbidity and mortality rates. Vancomycin remains the mainstay of treatment for MRSA bacteremia, but treatment failures can occur due to its slow bactericidal activity, resistance or strains with reduced susceptibility, and inadequate source control. Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of MRSA Infections recommend treatment with vancomycin or daptomycin, but are vague in reference to the escalation of antibiotic regimen, and predate the FDA approval of ceftaroline. Therefore, many questions remain surrounding optimal therapy including time to begin combination or alternative therapy, appropriate cadence of therapy, and antibiotic treatment superiority.
Ceftaroline is an anti-staphylococcal cephalosporin antibiotic used off-label for treatment of MRSA bacteremia. There exists a growing body of evidence for ceftaroline use in MRSA bacteremia, most of which is in combination with daptomycin or as monotherapy. However, limited data exist assessing the escalation of vancomycin to daptomycin versus ceftaroline for the treatment of MRSA bacteremia.
The aim of this study is to characterize MRSA bacteremia resolution with daptomycin compared to ceftaroline when used as monotherapy or in combination with vancomycin.

Methods: A single center, retrospective, electronic chart review of adult patients with positive MRSA blood cultures for more than 24 hours and received either daptomycin or ceftaroline during inpatient admission from January 1, 2015 to April 30, 2021. The data collected from Cerner Information Systems. Patients were excluded if they received both daptomycin and ceftaroline or received either agent for less than 48 hours or after culture clearance. The primary endpoint was time to culture clearance after change in antibiotic therapy. The secondary endpoints assessed vasopressor requirements, ICU and hospital length of stay, and survival to discharge.

Results: Of the 117 patients reviewed, 57 patients were included. Our findings showed time to culture clearance after initiating daptomycin (n= 9) was 32.6 hours (IQR 15.3 to 109.7) compared to ceftaroline (n= 48) was 65.5 hours (IQR 25.5 to 126.7), p= 0.206. Of note, patients in the ceftaroline group had significantly longer ICU length of stay (6.8 days $\pm$ 12.6, p=0.002) and hospital length of stay (24.7 days $\pm$ 17.4, p= 0.001) when compared to daptomycin.

Conclusion: Our findings characterize the escalation of antibiotic therapy for persistent MRSA bacteremia, and suggest the utility of a prospective study on this topic.

Table 1. Primary and Secondary Outcomes

Table 1.1 Primary Outcomes	**Daptomycin group (n= 9)**	**Ceftaroline group (n= 48)**	**P-value**
Time to culture clearance, hours [mean ± SD]	145.2 + 68.7	185.5 ± 89.1	0.206
Time to culture clearance after initiating alt antibiotic, hours [median (IQR)]	32.6 (15.3, 109.7)	65.5 (25.5, 126.7)	0.289
Table 1.2 Secondary Outcomes			
Use of vasoactive medication, yes [no. (%)]	1 (11.1)	18 (37.5)	0.096
ICU length of stay, days [mean + SD]	0.55 ± 1.7	6.8 ± 12.6	0.002
Hospital length of stay, days [mean ± SD]	15.8 ± 6.6	24.7 ± 17.4	0.001
Survival to discharge, yes [no. (%)]	9 (100)	43 (89.6)	0.179
Recurrence of MRSA bacteremia after study episode, yes [no./n (%)]	2/9 (22.2)	7/43 (16.3)	0.676