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Paper Poster Session
Endocarditis

Ceftaroline fosamil for the treatment of methicillin-resistant Staphylococcus aureus infective endocarditis

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Background: Despite the advent of novel treatment strategies for Methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections (BSI), outcomes remain poor with persistent BSI and mortality common. Moreover, the optimal treatment paradigm for persistent infection is unknown. The Infectious Diseases Society of America MRSA guidelines recommend assessing the need to change therapy if BSI has not cleared within 7 days, but clinical outcomes data supporting this recommendation are limited. The objective of this analysis was to determine the relationship between MRSA BSI duration and mortality.

Material/methods: Retrospective, single-center, observational cohort study from 2005 to 2015. Inclusion criteria: age ≥ 18 years; ≥ 1 positive MRSA blood culture. Second MRSA BSI episodes in patients experiencing > 1 episode during the study period were excluded. The primary outcome was 30-day mortality, defined as mortality from any cause within 30 days of index culture. Classification and regression tree (CART) analysis was used to determine BSI durations, measured in days from date of index culture, most strongly associated with 30-day mortality. Following determination of the CART breakpoints, demographics and clinical characteristics between 30-day survivors and non-survivors were compared using the Chi-squared or Fisher's exact test, and Student's *t*-test or Mann-Whitney *U* test where appropriate. The independent association between the CART breakpoints and 30-day mortality was then examined using backward, stepwise logistic regression.

Results: 575 patients were included. Demographics/clinical characteristics: mean (SD) age 55.9 (15.2); 63.3% male; 71% African American. Common co-morbidities: chronic kidney disease 22.7%; hemodialysis 14.6%; diabetes 32.5%; liver disease 20.3%; malignancy 5.2%; HIV/AIDS 6.6%; intravenous-drug user 33.2%. Sources of BSI: infective endocarditis 46.1%; skin and soft tissue 12.3%; pneumonia 12.5%; bone/joint 10.6%; other/unknown 8.0%; intravenous catheter 5.4%, deep abscess 4.2%. In the CART analysis, 30-day mortality was significantly higher among patients with BSI durations > 7 days compared with ≤ 7 days (21.4% versus 11.9% $P < 0.003$). Among the 402 patients with a BSI duration ≤ 7 days, a second CART breakpoint was discovered; 30-day mortality was numerically higher among patients with BSI durations of 3-7 days relative to 1-2 days (14.1% versus 7.9% $P < 0.070$). In logistic regression, BSI durations > 7 days (aOR 1.694; 95% CI 1.018-

2.819), pneumonia source (aOR 3.308; 95% CI 1.552-7.050), infective endocarditis source (aOR 2.691; 95% CI 1.473-4.914), and acute renal failure (aOR 2.233; 95% CI 1.383-3.605) were independently associated with 30-day mortality.

Conclusions: Mortality was highest among patients with MRSA BSI durations > 7 days. However, the incidence of mortality increased monotonically as BSI duration increased. A second increase in mortality was noted after 3 days of bacteremia, highlighting the importance of continual assessment of treatment adequacy when BSI fail to clear.