**Supplemental Table 1.** Baseline demographics, clinical characteristics, and outcomes of entire cohort

| | **N = 211** |
|---|---|
| **Demographics** | |
| Age, years | 59 (48 – 67) |
| Male sex | 126 (59.7) |
| Race | |
| African American | 140 (66.4) |
| Caucasian | 54 (25.6) |
| Hispanic/Latino | 1 (0.5) |
| Other | 16 (7.6) |
| Hospital System | |
| Detroit Medical Center | 136 (65.5) |
| UF Health – Shands Hospital | 38 (18.0) |
| Henry Ford Hospital | 37 (17.5) |
| | |
| **Comorbidities and past medical history** | |
| Prior hospitalization (1 year) | 129 (61.1) |
| Prior surgery (30 days) | 32 (15.2) |
| Prior antibiotics (90 days) | 51 (24.2) |
| Prior MRSA infection, (1 year) | 36 (17.1) |
| Obesity | 70 (33.2) |
| Diabetes mellitus | 77 (36.5) |
| Chronic kidney disease | 64 (30.3) |
| Chronic hemodialysis | 40 (19.0) |
| Liver disease | 34 (16.1) |
| Intravenous drug user | 37 (17.5) |
| Cerebrovascular accident | 11 (5.2) |
| COPD | 50 (23.7) |
| Heart failure | 60 (28.4) |
| Malignancy | 15 (7.1) |
| HIV/AIDS | 12 (5.7) |
| Neutropenia[a] | 7 (3.3) |
| Charlson comorbidity index | 3 (2-6) |
| | |
| **Clinical characteristics** | |
| Intensive care unit[b] | 70 (33.2) |
| APACHE II[b] | 16 (11-20) |

| | N = 211 |
|---|---|
| Lower respiratory tract source | 69 (32.7) |
| Infective endocarditis source | 49 (23.2) |
| Bone/joint source | 45 (21.3) |
| Intravenous catheter source | 31 (14.7) |
| Skin/soft tissue source | 17 (8.1) |
| Other source | 38 (18.0) |
| Polymicrobial BSI | 19 (9.0) |
| Vancomycin-susceptible[c] | 208 (98.6) |
| Daptomycin-susceptible[c,d] | 187 (95.4) |
| Ceftaroline-susceptible[e] | 155 (98.1) |
| BSI duration pre-ceftaroline, days | 5 (3-9) |
| | |
| **Treatment information** | |
| Infectious diseases consult | 189 (93.1) |
| Source control pursued | 75 (36.4) |
| Vancomycin prior directed therapy | 184 (87.2) |
| Daptomycin prior directed therapy | 86 (40.8) |
| Ceftaroline dosing frequency | |
| Every 8 hours | 108 (51.2) |
| Every 12 hours | 95 (45.0) |
| Every 24 hours | 8 (3.8) |
| Ceftaroline dose | |
| 600 mg | 129 (61.1) |
| 400 mg | 30 (14.2) |
| 300 mg | 15 (7.1) |
| 200 mg | 37 (17.5) |
| Ceftaroline inpatient duration, days | 11 (5 – 15) |
| Ceftaroline line of therapy | |
| Ceftaroline initial directed therapy | 8 (3.8) |
| Ceftaroline second directed therapy | 111 (52.6) |
| Ceftaroline third directed therapy | 79 (37.4) |
| Ceftaroline fourth directed therapy | 13 (6.2) |
| Combination therapy | 46 (21.8) |
| Common reasons to use ceftaroline | |
| Perceived failure of prior therapy | 102 (48.3) |
| Elevated vancomycin MIC | 47 (22.3) |
| Adverse reaction of prior therapy | 24 (11.4) |

| | N = 211 |
|---|---|
| Pulmonary coverage | 27 (12.8) |
| Polymicrobial infection/extend spectrum of activity | 15 (7.1) |
| Unknown/not documented | 20 (9.5) |
| | |
| **Outcomes** | |
| Clinical success | 153 (72.5) |
| In hospital mortality | 40 (19.0) |
| Cleared BSI on ceftaroline | - |
| BSI duration, days | 5 (3-9) |
| BSI duration post-ceftaroline initiation, days | - |
| Length of stay post-BSI, days | 16 (12-26.75) |
| Length of stay post-ceftaroline, days | 11 (7-19) |
| Inpatient adverse drug | |
| Clostridium difficile infection | 6 (2.8) |
| Rash | 7 (3.3) |
| Neutropenia[f] | 3 (1.4) |

Data presented as n (%) or median (IQR)

Abbreviations: UF, University of Florida; MRSA, methicillin-resistant *Staphylococcus aureus*; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; APACHE, acute physiology and chronic health evaluation; BSI, bloodstream infection; MIC, minimum inhibitory concentration

[a] Defined as absolute neutrophil count < 500 cells/$mm^3$ at ceftaroline initiation

[b] At time of index culture

[c] Susceptibility determined by Microscan, Vitek 2, BD Phoenix, or Etest.

[d] Daptomycin susceptibility available for 196 patients

[e] Ceftaroline susceptibility determined by Etest for 158

[f] Defined as decrease in neutrophil count to < 1,500 cells/$mm^3$ or > 50% decrease from baseline (first dose ceftaroline) if baseline ≤ 1, 500 cells/$mm^3$

**Supplemental Table 2.** Bivariate comparisons of patients in efficacy population experiencing clinical success or clinical failure

| | Failure N = 40 | Success N = 86 | *P* value |
|---|---|---|---|
| Age, years | 60 (47 – 66) | 57 (45 – 68) | 0.821 |
| Male sex | 20 (50.0) | 50 (58.1) | 0.392 |
| Race | | | 0.046 |
| African American | 21 (52.5) | 65 (75.6) | 0.010 |
| Caucasian | 17 (42.5) | 17 (19.8) | 0.007 |
| Hispanic/Latino | 0 (0.0) | 1 (1.2) | - |
| Other | 2 (5.0) | 3 (3.5) | 0.652 |
| Hospital System | | | 0.634 |
| Detroit Medical Center | 24 (60.0) | 59 (68.6) | |
| UF Health – Shands Hospital | 11 (27.5) | 19 (22.1) | |
| Henry Ford Hospital | 5 (12.5) | 8 (9.3) | |
| **Comorbidities & past medical history** | | | |
| Prior hospitalization (1 year) | 24 (60.0) | 47 (54.7) | 0.573 |
| Prior surgery (30 days) | 6 (15.0) | 13 (15.1) | 0.986 |
| Prior antibiotics (90 days) | 9 (22.5) | 24 (27.9) | 0.521 |
| Prior MRSA infection, (1 year) | 7 (17.5) | 13 (15.1) | 0.733 |
| Obesity | 17 (42.5) | 30 (36.1) | 0.497 |
| Diabetes mellitus | 14 (35.0) | 33 (38.4) | 0.716 |
| Chronic kidney disease | 12 (30.0) | 22 (25.6) | 0.603 |
| Chronic hemodialysis | 8 (20.0) | 18 (20.9) | 0.904 |
| Liver disease | 8 (20.0) | 12 (14.0) | 0.387 |
| Intravenous drug user | 5 (12.5) | 19 (22.1) | 0.202 |
| Cerebrovascular accident | 3 (7.5) | 5 (5.8) | 0.708 |
| COPD | 10 (25.0) | 19 (22.1) | 0.718 |
| Heart failure | 10 (25.0) | 24 (27.9) | 0.732 |
| Malignancy | 5 (12.5) | 2 (2.3) | 0.033 |
| HIV/AIDS | 0 (0.0) | 8 (9.3) | - |
| Neutropenia[b] | 2 (5.0 | 1 (1.2) | 0.236 |
| Charlson comorbidity index | 3.5 (2.0 – 5.0) | 3 (2.0 – 5.3) | 0.824 |
| **Clinical characteristics** | | | |
| Intensive care unit[c] | 21 (52.5) | 24 (27.9) | 0.007 |
| APACHE II[c] | 18.5 (15.3 – 23.8) | 15 (10 .0– 19.0) | 0.001 |
| Lower respiratory tract source | 19 (47.5) | 22 (25.6) | 0.015 |
| Infective endocarditis source | 7 (17.5) | 24 (27.9) | 0.207 |
| Bone/joint source | 5 (12.5) | 21 (24.4) | 0.124 |
| Intravenous catheter source | 8 (20.0) | 12 (14.0) | 0.387 |
| Skin/soft tissue source | 2 (5.0) | 9 (10.5) | 0.500 |
| Other source | 7 (17.5) | 15 (17.4) | 0.994 |
| Polymicrobial BSI | 5 (12.5) | 5 (5.8) | 0.287 |

| | Failure N = 40 | Success N = 86 | *P* value |
|---|---|---|---|
| Vancomycin-susceptible[d] | 40 (100.0) | 85 (98.8) | - |
| Daptomycin-susceptible[d,e] | 35 (94.5) | 81 (97.6) | 0.586 |
| Ceftaroline-susceptible[f] | 28 (96.6) | 66 (97.1) | 1.000 |
| Ceftaroline MIC[g], mg/L | 0.5 (0.5 – 0.75) | 0.5 (0.5 – 1.0) | 0.438 |
| BSI duration pre-ceftaroline, days | 3.5 (2.8 – 7.0) | 3.0 (2.0 – 6.0) | 0.284 |
| **Treatment information** | | | |
| Infectious diseases consult | 36 (94.7) | 77 (92.8) | 1.000 |
| Source control pursued | 12 (31.6) | 30 (36.1) | 0.624 |
| Vancomycin prior directed therapy | 32 (80.0) | 75 (87.2) | 0.292 |
| Daptomycin prior directed therapy | 18 (45.0) | 30 (34.9) | 0.276 |
| Ceftaroline dosing frequency | | | 0.753 |
| Every 8 hours | 19 (47.5) | 47 (54.7) | |
| Every 12 hours | 19 (47.5) | 35 (40.7) | |
| Every 24 hours | 2 (5.0) | 4 (4.7) | |
| Ceftaroline dose | | | 0.037 |
| 600 mg | 17 (42.5) | 59 (68.6) | 0.005 |
| 400 mg | 10 (25.0) | 9 (10.5) | 0.034 |
| 300 mg | 5 (12.5) | 6 (7.0) | 0.307 |
| 200 mg | 8 (20.0) | 12 (14.0) | 0.387 |
| Combination therapy | 13 (32.5) | 24 (27.9) | 0.598 |
| Combination with daptomycin | 11 (27.5) | 17 (19.8) | 0.331 |
| Combination with vancomycin | 1 (2.5) | 2 (2.3) | 1.000 |
| Combination with gentamicin | 1 (2.5) | 2 (2.3) | 1.000 |
| Combination with rifampin | 0 (0.0) | 5 (5.8) | - |

Data presented as n (%) or median (IQR)

Abbreviations: UF, University of Florida; MRSA, methicillin-resistant *Staphylococcus aureus*; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; APACHE, acute physiology and chronic health evaluation; BSI, bloodstream infection; MIC, minimum inhibitory concentration

[a] Blood cultures not cleared prior to first dose of ceftaroline.

[b] Defined as < 500 cells/$mm^3$.

[c] At time of index culture.

[d] Susceptibility determined by Microscan, Vitek 2, BD Phoenix, or Etest.

[e] Daptomycin susceptibility available for 120.

[f] Ceftaroline susceptibility determined by Etest for 97 patients.

[g] Ceftaroline minimum inhibitory concentration by Etest available for 81 patients.

**Supplemental Table 3.** Clinical success by ceftaroline dosing frequency stratified by FDA labeled renal function dose adjustment strata among efficacy population

| Renal function strata | Every 8 hours | Every 12 hours | Every 24 hours | *P* value |
|---|---|---|---|---|
| CrCl > 50 mL/min | 28/39 (71.8) | 11/17 (64.7) | - | 0.596 |
| CrCl 30.01 - 50 mL/min | 8/11 (72.7) | 10/13 (76.9) | - | 0.813 |
| CrCl 15 – 30 mL/min | 3/5 (60.0) | 5/8 (62.5) | - | 1.00 |
| CrCl < 15 mL/min or IHD | 8/11 (72.7) | 9/16 (56.3) | 4/6 (66.7) | 0.672 |

Data presented as n/N (%)

Abbreviations: CrCl, creatinine clearance; IHD, intermittent hemodialysis

**Supplemental Figure 1.** Clinical failure by ceftaroline minimum inhibitory concentration among patients in efficacy population and known ceftaroline minimum inhibitory concentration