**Re-Evaluation of cefepime or piperacillin-tazobactam to decrease the use of Carbapenems in ESBL-Producing Enterobacterales BloodStream Infections (REDUCE-BSI)**

Supplemental Materials

**Table S1. Dosing regimens adjusted for renal function**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Meropenem | | | | | | | | |
| eGFR | ≥ 50 | 26-50 | 10-25 | <10 | HD | CRRT | Empiric | Definitive |
| High dose | 2g q8h | 1g q8h | 1g q12h | 1g q24h | 1g q24h | 2g q12h | 9/21 (43%) | 11/25 (44%) |
| Standard dose | 1g q8h | 1g q12h | 0.5 g q12h | 0.5 g q24h | - | - | 10/21 (48%) | 12/25 (48%) |
| Other | - | - | - | - | - | - | 2/21 (10%) | 2/25 (8%) |
| Piperacillin-tazobactam | | | | | | | | |
| eGFR | - | >40 | 20-40 | <20 | HD | CRRT | Empiric | Definitive |
| High dose | - | 4.5g q6h | 3.375g q6h | 2.25g q6h | 2.25g q8h | 3.375g q8h | 8/33 (24%) | 2/10 (20%) |
| Standard dose | - | 3.375g q6h | 2.25g q6h | 2.25g q8h | - | - | 24/33 (73%) | 7/10 (70%) |
| Other | - | - | - | - | - | - | 1/33 (2%) | 1/10 (10%) |
| Cefepime | | | | | | | | |
| eGFR | ≥ 60 | 30-60 | <30 | <10 | HD | CRRT | Empiric | Definitive |
| High dose | 2g q8h | 2g q12h  1g q8h | 2g q24h  1g q12h | - | 1g q24h | 2g q12h | 44/65 (68%) | 19/30 (63%) |
| Standard dose | 1g q8h  2g q12h | 1g q12h  2g q24h | 1g q24h | 1g q24h | - | - | 20/65 (31%) | 9/30 (30%) |
| Other | - | - | - | - | - | - | 1/65 (2%) | 2/30 (7%) |

**Table S2. Patient Characteristics in Empiric Cohort**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Empiric Therapy Cohort | | |
|  | **CBP, N=25** | **NCBP, N=98** | **P** |
| Age (years), mean ± SD | 62.0 ± 12.0 | 61.0 ± 16.4 | 0.78 |
| Male, n (%) | 14 (56%) | 54 (55%) | 0.94 |
| White, n (%) | 17 (68%) | 66 (67%) | 0.51 |
| Admit Weight (kg), median (IQR) | 72.4 (54-83) | 79.4 (65-90) | 0.16 |
| Charlson Comorbidity Index, median (IQR) | **5 (2-10)** | **3 (1-4)** | **0.002** |
| Pitt Score ≥4, n (%) | 9 (36%) | 23 (23%) | 0.20 |
| WBC, median (IQR) | 13.4 (4-21) | 11.8 (9-18) | 0.75 |
| CRP, mean ± SD | 198.0 ± 138.0 | 165.5 ± 101.7 | 0.28 |
| Procalcitonin, median (IQR) | 4.8 (0.6-34.9) | 3.8 (0.5-16.2) | 0.87 |
| ICU Admission, n (%) | **17 (68%)** | **42 (43%)** | **0.02** |
| ID Consult, n (%) | 18 (72%) | 76 (78%) | 0.56 |
| Renal function, n (%) |  |  | 0.50 |
| *eGFR ≥60* | 10 (40%) | 50 (51%) |  |
| *eGFR 30-59* | 5 (20%) | 20 (20%) |  |
| *eGFR 10-29* | 8 (32%) | 22 (22%) |  |
| *eGFR <10* | 0 (0%) | 3 (3%) |  |
| *RRT* | 2 (8%) | 3 (3%) |  |
| Source, n (%) |  |  | 0.86 |
| *Genitourinary* | 14 (56%) | 51 (52%) |  |
| *Intra-abdominal* | 5 (20%) | 22 (22%) |  |
| *Respiratory* | 3 (12%) | 5 (5%) |  |
| *Skin* | 0 (0%) | 6 (6%) |  |
| *Other* | 3 (12%) | 14 (14%) |  |
| Concomitant Infection, n (%) | 7 (28%) | 30 (30%) | 0.80 |
| Source Control at 72h, n (%) | 5 (20%) | 15 (15%) | 0.55 |
| Organism, n (%) |  |  | 0.35 |
| *Klebsiella* spp. | 6 (24%) | 33 (34%) |  |
| *E. coli* | 19 (76%) | 65 (66%) |  |
| Beta-lactam TDM, n (%) | 4 (16%) | 17 (17%) |  |
| Hospital Length of Stay, median (IQR) | 12.0 (6-23) | 10.0 (6-21) | 0.55 |
| Length of Therapy (days), median (IQR) | 8.0 (5-14) | 8.0 (6-11) | 0.94 |
| Combination Therapy, n (%) | 7 (6%) | 14 (11%) | 0.14 |

**Table S3. Primary and Secondary Outcomes in Empiric Cohort**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Empiric Therapy Cohort | | |
|  | **CBP, N=25** | **NCBP, N=98** | **P** |
| In-Hospital Mortality | 7/25 (28.0%) | 6/98 (6.1%) | 0.005 |
| Clinical Cure | 18/25 (72.0%) | 86/97 (88.7%) | 0.055 |
| Microbiologic Cure | 22/25 (88.0%) | 85/91 (93.4%) | 0.403 |
| Recurrence of Infection | 1/25 (4.0%) | 4/98 (4.1%) | 0.99 |
| Development of Resistance | 1/74 (1.4%) | 0 (0%) | 0.99 |

**Table S4. Empiric therapy cox proportional hazards analysis**

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristic | HR | 95% CI | P value |
| Carbapenem Empirically | 2.66 | 0.88, 8.02 | 0.0815 |
| Charlson | 1.15 | 1.005, 1.29 | **0.0244** |
| Pitt ≥ 4 | 6.38 | 1.60, 25.45 | **0.0086** |
| ICU Admission | 5.45 | 0.61, 48.66 | 0.1289 |

**Table S5. Cefepime and piperacillin-tazobactam baseline characteristics for definitive therapy cohort**

|  |  |  |
| --- | --- | --- |
|  | FEP, N=30 | PT, N=10 |
| Age (years), mean ± SD | 60.2 ± 14.0 | 69.8 ± 22.3 |
| Male, n (%) | 18 (60%) | 3 (30%) |
| White, n (%) | 23 (77%) | 9 (90%) |
| Admit Weight (kg), median (IQR) | 82 (64-92) | 79 (68-86) |
| Charlson Comorbidity Index, median (IQR) | 3.0 (1.5-4) | 2.0 (1-5) |
| Pitt Score ≥4, n (%) | 5 (17%) | 1 (10%) |
| WBC, median (IQR) | 11.7 (9-17) | 12.7 (9-19) |
| CRP, mean ± SD | 173.0 ± 92.7 | 137.5 ± 113.6 |
| Procalcitonin, median (IQR) | 4.8 (0.5-14.7) | 3.2 (0.4-39.3) |
| ICU Admission, n (%) | 14 (47%) | 2 (20%) |
| ID Consult, n (%) | 24 (80%) | 3 (30%) |
| Renal function, n (%) |  |  |
| *eGFR ≥60* | 15 (50%) | 5 (50%) |
| *eGFR 30-59* | 5 (17%) | 4 (40%) |
| *eGFR 10-29* | 8 (27%) | 1 (10%) |
| *eGFR <10* | 1 (3%) | 0 (0%) |
| *RRT* | 1 (3%) | 0 (0%) |
| Source, n (%) |  |  |
| *Genitourinary* | 13 (43%) | 9 (90%) |
| *Intra-abdominal* | 5 (17%) | 1 (10%) |
| *Respiratory* | 3 (10%) | 0 (0%) |
| *Skin* | 1 (3%) | 0 (0%) |
| *Other* | 8 (27%) | 0 (0%) |
| Concomitant Infection, n (%) | 3 (10%) | 5 (50%) |
| Source Control at 72h, n (%) | 5 (17%) | 0 (0%) |
| Organism, n (%) |  |  |
| *Klebsiella* spp. | 13 (43%) | 1 (10%) |
| *E. coli* | 17 (57%) | 9 (90%) |
| Hospital Length of Stay, median (IQR) | 10.0 (6-22) | 10.0 (6-19) |
| Length of Therapy (days), median (IQR) | 8.0 (6-11) | 8.0 (5.5-13) |

**Table S6. Cefepime and piperacillin-tazobactam outcomes for definitive therapy cohort**

|  |  |  |
| --- | --- | --- |
| Outcome | FEP | PT |
| In-Hospital Mortality | 1/30 (3.3%) | 0 (0%) |
| Clinical Cure | 26/30 (86.7%) | 10/10 (100%) |
| Microbiologic Cure | 29/30 (96.7%) | 9/9 (100%) |
| Recurrence of Infection | 1/30 (3.3%) | 0 (0%) |
| Development of Resistance | 0 (0%) | 0 (0%) |

**Figure S1. Kaplan Meier Analysis of Survival Likelihood**

