**Table S7. Patient characteristics by subgroup.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | All | Baseline | Baseline | Baseline | 24 hours | 24 hours |
|  |  | Low | Medium | High | Low | High |
| Age, years  | 63 (50-72) | 64 (51-73) | 63 (50-71) | 57 (45-74) | 64 (51-72) | 62 (47-75) |
| Gender, Females | 147 (40) | 72 (38) | 53 (43) | 22 (47) | 112 (40) | 35 (43) |
| APACHEII score | 26 (22-32) | 25 (20-30) | 28 (23-32) | 31 (24-34) | 26 (21-31) | 29 (24-34) |
| Surgical Diagnosis | 86 (24) | 51 (27) | 29 (23) | 6 (13) | 74 (26) | 12 (15) |
| Severe septic shock | 204 (56) | 77 (40) | 85 (69) | 42 (89) | 144 (51) | 60 (74) |
| Vasopressin treatment | 188 (52) | 100 (52) | 66 (53) | 22 (47) | 147 (52) | 41 (51) |
| Activated Protein C treatment | 61 (17) | 20 (10) | 28 (23) | 13 (28) | 41 (15) | 20 (25) |
| Pre-existing conditions |  |  |  |  |  |  |
|  Chronic heart failure | 73 (20) | 46 (24) | 20 (16) | 7 (15) | 58 (21) | 15 (19) |
|  Chronic lung disease  | 22 (6.1) | 20 (10) | 1 (0.81) | 1 (2.1) | 21 (7.4) | 1 (1.2) |
|  Chronic liver disease | 42 (12) | 25 (13) | 14 (11) | 3 (6.4) | 32 (11) | 10 (12) |
|  Chronic renal failure | 241 (66) | 116 (60) | 91 (73) | 34 (72) | 176 (62) | 65 (80) |
|  COPD | 60 (17) | 42 (22) | 14 (11) | 4 (8.5) | 50 (18) | 10 (12) |
|  Cancer | 68 (19) | 29 (15) | 23 (19) | 16 (34) | 47 (17) | 21 (26) |
|  Intravenous drug use | 15 (4.1) | 8 (4.2) | 7 (5.6) | 2 (2-2) | 13 (4.6) | 2 (2.5) |
|  Alcoholism | 54 (15) | 32 (17) | 19 (15) | 3 (6.4) | 46 (16) | 8 (9.9) |
|  Solid organ transplant | 10 (2.8) | 7 (3.6) | 2 (1.6) | 1 (2.1) | 7 (2.5) | 3 (3.7) |
|  Recent trauma | 20 (5.5) | 13 (6.8) | 6 (4.8) | 1 (2.1) | 15 (5.3) | 5 (6.2) |
|  Immuno-compromised | 45 (12) | 17 (8.9) | 14 (11) | 14 (30) | 26 (9.2) | 19 (23) |
|  Chronic steroid use | 69 (19) | 39 (20) | 16 (13) | 14 (30) | 46 (16) | 23 (28) |
| Patient clinical measures at baseline |  |  |  |  |  |  |
|  Body temperature (°C) | 38 (37-38) | 37 (37-38) | 38 (37-39) | 37 (37-38) | 38 (37-38) | 38 (37-38) |
|  Maximum heart rate (beats per minute) | 128 (112-140) | 125 (108-135) | 130 (116-140) | 132 (119-144) | 125 (110-138) | 134 (120-140) |
|  MAP | 72 (67-78) | 74 (68-79) | 71 (66-75) | 70 (65-74) | 73 (68-78) | 71 (65-76) |
|  WBC | 14 ( 7.8-21.1) | 15 ( 9.9-21.2) | 14 ( 6.9-22.5) | 7.1 ( 1.8-10.7) | 15 ( 9.3-21.1) | 8.4 ( 3.7-19.2) |
|  Platelets | 167 ( 89-257) | 195 (109-291) | 154 ( 94-242) | 72 ( 49-144) | 180 (106-290) | 120 ( 54-191) |
|  Pao2Fio2 | 194 (143-260) | 206 (158-275) | 195 (139-230) | 142 ( 95-208) | 202 (154-270) | 162 (112-214) |
|  Creatinine | 155 (44) | 81 (43) | 61 (49) | 13 (29) | 121 (44) | 34 (42) |
| Pathogen |  |  |  |  |  |  |
|  Gram positive only | 76 (35) | 42 (37) | 21 (30) | 13 (37) | 58 (35) | 18 (35) |
|  Gram negative only | 44 (20) | 18 (16) | 15 (22) | 11 (31) | 30 (18) | 14 (27) |
|  Fungus only | 38 (18) | 23 (20) | 13 (19) | 2 (5.7) | 32 (19) | 6 (12) |
|  Virus only | 2 (0.92) | 2 (1.8) | 0 (0-0) | 0 (0-0) | 2 (1.2) | 0 (0-0) |
|  Mixed infection | 52 (24) | 28 (25) | 17 (25) | 7 (20) | 40 (24) | 12 (23) |
| Initial site of infection |  |  |  |  |  |  |
|  Lung | 155 (44) | 81 (43) | 61 (49) | 13 (29) | 121 (44) | 34 (42) |
|  Intravascular | 17 (4.8) | 6 (3.2) | 6 (4.8) | 5 (11) | 10 (3.6) | 7 (8.8) |
|  Abdomen | 99 (28) | 53 (28) | 37 (30) | 9 (20) | 84 (30) | 15 (19) |
|  Skin | 32 (9) | 19 (10) | 7 (5.6) | 6 (13) | 23 (8.3) | 9 (11) |
|  Genitourinary | 18 (5.1) | 8 (4.3) | 7 (5.6) | 3 (6.7) | 14 (5.1) | 4 (5) |
|  CNS | 2 (0.56) | 1 (0.53) | 0 (0-0) | 1 (2.2) | 1 (0.36) | 1 (1.2) |
|  Bone/joint | 5 (1.4) | 4 (2.1) | 1 (0.81) | 0 (0-0) | 5 (1.8) | 0 (0-0) |
|  Other site | 28 (7.9) | 15 (8) | 5 (4) | 8 (18) | 18 (6.5) | 10 (12) |