**Supplemental Digital Content 1:** *Serum cytokine/chemokine data and mortality analyses (Mann-Whitney)*.

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|  | **Survivors (n = 44)** | **Non-survivors (n = 8)** |  |
| **Cytokine/chemokine** | **Median (IQR) pg/ml** | **Median (IQR) pg/ml** | **p value** |
| IFN-α2 | 10 (0 – 25) | 15 (7.0 – 85) | 0.22 |
| IFNβ | 0 (0 – 0) | 0 (0 – 106) | 0.14 |
| IFNγ | 0 (0 – 0) | 9.5 (0 – 33) | 0.01 |
| Eotaxin | 55 (34 – 93) | 124 (65 – 193) | 0.03 |
| GCSF | 107 (65 – 523) | 6259 (379 – 10000) | 0.01 |
| **GM-CSF** | **0 (0 – 0)** | **52 (3.9 – 451)** | **< 0.0001** |
| GRO | 1064 (577 – 2041) | 3015 (1667 – 10000) | 0.01 |
| IL-1α | 0 (0 – 1.9) | 0.35 (0 – 45) | 0.37 |
| IL-1β | 2.7 (0.63 – 5.0) | 4.8 (1.8 – 5.8) | 0.21 |
| IL-1ra | 36 (11 – 140) | 1661 (113 – 6933) | 0.002 |
| IL-2 | 0 (0 – 0.69) | 0.85 (0.11 – 4.0) | 0.02 |
| IL-4 | 0.9 (0 – 6.6) | 0 (0 – 6.2) | 0.44 |
| IL-5 | 0 (0 – 0.12) | 0 (0 – 0.40) | 0.76 |
| **IL-6** | **16 (4.7 – 52)** | **4426 (260 – 8877)** | **< 0.0001** |
| IL-7 | 4.3 (0 – 8.4) | 0 (0 – 3.3) | 0.08 |
| **IL-8** | **7.0 (0 – 34)** | **1211 (14 – 4938)** | **< 0.0001** |
| IL-10 | 19 (8.8 – 47) | 451 (66 – 1559) | 0.003 |
| IL-12 p40 | 31 (10 – 66) | 38 (16 – 87) | 0.45 |
| IL-12 p70 | 0.20 (0 – 2.8) | 0.85 (0 – 4.0) | 0.77 |
| IL-13 | 0 (0 – 0.07) | 0 (0 – 2.1) | 0.19 |
| IL-17 | 0 (0 – 0) | 0 (0 – 16) | 0.24 |
| **IP-10** | **1905 (620 – 3956)** | **17200 (4132 – 27270)** | **0.0004** |
| **MCP-1** | **375 (226 – 700)** | **5265 (1852 – 7124)** | **< 0.0001** |
| MDC | 1558 (951 – 2347) | 1797 (1371 – 2319) | 0.59 |
| **MIP-1α** | **0 (0 – 0)** | **68 (3.3 – 231)** | **0.0008** |
| MIP-1β | 32 (20 – 43) | 120 (30 – 288) | 0.01 |
| RANTES | 4599 (2868 – 7391) | 5393 (3990 – 7703) | 0.37 |
| sCD40L | 8144 (1350 – 14500) | 5855 (2823 – 8058) | 0.67 |
| TNFα | 5.3 (3.4 – 8.5) | 17 (7.6 – 125) | 0.003 |
| VEGF | 0 (0 – 0) | 0 (0 – 614) | 0.30 |
| Fractalkine | 67 (32 – 105) | 105 (43 – 233) | 0.19 |

IQR: interquartile range, IFN: interferon, GCSF: granulocyte colony stimulating factor, GM-CSF: granulocyte macrophage colony stimulating factor, GRO: growth-related oncogene, IL: interleukin, IL-1ra: IL-1 receptor antagonist, MCP: monocyte chemotactic protein, MDC: macrophage-derived chemokine, MIP: macrophage inflammatory protein, RANTES: regulated on activation normal T cell expressed and secreted, sCD40L: soluble CD40 ligand, TNF: tumor necrosis factor, VEGF: vascular endothelial growth factor.

Biomarkers with a p value < 0.0016 (to allow for multiple comparisons) are shown in bold.

**Supplemental Digital Content 2:** *Serum cytokine/chemokine analyses by 2009 H1N1 status (Mann-Whitney)*.

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|  | **2009 H1N1 (n = 25)** | **Other influenza (n = 27)** |  |
| **Cytokine/chemokine** | **Median (IQR) pg/ml** | **Median (IQR) pg/ml** | **p value** |
| IFN-α2 | 14 (1.6 – 23) | 12 (0 – 27) | 0.91 |
| IFNβ | 0 (0 – 0) | 0 (0 – 0) | 0.59 |
| **IFNγ** | **3.8 (0 – 15)** | **0 (0 – 0)** | **< 0.0001** |
| Eotaxin | 74 (47 – 172) | 53 (34 – 87) | 0.11 |
| GCSF | 169 (63 – 2010) | 118 (70 – 525) | 0.61 |
| **GM-CSF** | **5.6 (0 – 119)** | **0 (0 – 0)** | **< 0.0001** |
| GRO | 1189 (726 – 2838) | 1067 (560 – 2699) | 0.62 |
| IL-1α | 0 (0 – 11) | 0 (0 – 1.9) | 0.57 |
| IL-1β | 1.2 (0 – 5.1) | 3.5 (1.9 – 6.9) | 0.047 |
| IL-1ra | 44 (15 – 362) | 36 (11 – 160) | 0.68 |
| **IL-2** | **0.70 (0.30 – 1.5)** | **0 (0 – 0)** | **< 0.0001** |
| IL-4 | 0 (0 – 4.8) | 1.1 (0 – 6.8) | 0.28 |
| IL-5 | 0 (0 – 0.35) | 0 (0 – 0) | 0.11 |
| IL-6 | 49 (12 – 268) | 9.7 (1.7 – 27) | 0.008 |
| IL-7 | 0 (0 – 6.1) | 4.6 (2.2 – 15) | 0.01 |
| **IL-8** | **55 (13 – 201)** | **0 (0 – 13)** | **< 0.0001** |
| IL-10 | 18 (6.8 – 100) | 30 (11 – 94) | 0.46 |
| IL-12 p40 | 24 (0 – 79) | 40 (14 – 69) | 0.43 |
| IL-12 p70 | 1.2 (0 – 5.0) | 0 (0 – 2.7) | 0.009 |
| IL-13 | 0 (0 – 0.52) | 0 (0 – 0) | 0.06 |
| **IL-17** | **0 (0 – 9.9)** | **0 (0 – 0)** | **0.0002** |
| IP-10 | 3359 (1223 – 9152) | 1650 (534 – 3830) | 0.03 |
| MCP-1 | 760 (375 – 2111) | 304 (185 – 593) | 0.004 |
| MDC | 1449 (978 – 2104) | 1711 (1000 – 2719) | 0.33 |
| **MIP-1α** | **13 (0 – 38)** | **0 (0 – 0)** | **< 0.0001** |
| MIP-1β | 34 (20 – 61) | 33 (24 – 42) | 0.48 |
| RANTES | 3831 (2589 – 6330) | 5890 (3697 – 8744) | 0.10 |
| sCD40L | 6302 (2756 – 16460) | 5783 (1149 – 14500) | 0.36 |
| TNFα | 8.5 (3.7 – 18) | 4.8 (4.2 – 7.2) | 0.047 |
| **VEGF** | **0 (0 – 416)** | **0 (0 – 0)** | **0.0002** |
| Fractalkine | 70 (20 – 99) | 73 (55 – 128) | 0.59 |

IQR: interquartile range, IFN: interferon, GCSF: granulocyte colony stimulating factor, GM-CSF: granulocyte macrophage colony stimulating factor, GRO: growth-related oncogene, IL: interleukin, IL-1ra: IL-1 receptor antagonist, MCP: monocyte chemotactic protein, MDC: macrophage-derived chemokine, MIP: macrophage inflammatory protein, RANTES: regulated on activation normal T cell expressed and secreted, sCD40L: soluble CD40 ligand, TNF: tumor necrosis factor, VEGF: vascular endothelial growth factor.

Biomarkers with a p value < 0.0016 (to allow for multiple comparisons) are shown in bold.

**Supplemental Digital Content 3:** *Serum cytokine/chemokine analyses by S. aureus status (Mann-Whitney)*.

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|  | ***S. aureus* secondary infection (n = 11)** | **Other or no secondary infection (n = 41)** |  |
| **Cytokine/chemokine** | **Median (IQR) pg/ml** | **Median (IQR) pg/ml** | **p value** |
| IFN-α2 | 6.1 (3.8 – 14) | 25 (0 – 33) | 0.19 |
| IFNβ | 0 (0 – 0) | 0 (0 – 0) | 0.33 |
| **IFNγ** | **9.1 (3.8 – 16)** | **0 (0 – 0)** | **< 0.0001** |
| Eotaxin | 96 (50 – 167) | 56 (35 – 92) | 0.27 |
| GCSF | 950 (41 – 10000) | 123 (70 – 637) | 0.23 |
| **GM-CSF** | **99 (20 – 321)** | **0 (0 – 0)** | **< 0.0001** |
| GRO | 1361 (1061 – 10000) | 1067 (464 – 2677) | 0.049 |
| IL-1α | 0 (0 – 55) | 0 (0 – 0) | 0.55 |
| IL-1β | 1.1 (0.29 – 4.3) | 3.5 (1.3 – 5.6) | 0.14 |
| IL-1ra | 25 (12 – 245) | 40 (13 – 182) | 0.90 |
| IL-2 | 0.70 (0 – 0.86) | 0 (0 – 0.70) | 0.06 |
| IL-4 | 0 (0 – 0) | 1.1 (0 – 6.8) | 0.004 |
| IL-5 | 0.12 (0 – 0.49) | 0 (0 – 0) | 0.02 |
| IL-6 | 65 (13 – 4794) | 16 (3.1 – 62) | 0.02 |
| IL-7 | 0 (0 – 4.4) | 4.6 (0 – 9.8) | 0.01 |
| **IL-8** | **164 (52 – 4424)** | **6.1 (0 – 22)** | **0.0002** |
| IL-10 | 30 (10 – 710) | 23 (9.1 – 56) | 0.22 |
| IL-12 p40 | 9.9 (0 – 50) | 40 (15 – 77) | 0.046 |
| IL-12 p70 | 1.2 (0.50 – 4.9) | 0 (0 – 2.8) | 0.05 |
| IL-13 | 0 (0 – 2.7) | 0 (0 – 0) | 0.36 |
| **IL-17** | **0 (0 – 20)** | **0 (0 – 0)** | **0.0006** |
| IP-10 | 2742 (1406 – 8303) | 2100 (643 – 5172) | 0.43 |
| MCP-1 | 688 (415 – 6173) | 372 (203 – 880) | 0.009 |
| MDC | 1689 (1035 – 2365) | 1559 (967 – 2452) | 1.0 |
| MIP-1α | **21 (7 – 120)** | **0 (0 – 0)** | **< 0.0001** |
| MIP-1β | 36 (20 – 159) | 31 (21 – 49) | 0.37 |
| RANTES | 3730 (3090 – 4344) | 5445 (2568 – 7784) | 0.10 |
| sCD40L | 8643 (5783 – 15755) | 3640 (1219 – 14500) | 0.08 |
| TNFα | 7.0 (4.7 – 21) | 5.4 (3.6 – 8.9) | 0.21 |
| **VEGF** | **306 (0 – 744)** | **0 (0 – 0)** | **0.0004** |
| Fractalkine | 55 (22 – 82) | 73 (52 – 124) | 0.44 |

IQR: interquartile range, IFN: interferon, GCSF: granulocyte colony stimulating factor, GM-CSF: granulocyte macrophage colony stimulating factor, GRO: growth-related oncogene, IL: interleukin, IL-1ra: IL-1 receptor antagonist, MCP: monocyte chemotactic protein, MDC: macrophage-derived chemokine, MIP: macrophage inflammatory protein, RANTES: regulated on activation normal T cell expressed and secreted, sCD40L: soluble CD40 ligand, TNF: tumor necrosis factor, VEGF: vascular endothelial growth factor.

Biomarkers with a p value < 0.0016 (to allow for multiple comparisons) are shown in bold.