

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

	<b>Survivors (n = 44)</b>	<b>Non-survivors (n = 8)</b>	
<b>Cytokine/chemokine</b>	<b>Median (IQR) pg/ml</b>	<b>Median (IQR) pg/ml</b>	<b>p value</b>
IFN- $\alpha$ 2	10 (0 – 25)	15 (7.0 – 85)	0.22
IFN $\beta$	0 (0 – 0)	0 (0 – 106)	0.14
IFN $\gamma$	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
<b>GM-CSF</b>	<b>0 (0 – 0)</b>	<b>52 (3.9 – 451)</b>	<b>&lt; 0.0001</b>
GRO	1064 (577 – 2041)	3015 (1667 – 10000)	0.01
IL-1 $\alpha$	0 (0 – 1.9)	0.35 (0 – 45)	0.37
IL-1 $\beta$	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
<b>IL-6</b>	<b>16 (4.7 – 52)</b>	<b>4426 (260 – 8877)</b>	<b>&lt; 0.0001</b>
IL-7	4.3 (0 – 8.4)	0 (0 – 3.3)	0.08
<b>IL-8</b>	<b>7.0 (0 – 34)</b>	<b>1211 (14 – 4938)</b>	<b>&lt; 0.0001</b>
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
<b>IP-10</b>	<b>1905 (620 – 3956)</b>	<b>17200 (4132 – 27270)</b>	<b>0.0004</b>
<b>MCP-1</b>	<b>375 (226 – 700)</b>	<b>5265 (1852 – 7124)</b>	<b>&lt; 0.0001</b>
MDC	1558 (951 – 2347)	1797 (1371 – 2319)	0.59
<b>MIP-1<math>\alpha</math></b>	<b>0 (0 – 0)</b>	<b>68 (3.3 – 231)</b>	<b>0.0008</b>
MIP-1 $\beta$	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
TNF $\alpha$	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).**

	<b>2009 H1N1 (n = 25)</b>	<b>Other influenza (n = 27)</b>	
<b>Cytokine/chemokine</b>	<b>Median (IQR) pg/ml</b>	<b>Median (IQR) pg/ml</b>	<b>p value</b>
IFN- $\alpha$ 2	14 (1.6 – 23)	12 (0 – 27)	0.91
IFN $\beta$	0 (0 – 0)	0 (0 – 0)	0.59
<b>IFN<math>\gamma</math></b>	<b>3.8 (0 – 15)</b>	<b>0 (0 – 0)</b>	<b>&lt; 0.0001</b>
Eotaxin	74 (47 – 172)	53 (34 – 87)	0.11
GCSF	169 (63 – 2010)	118 (70 – 525)	0.61
<b>GM-CSF</b>	<b>5.6 (0 – 119)</b>	<b>0 (0 – 0)</b>	<b>&lt; 0.0001</b>
GRO	1189 (726 – 2838)	1067 (560 – 2699)	0.62
IL-1 $\alpha$	0 (0 – 11)	0 (0 – 1.9)	0.57
IL-1 $\beta$	1.2 (0 – 5.1)	3.5 (1.9 – 6.9)	0.047
IL-1ra	44 (15 – 362)	36 (11 – 160)	0.68
<b>IL-2</b>	<b>0.70 (0.30 – 1.5)</b>	<b>0 (0 – 0)</b>	<b>&lt; 0.0001</b>
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
<b>IL-8</b>	<b>55 (13 – 201)</b>	<b>0 (0 – 13)</b>	<b>&lt; 0.0001</b>
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
<b>IL-17</b>	<b>0 (0 – 9.9)</b>	<b>0 (0 – 0)</b>	<b>0.0002</b>
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
<b>MIP-1<math>\alpha</math></b>	<b>13 (0 – 38)</b>	<b>0 (0 – 0)</b>	<b>&lt; 0.0001</b>
MIP-1 $\beta$	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
TNF $\alpha$	8.5 (3.7 – 18)	4.8 (4.2 – 7.2)	0.047

<b>VEGF</b>	<b>0 (0 – 416)</b>	<b>0 (0 – 0)</b>	<b>0.0002</b>
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).**

	<i>S. aureus</i> secondary infection (n = 11)	Other or no secondary infection (n = 41)	
Cytokine/chemokine	Median (IQR) pg/ml	Median (IQR) pg/ml	p value
IFN- $\alpha$ 2	6.1 (3.8 – 14)	25 (0 – 33)	0.19
IFN $\beta$	0 (0 – 0)	0 (0 – 0)	0.33
<b>IFN<math>\gamma</math></b>	<b>9.1 (3.8 – 16)</b>	<b>0 (0 – 0)</b>	<b>&lt; 0.0001</b>
Eotaxin	96 (50 – 167)	56 (35 – 92)	0.27
GCSF	950 (41 – 10000)	123 (70 – 637)	0.23
<b>GM-CSF</b>	<b>99 (20 – 321)</b>	<b>0 (0 – 0)</b>	<b>&lt; 0.0001</b>
GRO	1361 (1061 – 10000)	1067 (464 – 2677)	0.049
IL-1 $\alpha$	0 (0 – 55)	0 (0 – 0)	0.55
IL-1 $\beta$	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
<b>IL-8</b>	<b>164 (52 – 4424)</b>	<b>6.1 (0 – 22)</b>	<b>0.0002</b>
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
<b>IL-17</b>	<b>0 (0 – 20)</b>	<b>0 (0 – 0)</b>	<b>0.0006</b>
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-1 $\alpha$	<b>21 (7 – 120)</b>	<b>0 (0 – 0)</b>	<b>&lt; 0.0001</b>
MIP-1 $\beta$	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
TNF $\alpha$	7.0 (4.7 – 21)	5.4 (3.6 – 8.9)	0.21

<b>VEGF</b>	<b>306 (0 – 744)</b>	<b>0 (0 – 0)</b>	<b>0.0004</b>
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.