**Supplemental Data**

**Strong Viral Associations with Systemic Lupus Erythematosus among Filipinos**

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**Supplemental Table 3.** Number of positive autoantibodies detected by Bioplex assay in Filipino SLE patients, based on seropositivity for common herpes viruses (EBV, CMV, HSV-1, and HSV-2), EBV-EA, or EBV-EBNA-1.

**Supplemental Table 1.** Distribution of ACR scores in Filipino SLE patients, based on seropositivity for common herpes viruses (EBV, CMV, HSV-1, and HSV-2), EBV-EA, or EBV-EBNA-1. *P* values compare seropositive and seronegative patients for each antigen.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Number of Positive ACR Criteria** | | | | | | | |  |
|  | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **Median** | ***P*** |
| **EBV VCA -** | 0 | 1 | 0 | 0 | 0 | 0 | 0 | n/a | 0.310 |
| **EBV VCA +** | 20 | 59 | 68 | 48 | 24 | 12 | 1 | 6 |
| **CMV -** | 1 | 6 | 3 | 2 | 1 | 0 | 0 | 5 | 0.177 |
| **CMV +** | 19 | 54 | 65 | 46 | 23 | 12 | 1 | 6 |
| **HSV1 -** | 5 | 11 | 7 | 2 | 4 | 0 | 0 | 5 | **0.0150** |
| **HSV1 +** | 15 | 49 | 61 | 46 | 20 | 12 | 1 | 6 |
| **HSV2 -** | 12 | 14 | 10 | 2 | 7 | 3 | 0 | 5 | **0.00438** |
| **HSV2 +** | 8 | 46 | 58 | 46 | 17 | 9 | 1 | 6 |
| **EBV EA -** | 3 | 5 | 6 | 2 | 1 | 1 | 0 | 6 | 0.184 |
| **EBV EA +** | 17 | 55 | 62 | 46 | 23 | 11 | 1 | 6 |
| **EBV EBNA1 -** | 4 | 5 | 11 | 5 | 4 | 2 | 1 | 6 | 0.576 |
| **EBV EBNA1 +** | 16 | 55 | 57 | 43 | 20 | 10 | 0 | 6 |

**Supplemental Table 2.** Associations between viral seropositivity and the presence of ACR criteria in Filipino SLE patients.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **ACR Criteria** | **EBV-VCA**  **OR (95% CI)**  ***Padj*** | **CMV**  **OR (95% CI)**  ***Padj*** | **HSV-1**  **OR (95% CI)**  ***Padj*** | **HSV-2**  **OR (95% CI)**  ***Padj*** | **EBV-EA**  **OR (95% CI)**  ***Padj*** | **EBNA-1**  **OR (95% CI)**  ***Padj*** |
| **Malar** | 0 (0, 171)  1.00 | 0.79 (0.08, 3.8)  1.00 | 1.17 (0.45, 3.1)  0.89 | 1.2 (0.55, 2.7)  0.84 | 0.53 (0.06, 2.4)  0.67 | 0.41 (0.12, 1.4)  0.88 |
| **Discoid** | Inf (0.01, Inf)  1.00 | Inf (0.86, Inf)  0.75 | 2.61 (0.76, 9.0)  0.58 | 1.48 (0.64, 3.4)  0.84 | 5.0 (0.75, 215)  0.44 | 0.98 (0.4, 2.4)  1.00 |
| **Photosens** | 0 (0, 142)  1.00 | 0.65 (0.07, 3.1)  0.99 | 1.46 (0.6, 3.5)  0.68 | 1.28 (0.61, 2.7)  0.84 | 1.93 (0.56, 5.9)  0.45 | 0.64 (0.23, 1.8)  0.88 |
| **Oral Ulcers** | Inf (0.03, Inf)  1.00 | 1.98 (0.63, 6.2)  0.86 | 1.81 (0.82, 4.0)  0.58 | 1.12 (0.59, 2.1)  0.84 | 0.43 (0.15, 1.2)  0.44 | 0.79 (0.37, 1.7)  0.88 |
| **Arthritis** | 0 (0, 107)  1.00 | 1.23 (0.27, 4.6)  0.99 | 1.53 (0.67, 3.5)  0.68 | 1.5 (0.75, 3.0)  0.84 | 1.83 (0.57, 5.5)  0.45 | 1.29 (0.57, 2.9)  0.88 |
| **Serositis** | Inf (0.005, Inf)  1.00 | 2.3 (0.32, 100)  0.99 | 0.87 (0.29, 3.1)  0.89 | 1.1 (0.45, 2.7)  1.00 | 0.62 (0.18, 2.7)  0.67 | 1.33 (0.42, 5.6)  0.88 |
| **Renal** | Inf (0.03, Inf)  1.00 | 0.87 (0.28, 2.7)  1.00 | 0.69 (0.31, 1.5)  0.68 | 1.14 (0.60, 2.1)  0.84 | 0.80 (0.30, 2.1)  0.81 | 0.57 (0.26, 1.2)  0.88 |
| **Neurologic** | Inf (0.004, Inf)  1.00 | 0.87 (0.18, 8.5)  0.99 | 1.00 (0.31, 4.2)  1.00 | 0.62 (0.27, 1.4)  0.84 | 0.78 (0.20, 4.5)  0.80 | 0.84 (0.29, 3.0)  0.88 |
| **Hematologic** | Inf (0.02, Inf)  1.00 | 0.76 (0.25, 2.3)  0.99 | 1.56 (0.7, 3.5)  0.68 | 1.49 (0.78, 2.8)  0.84 | 1.89 (0.68, 5.2)  0.45 | 1.19 (0.56, 2.5)  0.88 |
| **Immunologic** | 0 (0, 149)  1.00 | 2.55 (0.62, 9.4)  0.75 | 2.29 (0.98, 5.3)  0.58 | 3.08 (1.52, 6.2)  **0.03** | 3.46 (1.1, 10.4)  0.16 | 1.62 (0.69, 3.8)  0.88 |
| Odds ratios and *P* values compare the percent of virus seropositive vs. seronegative patients who met each ACR criterion. Odds ratios >1 indicate that virus seropositive patients were more likely to meet the criterion. *P* values were adjusted by the false discovery rate method. The ANA criterion could not be analyzed because all patients were ANA-positive, regardless of virus seropositivity. | | | | | | |

**Supplemental Table 3.** Number of positive autoantibodies detected by Bioplex assay in Filipino SLE patients, based on seropositivity for common herpes viruses (EBV, CMV, HSV-1, and HSV-2), EBV-EA, or EBV-EBNA-1. *P* values compare seropositive and seronegative patients for each antigen.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Number of Positive Autoantibodies by Bioplex** | | | | | | | | | | | | | |  |
|  | **0** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **Median** | ***P*** |
| **EBV VCA -** | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | n/a | 0.893 |
| **EBV VCA +** | 31 | 8 | 20 | 21 | 18 | 18 | 18 | 27 | 21 | 24 | 17 | 8 | 1 | 5.5 |
| **CMV -** | 1 | 2 | 2 | 1 | 1 | 2 | 2 | 0 | 1 | 0 | 1 | 0 | 0 | 4 | 0.174 |
| **CMV +** | 30 | 6 | 18 | 20 | 17 | 16 | 17 | 27 | 20 | 24 | 16 | 8 | 1 | 6 |
| **HSV1 -** | 5 | 2 | 3 | 5 | 2 | 3 | 3 | 0 | 4 | 1 | 1 | 0 | 0 | 3 | **0.0245** |
| **HSV1 +** | 26 | 6 | 17 | 16 | 16 | 15 | 16 | 27 | 17 | 23 | 16 | 8 | 1 | 6 |
| **HSV2 -** | 10 | 4 | 4 | 4 | 3 | 5 | 5 | 1 | 6 | 4 | 2 | 0 | 0 | 4 | **0.0159** |
| **HSV2 +** | 21 | 4 | 16 | 17 | 15 | 13 | 14 | 26 | 15 | 20 | 15 | 8 | 1 | 6 |
| **EBV EA -** | 11 | 0 | 1 | 1 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **2.37E-06** |
| **EBV EA +** | 20 | 8 | 19 | 20 | 16 | 16 | 18 | 27 | 21 | 24 | 17 | 8 | 1 | 6 |
| **EBV EBNA -** | 7 | 0 | 3 | 2 | 1 | 1 | 2 | 5 | 5 | 4 | 2 | 0 | 0 | 6.5 | 0.842 |
| **EBV EBNA +** | 24 | 8 | 17 | 19 | 17 | 17 | 17 | 22 | 16 | 20 | 15 | 8 | 1 | 5 |