**Supplemental Figure 1: Comparison of plasma cytokine/chemokine levels in SSc patients not treated with immunosuppressive agents vs. control subjects**



**Supplemental Table 1: Study Subject characteristics.**

|  |  |  |  |
| --- | --- | --- | --- |
|  **Characteristics** | **GENISOS Cohort****SSC (n=266) (%)** | **Control Subjects****(n=97) (%)** | **Canadian Cohort****SSc (n=171) (%)** |
| Female gender | 221 (83%) | 78 (80%) | 142 (83%) |
| Age at first study visit, mean ±SD years | 48.6 ±13.5 | 48 ±12.7 | 53.1 ±11.9 |
| Diffuse cutaneous involvement | 156 (59%) |   | 66 (39%) |
| Disease duration, mean ±SD years | 2.5 ±1.6 |   | 2.2 ±1.2 |
| *Ethnicity*   | White | 125 (47%) | 48 (49%) | 147 (86%) |
| African American | 54 (20%) | 17 (18%) | 3 (2%) |
| Latino | 77 (29%) | 27 (29%) | 2 (1%) |
|  | Others | 10 (4%) |  |  |
| *Antibodies* | Anti-centromere antibody | 32 (12%) |  | 46 (27%) |
| Anti-topoisomerase I antibody | 49 (18%) |  | 32 (19%) |
| Anti-RNA polymerase III antibody | 61 (23%) |  | 19 (11%) |
| Anti-U1 RNP antibody | 30 (11%) |  | 8 (5%) |
| Immunosuppression | 82 (32%) |  | 49 (29%) |

**Supplemental Table 2: Comparison of plasma cytokine levels between SSc patients vs controls in GENOSIS Cohort**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Cytokine/ Chemokine |  *b* |  95% CI | p-value | Subgroup analysis for patients not treated with immunosuppressive agents *b* 95% CI p-value |
| IL-1β | -0.021 | (-0.350; 0.309) | 0.903 | -0.007 | (-0.366; 0.352) | 0.969 |
| IL5 | -0.243 | (-0.548; 0.061) | 0.117 | -0.341 | (-0.680; -0.002) | 0.049 |
| IL6 | **-0.893** | **(-1.130; -0.656)** | **<0.001** | **-0.938** | **(-1.185; -0.691)** | **<0.001** |
| IL8 | **-0.491** | **(-0.814; -0.168)** | **0.003** | **-0.476** | **(-0.817; -0.135)** | **0.006** |
| IL10 | **-0.540** | **(-0.877; -0.202)** | **0.002** | **-0.556** | **(-0.935; -0.178)** | **0.004** |
| IL12 | -0.186 | (-0.603; 0.232) | 0.382 | -0.297 | (-0.767; 0.172) | 0.214 |
| IL13 | 0.068 | (-0.296; 0.433) | 0.713 | -0.092 | (-0.503; 0.318) | 0.658 |
| TNF-α | **-0.446** | **(-0.612; 0.280)** | **<0.001** | **-0.468** | **(-0.648; -0.286)** | **<0.001** |
| CCL2 | **-0.393** | **(-0.522; -0.265)** | **<0.001** | **-0.351** | **(-0.482; -0.220)** | **<0.001** |
| ITAC | **-0.689** | **(-0.902; -0.475)** | **<0.001** | **-0.601** | **(-0.822; -0.380)** | **<0.001** |
| IP10 | **-0.760** | **(-0.987; -0.533)** | **<0.001** | **-0.699** | **(-0.927; -0.472)** | **<0.001** |

\* Adjusted for age, gender, and ethnicity at enrollment.

**Supplemental Table 3. Correlation (r) between cytokines in GENOSIS cohort**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | IL5 | IL10 | IL12 | CCL2 |
| IL5 | 1.0000 | **0.8269** | **0.8738** | 0.0251 |
| IL10 |  | 1.0000 | **0.8333** | 0.0509 |
| IL12 |  |  | 1.0000 | 0.0119 |
| CCL2 |  |  |  | 1.0000 |

**Supplemental Table 4: Longitudinal analysis of predictive significance of CCL-2 and IL-10 for mRSS in dcSSc patients in the GENOSIS cohort \***

|  |  |  |
| --- | --- | --- |
| Cytokine/Chemokine |  Main effect of cytokine *b* 95% CI *p -*value |  Interaction term between baseline cytokine and follow up-time *b* 95% CI *p -*value |
| CCL2  | **1.15** | **(-2.02; 4.31)** | **0.477** | **-0.38** | **(-1.07; 0.31)** | **0.280** |
| IL10 | **0.37** | **(-0.73; 1.47)** | **0.509** | **-0.16** | **(-0.45; 0.13)** | **0.290** |
|  |  |  |  |  |  |  |

**\* Adjusted for age at enrollment and gender.**

**Supplemental Table 5: Longitudinal analysis of predictive significance of CCL-2, IL-10 and IL-6 for the decline of FVC% in the CSRG cohort \***

|  |  |  |
| --- | --- | --- |
| Cytokine/Chemokine |  Main effect of cytokine *b* 95% CI *p -*value | Interaction term between baseline cytokine and follow up-time *b* 95% CI *p -*value |
| CCL2  | **-4.53** | **(-8.56; -0.49)** | **0.028** | **-0.58** | **(-1.14; -0.03)** | **0.038** |
| IL10 | **-4.94** | **(-8.92; -0.96)** | **0.015** | -0.06 | (-0.75; 0.63) | 0.859 |
| IL6 | **-6.04** | **(-10.06; -2.02)** | **0.003** | -0.58 | (-1.21; 0.04) | 0.068 |

\* Adjusted for age at enrollment and gender.

**Supplemental Table 6: Immunosuppressive treatment at the baseline visit and follow-up time in the GENOSIS cohort\***

|  |  |  |
| --- | --- | --- |
| Treatment |  Baseline (%) |  Follow-up (%) # |
| Prednisone >5mg | 59 | (22.2%) | 29 | (13.2%) |
| Azathioprine | 6 | (2.3%) | 4 | (1.8%) |
| Methotrexate | 25 | (9.4%) | 22 | (10.0%) |
| MMF | 4 | (1.5%) | 11 | (5 %) |
| Cytoxan | 8 | (3.0%) | 24 | (10.9%) |
| Immunosup | 43 | (16.2%) | 54 | (24.5%) |
| Immunosup/pre | 82 | (30.8%) | 70 | (31.8%) |

\* Due to logistical reasons, only patients enrolled before 2010 were included in the present study.

# Medication regimen during the first year of follow-up.