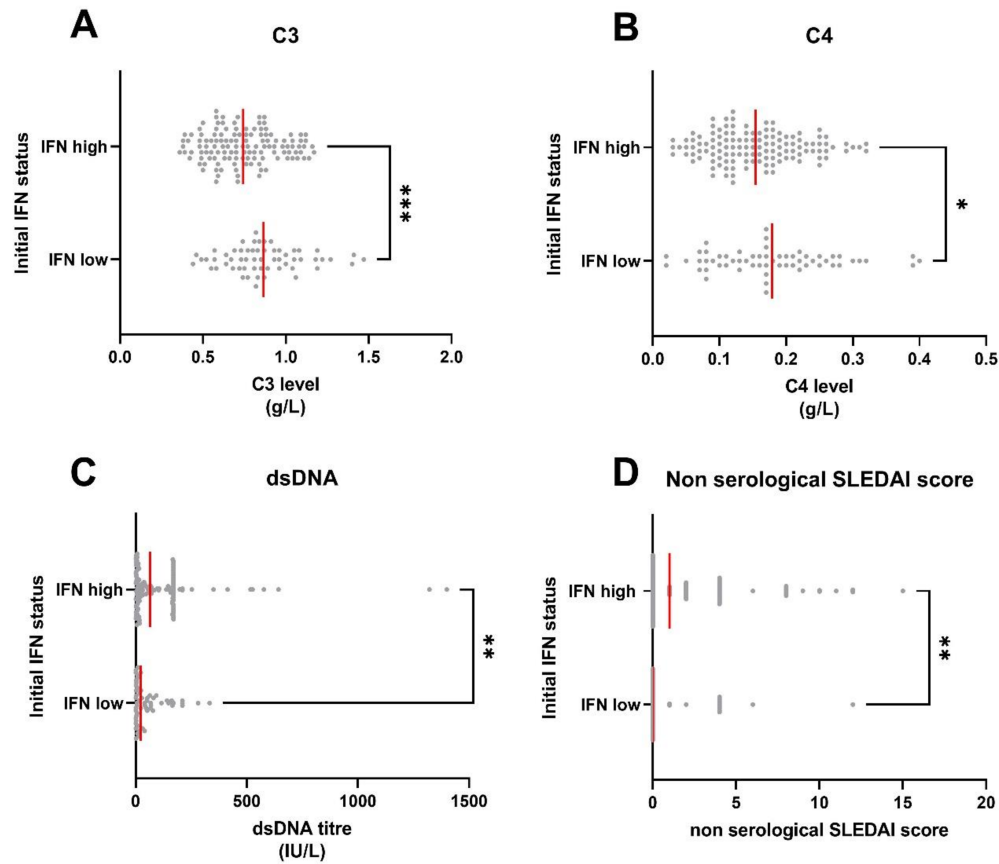
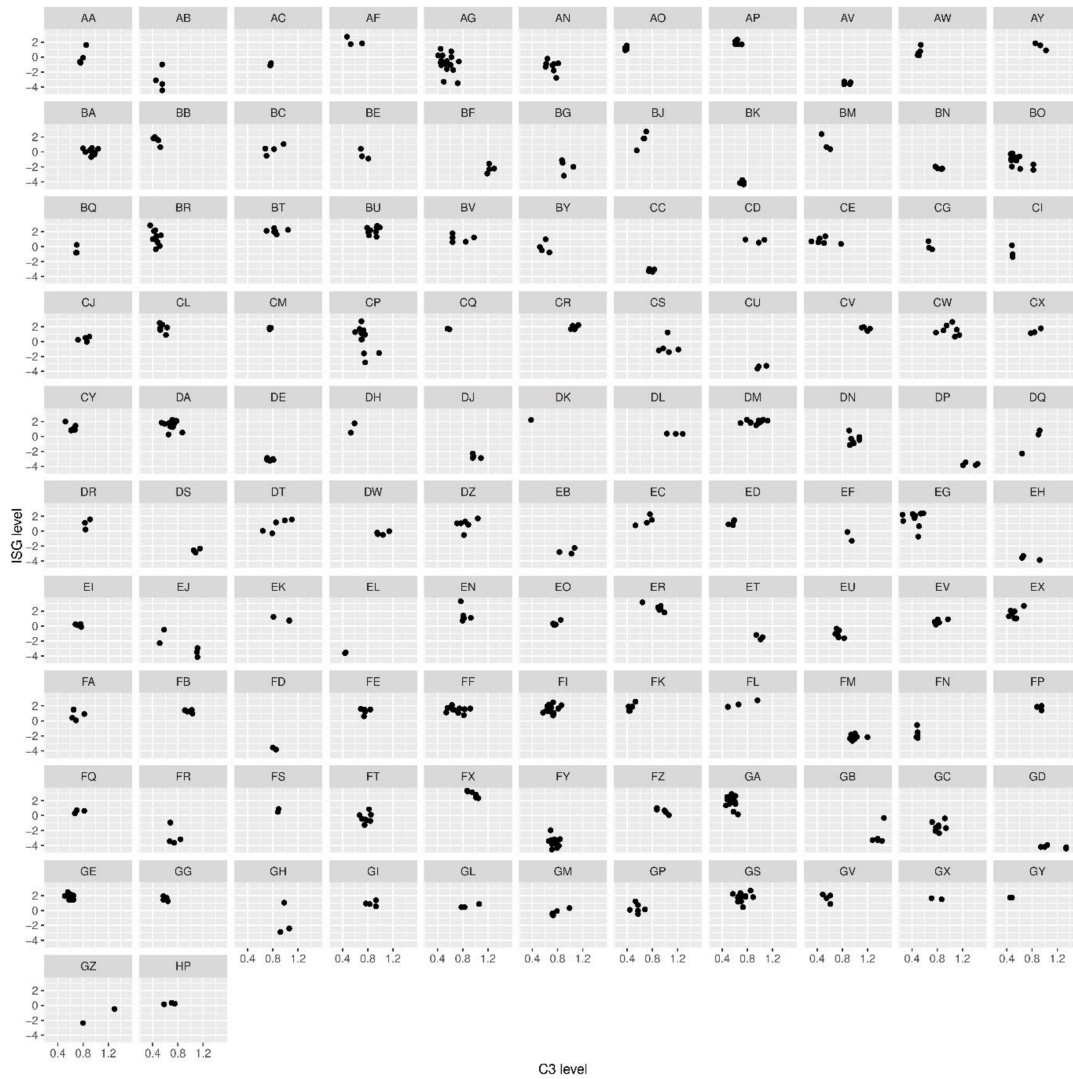


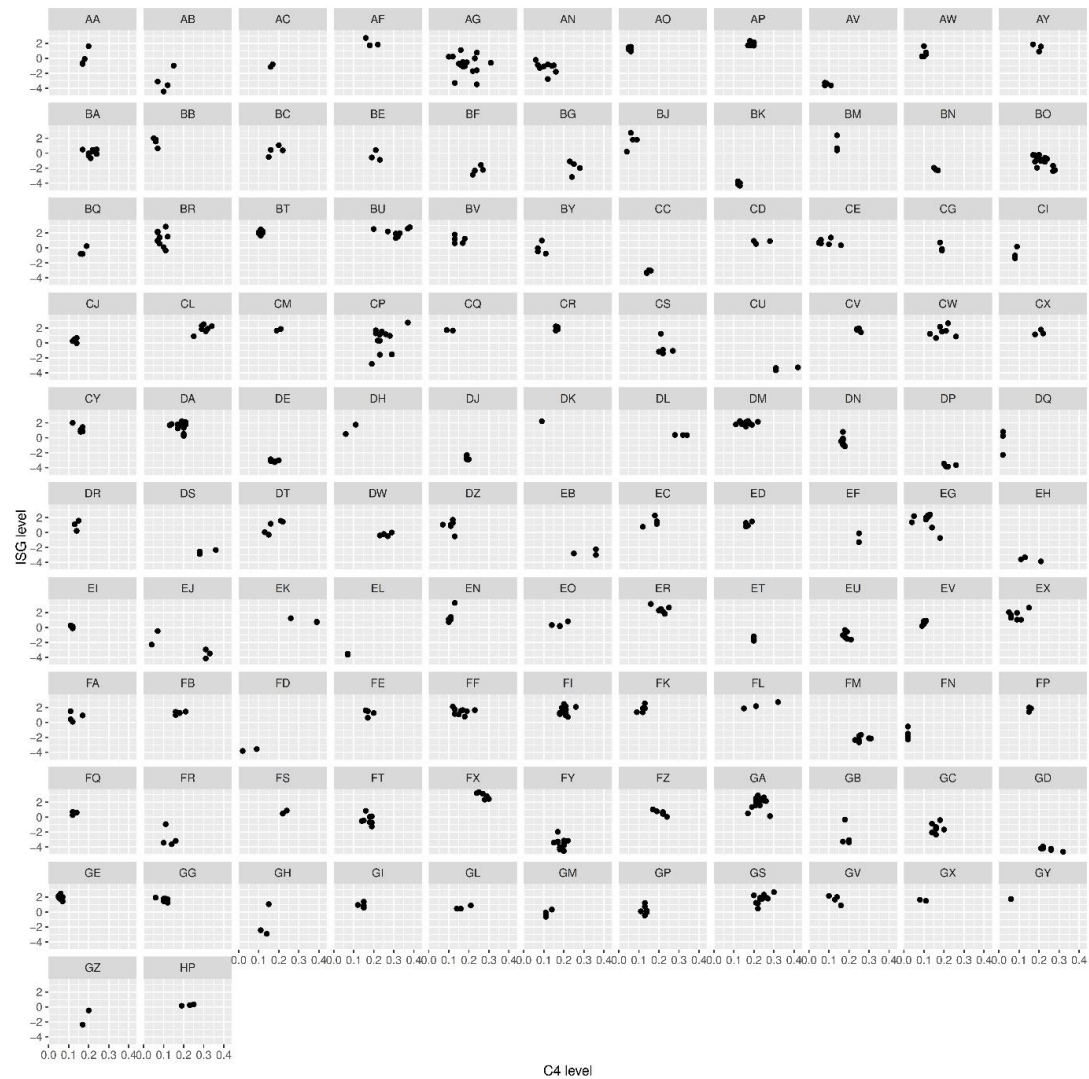
## Supplementary Data



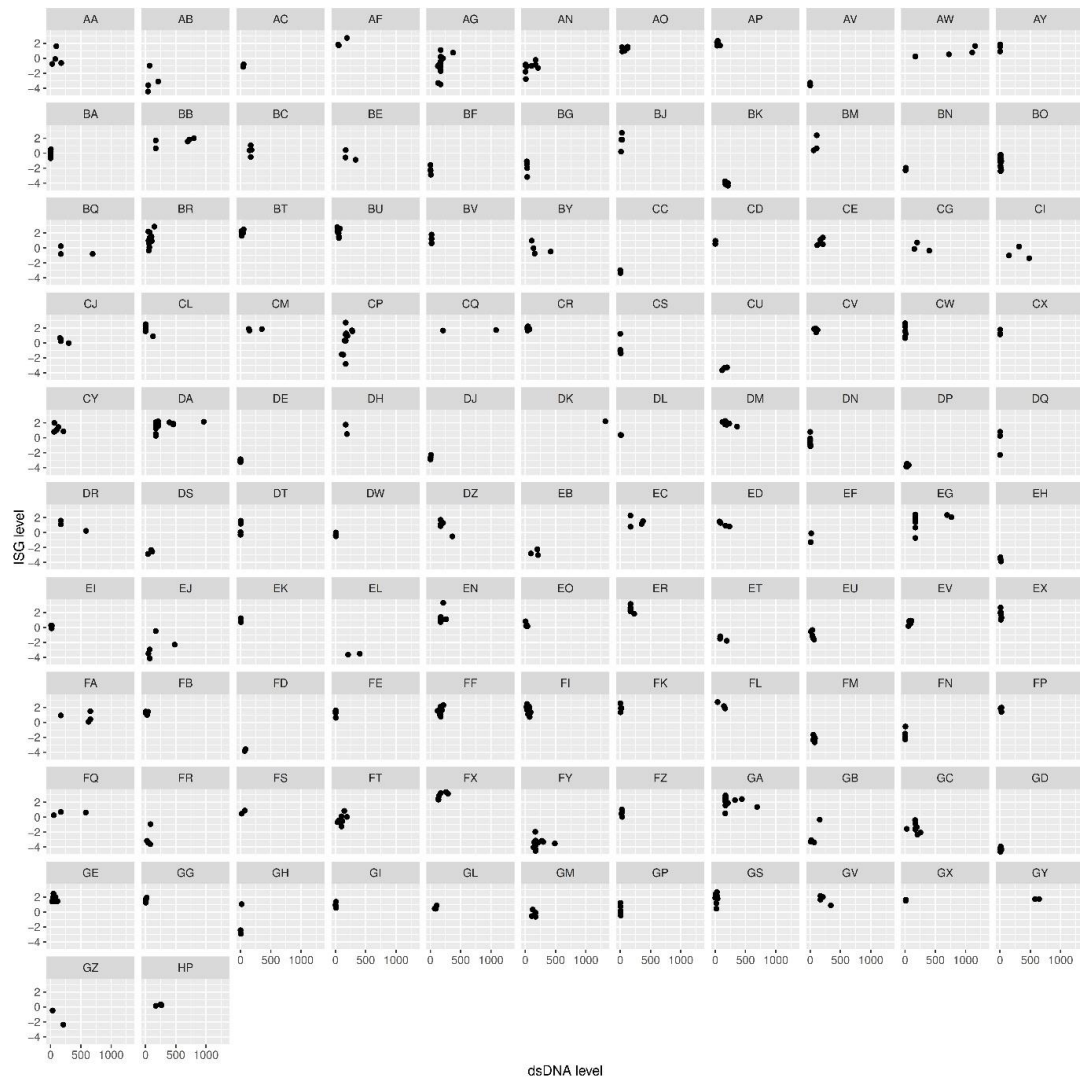
**Supplementary figure S1:** A) C3 levels in patients with IFN high status on initial testing vs IFN low status on initial testing. B) C4 levels in patients with IFN high status on initial testing vs IFN low status on initial testing. C) anti-dsDNA antibody titres in patients with IFN high status on initial testing vs IFN low status on initial testing. D) Non serological SLEDAI score (SLEDAI score excluding anti-dsDNA antibody and complement scores) in patients with IFN high status on initial testing vs IFN low status on initial testing. Red lines represent mean in figures A) and B) (parametric data) and median in figures C) and D) (non parametric data).



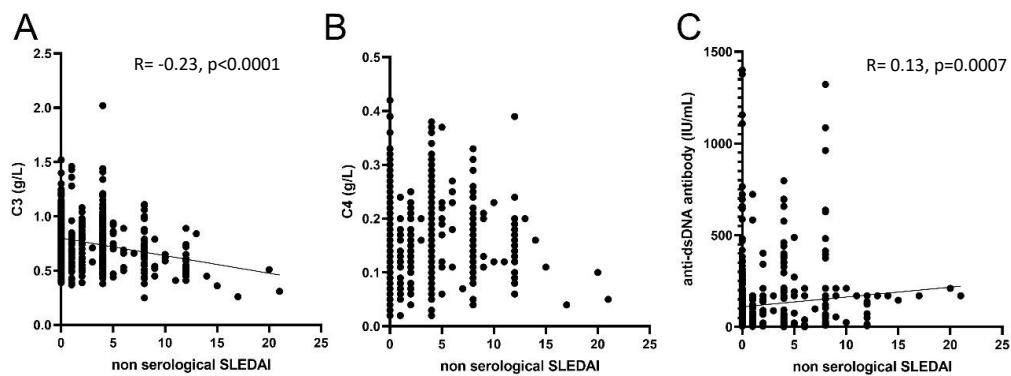
**Supplementary figure S2:** C3 levels (g/L) (x axis) and ISG levels (y axis) in patients with 3 or more longitudinal ISG results. Each graph represents one patient.



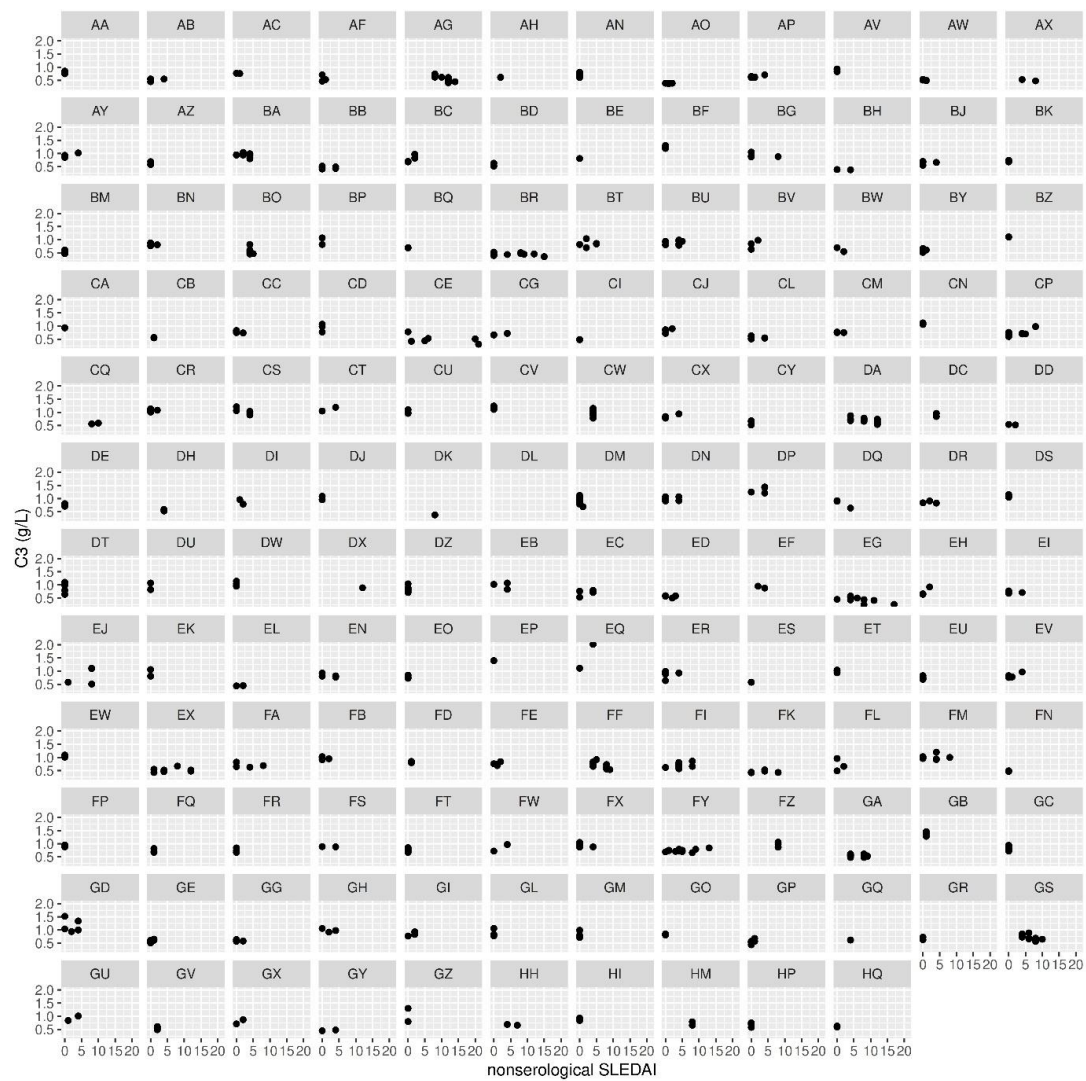
**Supplementary figure S3:** C4 levels (g/L) (x axis) and ISG levels (y axis) in patients with 3 or more longitudinal ISG results. Each graph represents one patient.



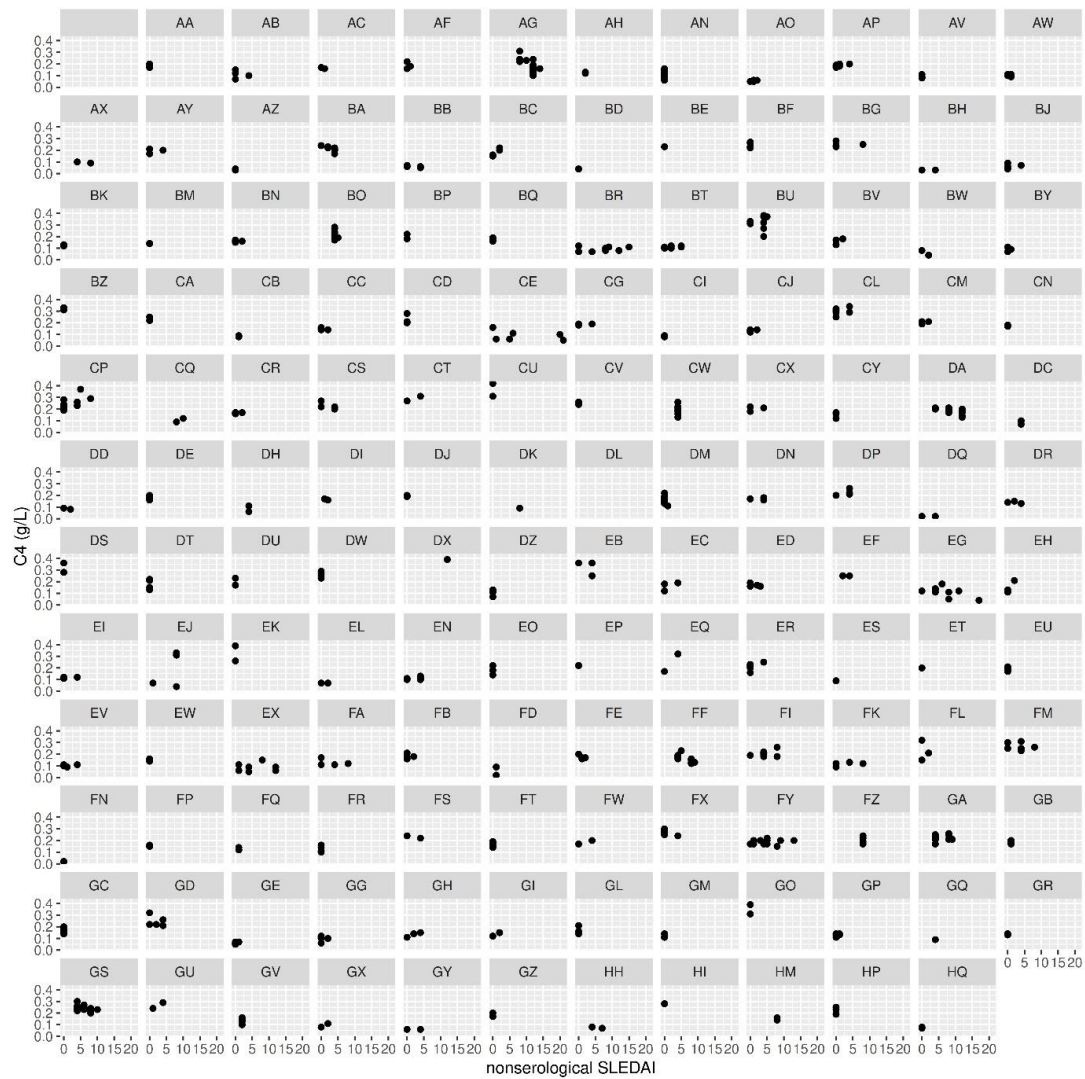
**Supplementary figure S4:** anti-dsDNA titres (IU/L) (x axis) and ISG levels (y axis) in patients with 3 or more longitudinal ISG results. Each graph represents one patient.



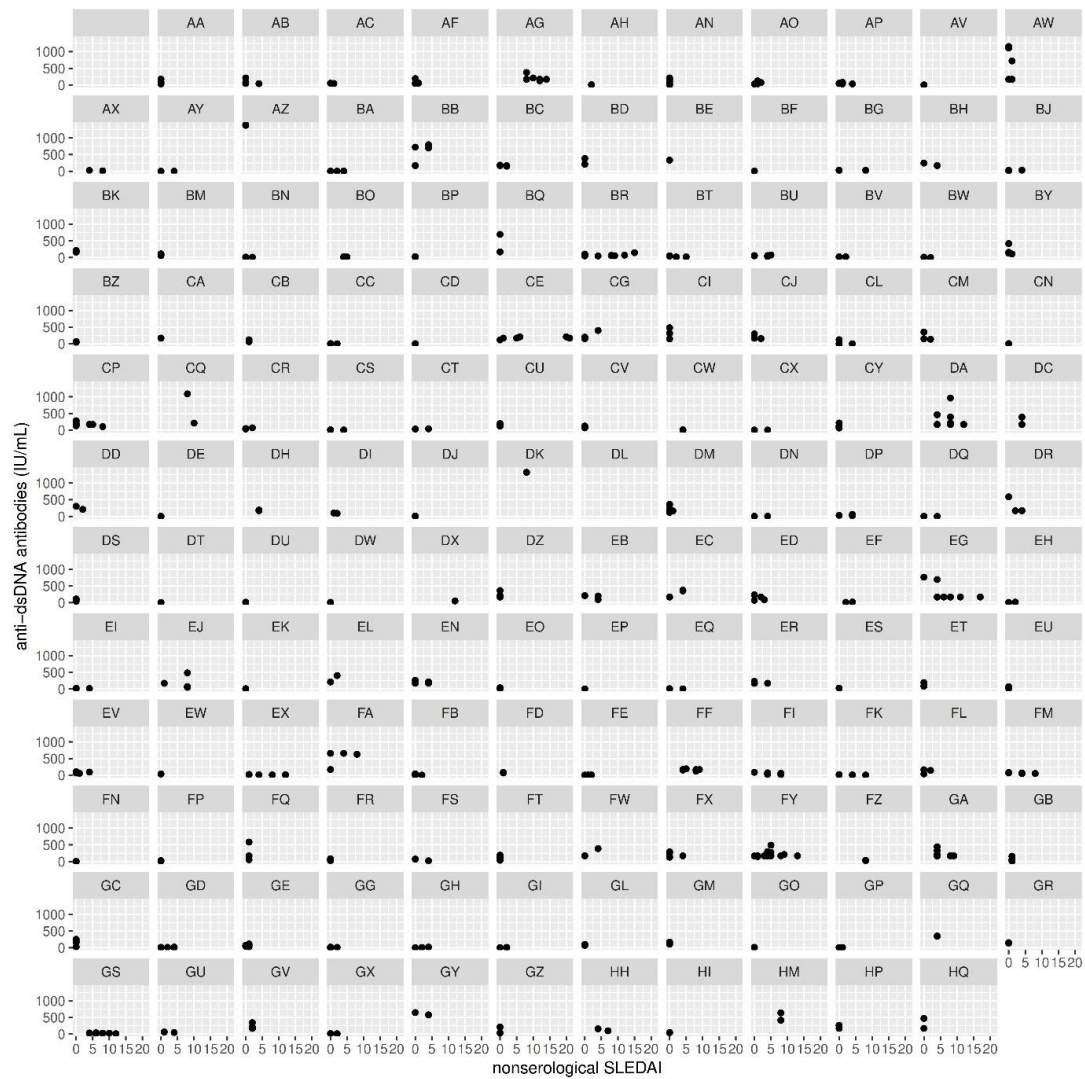
**Supplementary figure S5:** The relationship between non serological SLEDAI and serological components for the SLEDAI across the whole cohort.



**Supplementary Figure S6:** The relationship between non-serological SLEDAI and C3 in individual patients. Each square represents samples from one patient.

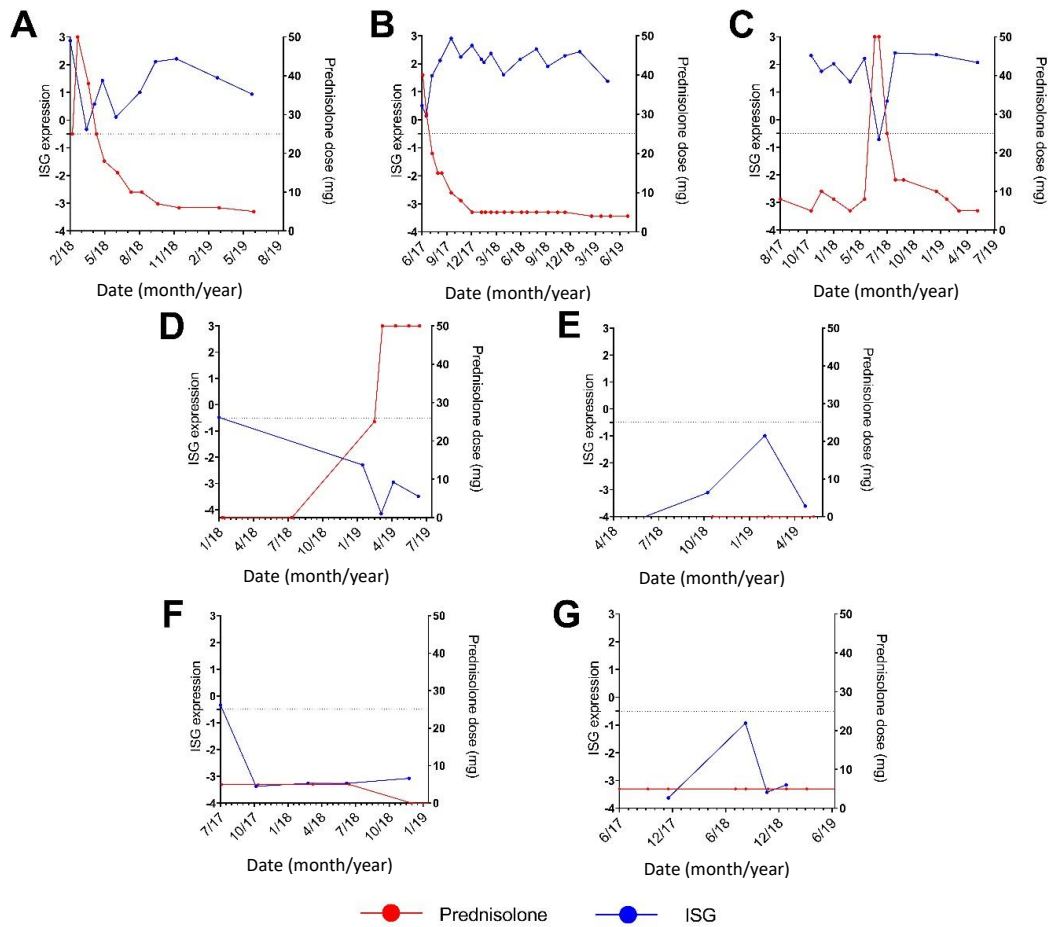


**Supplementary Figure S7:** The relationship between non-serological SLEDAI and C4 in individual patients. Each square represents samples from one patient.



**Supplementary Figure S8:** The relationship between non-serological SLEDAI and anti-dsDNA antibody levels in individual patients. Each square represents samples from one patient.





**Supplementary figure S9:** Each graph in this figure represents ISG levels from one individual patient over time with their corresponding glucocorticoid dose. **A-C)** IFN high patients who have fluctuations in ISG levels  $>2$  SD from mean fluctuation temporally related to high dose prednisolone use. **D)** IFN low patient who had ISG level fluctuation  $>2$  SD from mean fluctuation temporally related to high dose prednisolone use. **E-G)** IFN low patients who had ISG fluctuation  $>2$  SD from mean fluctuation in ISG expression level that was not related to prednisolone dose.

<b>Supplementary table S1: Composite disease activity measurements</b>								
	<b>Initial IFN HIGH</b>	<b>Initial IFN LOW</b>	<b>P value (Initial HIGH vs Initial LOW)</b>	<b>Multivariate analysis</b>	<b>Stable IFN HIGH</b>	<b>Stable IFN LOW</b>	<b>P value (Stable HIGH vs stable LOW)</b>	<b>Multivariate analysis</b>
Time adjusted mean SLEDAI (AMS) Median [range]	4.2 [0-14.3]	2.0 [0-10.0]	<b>P=&lt;0.0001</b>	<b>P=0.01</b>	4.2 [0-13.0]	2.6 [0-8.0]	<b>P=0.001</b>	P=0.07
Percentage time spent in LLDAS Median [range]	55.5 [0-100]	84.0 [0-100]	<b>P=0.0003</b>	P=0.06	61.0 [0-100]	91.0 [0-100]	<b>P=0.001</b>	P=0.16
Mild/Moderate flare during study period (n (%) of patients with at least one flare)	69(53.5%)	16(25.8%)	<b>OR 3.31 [1.72-6.58]</b> <b>P=0.0004</b>	<b>OR 2.87 [1.44-5.93]</b> <b>P=0.003</b>	46(54.1%)	12(30.8%)	<b>OR 2.65 [1.21-6.09]</b> <b>P=0.017</b>	OR 2.10[0.88-5.19] P=0.10
Severe flare during study period (% of patients with at least one flare)	34(26.4%)	4(6.5%)	<b>OR 5.19 [1.94-18.04]</b> <b>P=0.003</b>	<b>OR 5.35 [1.90-19.41]</b> <b>P=0.003</b>	27(31.8%)	3(7.7%)	<b>OR 5.59 [1.80-24.58]</b> <b>P=0.008</b>	<b>OR 5.69 [1.66-27.19]</b> <b>P=0.012</b>

<b>Supplementary table S2: Medication</b>							
		<b>Initial IFN HIGH</b>	<b>Initial IFN LOW</b>	<b>Initial HIGH vs Initial LOW p</b>	<b>Stable IFN HIGH</b>	<b>Stable IFN LOW</b>	<b>Stable HIGH vs stable LOW P</b>
Number of pts with medication data	200	127	59		83	38	
Hydroxychloroquine (N%)	180(90.0%)	115(90.6%)	52 (88.1%)	OR 1.08 [0.36-2.96] P=0.88	76 (91.6%)	35 (92.1%)	OR 0.93[0.19-3.57] P=0.92
Immunosuppressant (excluding biologic) (N%)	136(68.0%)	94 (74.0%)	32 (54.2%)	<b>OR 2.51 [1.34-4.75]</b> <b>P=0.004</b>	65 (78.3%)	21 (55.3%)	<b>OR 2.88 [1.24-6.29]</b> <b>P=0.012</b>
Azathioprine (N%)	48(24%)	39 (30.7%)	7 (11.9%)	<b>OR 3.29 [1.44-8.51]</b> <b>P=0.008</b>	20 (24.1%)	5 (13.2%)	<b>OR 2.10 [0.77-6.75]</b> <b>P=0.17</b>
Mycophenolate (N%)	74 (37.0%)	50 (39.4%)	18 (30.5%)	OR 1.48 [0.77-2.90] P=0.24	37 (44.6%)	13 (34.2%)	OR 1.54 [0.71-3.48] P=0.28
Methotrexate (N%)	31 (15.5%)	20 (15.7%)	9 (15.3%)	OR 1.03 [0.45-2.55] P=0.93	15 (18.1%)	4 (10.5%)	OR 1.85[0.62-6.94] P=0.29
Leflunomide N (%) (N%)	4 (2.0%)	2 (1.6%)	2 (33.9%)	OR 0.45[0.05-3.88] P=0.44	2 (2.4%)	1 (2.6%)	##
Cyclophosphamide (N%)	5 (2.5%)	4 (3.1%)	0 (0.0%)	##	2 (2.4%)	1 (2.6%)	##
Belimumab (N%)	4(2.0%)	3(2.4%)	1 (1.7%)	##	3 (3.6%)	1 (2.6%)	##
Rituximab (N%)	10 (5.0%)	4 (3.1%)	5(8.5%)	OR 0.35 [0.08-1.37] P=0.13	3 (3.6%)	3 (7.9%)	OR 0.44 [0.08-2.47] P=0.33
Glucocorticoid (any) (N%)	115 (57.5%)	81(63.8%)	27 (45.8%)	<b>OR 2.02[1.06-3.86]</b> <b>P=0.031</b>	52 (62.7%)	18 (47.4%)	OR 1.96[0.91-4.27] P=0.09
Time adjusted mean GC dose (mg) (median[range])	1.37[0-42.2]	1.7 [0-42.2]	0.0 [0-11.5]	<b>P = 0.005</b>	1.6 [0-42.2]	0.0 [0-16.25]	P=0.06
<b>## number of patients taking medication too small for meaningful analysis</b>							

Supplementary Table S3: Disease related damage scores								
	Initial IFN HIGH	Initial IFN LOW	Initial status Univariate analysis	Initial status Multivariate analysis adjusting for age and race	Stable IFN HIGH	Stable IFN LOW	Stable status Univariate analysis	Stable status Multivariate analysis adjusting for age and race
	<b>125</b>	<b>60</b>			<b>84</b>	<b>36</b>		
Total SLICC score Median [range]	1[0-6]	1[0-7]	P=0.10	P=0.25	0[0-6]	1[1-7]	P=0.22	P=0.73
Ocular (n(%))	7(5.6%)	8(13.3%)	OR 0.39 [0.13-1.13] P=0.08	OR 0.38 [0.12-1.22] P=0.10	4(4.8%)	4(11.1%)	OR 0.43 [0.10-1.91] P=0.26	OR 0.87 [0.15-5.35] P=0.87
Neuropsychiatric (n(%))	11(8.8%)	11(18.3%)	OR 0.43 [0.17-1.07] P=0.07	OR 0.45 [0.17-1.22] P=0.11	6(7.1%)	3(8.3%)	OR 0.91 [0.23-4.51] P=0.90	OR 1.29 [0.26-7.92] P=0.77
Renal (n(%))	10(8.0%)	13(21.7%)	<b>OR 0.32 [0.13-0.77] P=0.011</b>	<b>OR 0.26 [0.09-0.68] P=0.006</b>	5(6.0%)	4(11.1%)	OR 0.55 [0.14-2.32] P=0.39	OR 0.39 [0.08-1.95] P=0.23
Pulmonary (n(%))	13(10.4%)	3(5.0%)	OR 2.20 [0.68-9.88] P=0.23	OR 3.24 [0.89-16.02] P=0.10	6(7.1%)	3(8.3%)	OR 0.91 [0.23-4.51] P=0.90	OR 1.17 [0.24-7.06] P=0.85
Cardiac (n(%))	12(9.6%)	9(15.0%)	OR 0.60 [0.24-1.56] P=0.28	OR 0.66 [0.24-1.84] P=0.41	4(4.8%)	5(13.9%)	OR 0.33 [0.08-1.34] P=0.12	OR 0.63 [0.12-3.39] P=0.59
Peripheral vascular (n(%))	9(7.2%)	6(10.0%)	0.70 [0.24-2.18] P=0.52	0.58 [0.19-1.92] P=0.36	6(7.1%)	3(8.3%)	OR 0.91 [0.23-4.51] P=0.90	0.67[0.14-3.90] P=0.64
Gastrointestinal (n(%))	1(0.8%)	0(0.0%)	##	##	1(1.2%)	0(0.0%)	##	##
Musculoskeletal (n(%))	26(20.8%)	14(23.3%)	OR 0.87 [0.42-1.84] P=0.70	OR 1.11[0.50-2.60] P=0.79	17(20.2%)	8(22.2%)	OR 0.97 [0.38-2.59] P=0.95	OR 1.48[0.51-4.76] P=0.48
Skin (n(%))	24(19.2%)	5(8.3%)	OR 2.61 [1.00-8.06] P=0.06	OR 2.25 [0.83-7.25] P=0.13	17(20.2%)	3(8.3%)	OR 3.0 [0.93-13.46] P=0.10	OR 3.3 [0.91-16.63] P=0.10
Gonadal failure (n(%))	2(1.6%)	2(3.3%)	OR 0.23 [0.01-2.49] P=0.24	##	2(2.4%)	2(5.6%)	OR 0.22 [0.01-2.37] P=0.22	##
Diabetes (n(%))	2(1.6%)	8(13.3%)	<b>OR 0.11 [0.02-0.44] P=0.005</b>	OR 0.21 [0.03-1.16] P=0.09	2(2.4%)	5(13.9%)	<b>OR 0.16 [0.02-0.80] P=0.036</b>	OR 0.34 [0.04-2.48] P=0.30
Malignancy (n(%))	3(2.4%)	7(11.6%)	<b>OR 0.19 [0.04-0.70] P=0.018</b>	OR 0.26 [0.05-1.09] P=0.07	3(3.6%)	6(16.7%)	<b>OR 0.20 [0.04-0.81] P=0.029</b>	OR 0.48 [0.08-2.63] P=0.40
## number of patients too small for meaningful analysis								