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).

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**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.

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**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.

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**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.

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

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

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**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.

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

Supplementary table S2	: Medication						
		Initial IFN HIGH	Initial IFN LOW	Initial HIGH vs Initial LOW	Stable IFN HIGH	Stable IFN LOW	Stable HIGH vs stable LOW P
				р			
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%)	OR 2.51 [1.34-4.75] P=0.004	65 (78.3%)	21 (55.3%)	OR 2.88 [1.24-6.29] P=0.012
Azathioprine (N%)	48(24%)	39 (30.7%)	7 (11.9%)	OR 3.29 [1.44-8.51] P=0.008	20 (24.1%)	5 (13.2%)	OR 2.10 [0.77-6.75] P=0.17
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%)	OR 2.02[1.06-3.86] P=0.031	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]	P = 0.005	1.6 [0-42.2]	0.0 [0-16.25]	P=0.06
## number of patients taki	ng medication	too small for n	neaningful and	alysis			

Supplementary	Table S3: Di	sease relate	ed damage scores					
	Initial IFN	Initial IFN	Initial status	Initial status	Stable	Stable	Stable status	Stable status
	HIGH	LOW	Univariate analysis	Multivariate analysis	IFN HIGH	IFN LOW	Univariate analysis	Multivariate analysis
				adjusting for age and				adjusting for age and race
				race				
	125	60			84	36		
Total SLICC score	1[0-6]	1[0-7]	P=0.10	P=0·25	0[0-6]	1[1-7]	P=0·22	P=0·73
Median [range]								
Ocular	7(5·6%)	8(13·3%)	OR 0·39 [0·13-1·13]	OR 0·38 [0·12-1·22]	4(4·8%)	4(11·1%)	OR 0·43 [0·10-1·91]	OR 0.87 [0.15-5.35]
(n(%))			P=0.08	P=0.10			P=0·26	P=0.87
Neuropsychiatric	11(8.8%)	11(18·3%)	OR 0·43 [0·17-1·07]	OR 0.45 [0.17-1.22]	6(7·1%)	3(8·3%)	OR 0.91 [0.23-4.51]	OR 1·29 [0·26-7·92]
(n(%))			P=0.07	P=0·11	- ( ( )		P=0.90	P=0.77
Renal	10(8.0%)	13(21.7%)	OR 0.32 [0.13-0.77]	OR 0·26 [0·09-0·68]	5(6·0%)	4(11·1 %)	OR 0.55 [0.14-2.32]	OR 0.39 [0.08-1.95]
(n(%))	12(10, 10()	2(5.0%)	P=0.011	P=0.006	C(7.40()	2(0,20/)	P=0-39	P=0·23
Pulmonary	13(10.4%)	3(5.0%)	OR 2-20 [0-68-9-88]	OR 3-24 [0-89-16-02]	6(7.1%)	3(8·3%)	OR 0.91 [0.23-4.51]	OR 1.17 [0.24-7.06]
(n(%))	12/0 (0/)	0(15,00()	P=0·23	P=0·10	4(4.00/)	F(12.00/)	P=0.90	P=0.85
	12(9.6%)	9(15.0%)	DR 0.00 [0.24-1.20]	DR 0.00 [0.24-1.84]	4(4·8%)	2(13.9%)	DR 0.33 [0.08-1.34]	DR 0.63 [0.12-3.39]
(II(70)) Deriphoral	0(7,2%)	6(10,0)%	0.70 [0.24 2.19]	0.59 [0.10 1.02]	6(7,10/)	2(0,20/)	P-0.12	P=0.39
vascular	9(7.2%)	0(10.0)%	D-0.52	D-0.36	0(7.1%)	5(0.2%)	DR 0.91 [0.25-4.51]	D-0.64
(n(%))			F -0'52	F =0.30			F -0-50	F = 0°04
Gastrointestinal	1(0.8%)	0(0.0%)	##	##	1(1.2%)	0(0.0%)	##	##
(n(%))	1(0 0/0)	0(0 0/0)			1(1 2/0)	0(0 070)		
Musculoskeletal	26(20.8%)	14(23.3%)	OR 0.87 [0.42-1.84]	OR 1.11[0.50-2.60]	17(20.2%)	8(22·2%)	OR 0.97 [0.38-2.59]	OR 1·48[0·51-4·76]
(n(%))	,	( <i>,</i>	P=0.70	P=0.79	( /	- ( - )	P=0.95	P=0.48
Skin	24(19.2%)	5(8.3%)	OR 2.61 [1.00-8.06]	OR 2·25 [0·83-7·25]	17(20.2%)	3(8·3%)	OR 3·0 [0·93-13·46]	OR 3·3 [0·91-16·63]
(n(%))			P=0.06	P=0.13			P=0.10	P=0.10
Gonadal failure	2(1.6%)	2(3·3%)	OR 0·23 [0·01-2·49]	##	2(2·4%)	2(5.6%)	OR 0·22 [0·01-2·37]	##
(n(%))			P=0·24				P=0.22	
Diabetes	2(1.6%)	8(13·3%)	OR 0·11 [0·02-0·44]	OR 0·21 [0·03-1·16]	2(2·4%)	5(13·9%)	OR 0·16 [0·02-0·80]	OR 0·34 [0·04-2·48]
(n(%))			P=0.005	P=0·09			P=0.036	P=0·30
Malignancy	3(2·4%)	7(11.6%)	OR 0·19 [0·04-0·70]	OR 0·26 [0·05-1·09]	3(3·6%)	6(16·7%)	OR 0·20 [0·04-0·81]	OR 0·48 [0·08-2·63]
(n(%))			P=0.018	P=0·07			P=0.029	P=0·40
## number of pati	ents too sma	ll for meanin	gful analysis					