

Table e-1: Baseline clinical and demographic data of relapse responders (Resp) and non-responders (Non Resp).

Variable	Resp	Non-Resp	P-values
n	90	67	
Diagnosis [RRMS/CIS (%RRMS)]	64/26 (71.1)	50/17 (74.6)	0.6251 ^a
Age (SD)	37.1 (8.7)	35.6 (8.7)	0.2622 ^b
Disease duration (SD)	4.9 (6.1)	4.7 (5.8)	0.5585 ^b
Sex F/M (% F)	59/31 (65.5)	49/18 (73.1)	0.3107 ^a
Baseline EDSS (SD)	1.6 (1.3)	1.7 (1.4)	0.4165 ^b
Number of relapses 2 yrs before BL (SD)	1.3 (0.7)	1.6 (0.7)	0.0074 ^b
Mean time between HDMP and BL, months (SD)	10.8 (9.0)	8.6 (8.3)	0.1718 ^b
Previous DMT use before BL [n(%)]	6 (6.7)	9 (13.4)	0.2466 ^a
IFN preparation [n (%)]			
IM IFNβ-1a	46 (51.1)	32 (47.8)	0.5917 ^a
SC IFNβ-1b	18 (20.0)	18 (26.9)	
SC IFNβ-1a	26 (28.9)	17 (25.4)	

Notes: n = number, RRMS = relapsing remitting multiple sclerosis; CIS = clinically isolated syndrome, SD = standard deviation, F = Female, M = Male, EDSS = Expanded Disability Status Scale, IM = intramuscular, SC = subcutaneous, Resp = Responders, Non-Resp = Non-responders. HDMP = High dose methylprednisolone, DMT = Disease modifying therapy, BL = Baseline, Yrs = years.

Responders were defined as having no relapses during the 2 years post initiation of IFN- β Therapy. P-values were evaluated using ^aChi square tests or ^bMann Whitney T-tests.

Table e-2. Previous Treatments of relapse responders and non-responders.

Previous Treatment	No Relapse	Relapses
	n	n
GLAT	2	5
IVIg	1	1
Azathioprin	0	1
Investigational medication	3	2
No previous treatment	84	58

Notes: GLAT = glatiramer acetate, IVIg = intravenous immunoglobulins

Table e-3: Differences in baseline cytokine concentrations in relapse responders and non-responders.

Cytokine	Risk of Relapse while on IFN- β therapy	
	OR(95%CI)	P-value
IL1 β	1.45(1.09-1.93)	0.0105
CCL2/MCP1	1.3(0.98-1.72)	0.0672
LIF	0.85(0.7-1.04)	0.1138
IL1RA	1.14(0.95-1.36)	0.1603
IL-8	1.07(0.97-1.18)	0.1773
TNF β	0.68(0.38-1.22)	0.1982
CXCL1/Gro α	1.2(0.9-1.6)	0.2143
MIP1 α	1.16(0.91-1.48)	0.2394
IL-13	0.74(0.44-1.23)	0.2465
IL-5	0.77(0.49-1.21)	0.2592
Eotaxin	0.8(0.52-1.22)	0.2959
TNF α	0.68(0.33-1.42)	0.3065
PAI	1.4(0.73-2.71)	0.3149
NGF	0.85(0.61-1.17)	0.3176
IL-17F	1.19(0.83-1.71)	0.3421
IL-10	0.82(0.55-1.24)	0.3447
Resistin	1.15(0.86-1.53)	0.3565
CXCL10/IP10	0.67(0.28-1.58)	0.3574
IL12p40	0.85(0.59-1.22)	0.3762
IL12p70	0.83(0.56-1.25)	0.3815
IL-7	0.78(0.44-1.39)	0.4064
IL-1a	0.82(0.5-1.32)	0.4122
GMCSF	0.85(0.55-1.29)	0.4406
MIP1 β	1.3(0.66-2.56)	0.4429
IFN β	1.13(0.83-1.54)	0.4483
IL-2	0.83(0.5-1.37)	0.4576
IL-4	0.82(0.46-1.46)	0.4898
HGF	0.87(0.59-1.28)	0.4901
PDGF	0.86(0.57-1.31)	0.4923
VCAM	1.09(0.84-1.42)	0.5078
Rantes	1.08(0.87-1.34)	0.5122
ICAM	1.07(0.86-1.35)	0.5309
CD40L	0.97(0.87-1.08)	0.5373
VEGF	0.9(0.64-1.26)	0.5399
IL-6	1.18(0.69-2.01)	0.5428
IFN α	0.94(0.76-1.16)	0.5469
Leptin	0.88(0.55-1.42)	0.6123
GCSF	1.05(0.86-1.28)	0.6247
TGF β	0.89(0.54-1.45)	0.6325
IL-15	0.92(0.65-1.32)	0.6640
sFasL	0.88(0.48-1.6)	0.6662
ENA	1.1(0.7-1.74)	0.6696
TGF α	0.91(0.58-1.42)	0.6754
SCF	0.8(0.28-2.28)	0.6803
MCSF	1.11(0.68-1.79)	0.6808
MCP3	0.92(0.62-1.38)	0.6961
FGF	0.88(0.44-1.75)	0.7129
IFN γ	0.89(0.46-1.71)	0.7305
IL-17	0.96(0.69-1.32)	0.7877
MIG	1.01(0.84-1.22)	0.9162
sTRAIL	0.99(0.74-1.32)	0.9280

Note: Baseline cytokine values were 2-log transformed. Odds ratios (OR), confidence intervals (CI) and p-values were assessed using logistic regression.

Table e-4: Serum cytokine concentrations with statistically significant changes from baseline to 3 months in relapse responders and non-responders.

Cytokine (pg/ml)	Responders (n=90)					
	Baseline		3 Month		Δ from BL to 3M	
	Mean	SD	Mean	SD	P-value	Direction
CXCL10/IP10	68.0	17.1	246.5	181.4	< 0.0001	up
CCL2/MCP1	49.4	72.0	125.2	202.4	0.0006	up
IL-1α	36.2	34.8	46.5	22.7	0.0135	up
IFNβ	6.3	13.7	11.4	26.4	0.0179	up
GCSF	3.5	4.6	5.1	6.7	0.0191	up
TGFβ	21.7	10.0	24.3	12.4	0.0216	up
ICAM	23924.4	18247.1	25790.5	18162.8	0.0242	up
IL12p40	73.2	29.9	79.4	34.8	0.0246	up
MIP1β	1254.8	409.8	1361.0	622.6	0.0287	up
sTRAIL	56.3	29.0	64.0	33.4	0.0290	up
CD40L	7594.1	7727.2	9420.8	10852.4	0.0315	up
IL1RA	617.4	1211.9	1665.2	4627.5	0.0382	up
MIP1α	59.6	70.8	88.6	143.2	0.0453	up
sVCAM	11249.3	5327.1	12828.1	9064.8	0.0498	up
Cytokine (pg/ml)	Non Responders (N=67)					
	Baseline		3 Month		Δ from BL to 3M	
	Mean	SD	Mean	SD	P-value	Direction
CXCL10/IP10	65.8	18.2	256.8	197.8	< 0.0001	up
IL-1α	32.4	14.3	47.5	25.6	< 0.0001	up
IFNβ	7.0	10.5	10.5	16.4	0.0004	up
IFNα	59.5	57.5	86.4	71.5	0.0024	up
CCL2/MCP1	91.2	150.2	167.9	251.8	0.0124	up
sVCAM	11866.4	6006.0	13284.5	6496.9	0.0149	up
IL-8	859.3	1589.7	488.7	1211.5	0.0198	down
TNFβ	18.2	6.1	19.8	7.8	0.0413	up

Note: BL = baseline, 3M = 3 months, SD = standard deviation. P-values were determined using a paired t-test. Up = increase in concentration; Down = decrease in concentration.

Table e-5: Baseline clinical and demographic data of EDSS responders (Resp) and non-responders (Non Resp).

Variable	Resp	Non Resp	P-values
n	114	39	
Diagnosis [RRMS/CIS (%RRMS)]	80/34 (70.2)	31/8 (79.5)	0.2607 ^a
Age, yrs (SD)	36.1 (9.0)	36.9 (7.6)	0.5697 ^b
Disease duration, yrs (SD)	4.6 (6.2)	5.5 (5.3)	0.0817 ^b
Sex F/M (% F)	81/33 (71.1)	26/13 (66.7)	0.6061 ^a
Baseline EDSS (SD)	1.8 (1.2)	1.2 (1.6)	0.0034 ^b
Number of relapses 2 yrs before BL (SD)	1.5 (0.7)	1.4 (0.7)	0.7349 ^b
Mean time between HDMP and BL, months (SD)	8.9 (9.5)	12.0 (8.3)	0.0283 ^b
Previous DMT use before BL [N(%)]	12 (10.5)	3 (7.7)	0.6074 ^a
IFN preparation [n (%)]			
IM IFNβ-1a	58 (51.0)	19 (47.8)	0.9729 ^a
SC IFNβ-1b	25 (22.0)	9 (23.1)	
SC IFNβ-1a	31 (27.2)	11 (28.2)	

Notes: n = number, RRMS = relapsing remitting multiple sclerosis; CIS = clinically isolated syndrome, SD = standard deviation, F = Female, M = Male, EDSS = Expanded Disability Status Scale, IM = intramuscular, SC = subcutaneous, Resp = Responders, Non-Resp = Non-responders. HDMP = High dose methylprednisolone, DMT = Disease modifying therapy, BL = Baseline, Yrs = years. Non-Responders were defined as having at least 1 point increase of EDSS score 2 years post initiation of IFN- β Therapy. P-values were evaluated using ^aChi square tests or ^bMann Whitney T-tests.

Table e-6. Previous Treatments of EDSS responders and non-responders.

Previous Treatment	No Relapse	Relapses
	n	n
GLAT	6	1
IVIg	1	1
Azathioprin	1	0
Investigational medication	4	1
No previous treatment	102	36

Notes: GLAT = glatiramer acetate, IVIg = intravenous immunoglobulins

Table e-7: Differences in baseline cytokine concentrations in EDSS responders and non-responders.

Cytokine	Risk of Increasing EDSS while on IFN β	
	OR(95%CI)	P-values
MIG	0.81(0.66-1)	0.0485
TNF β	0.61(0.32-1.16)	0.1308
PAI	0.56(0.25-1.23)	0.1471
CXCL1/Gro α	0.75(0.51-1.11)	0.1489
IL1RA	0.84(0.66-1.07)	0.1667
VEGF	0.77(0.52-1.12)	0.1696
IL-8	0.92(0.81-1.04)	0.1990
PDGF	0.75(0.47-1.2)	0.2293
IL-1 β	0.83(0.6-1.14)	0.2490
MCP3	0.77(0.49-1.2)	0.2495
MIP1 α	0.85(0.64-1.14)	0.2847
ENA	0.76(0.45-1.27)	0.2919
MIP1 β	0.66(0.3-1.46)	0.3037
HGF	0.79(0.5-1.25)	0.3199
CXCL1/MCP1	0.85(0.61-1.19)	0.3388
Eotaxin	0.79(0.49-1.29)	0.3451
IL-6	0.74(0.39-1.42)	0.3652
Rantes	0.91(0.74-1.12)	0.3674
IL-7	0.74(0.39-1.42)	0.3690
IL12p40	0.84(0.56-1.24)	0.3804
LIF	0.91(0.73-1.13)	0.3856
sFasL	0.77(0.39-1.51)	0.4397
IL-2	0.8(0.45-1.42)	0.4526
IL-4	0.8(0.42-1.54)	0.5066
IL-1 α	0.83(0.48-1.44)	0.5129
IL-5	0.85(0.51-1.42)	0.5333
CD40L	0.96(0.85-1.09)	0.5561
CXCL10/IP10	0.76(0.28-2.02)	0.5786
MCSF	0.87(0.53-1.44)	0.5985
TNF α	0.81(0.36-1.83)	0.6085
ICAM	1.06(0.81-1.39)	0.6504
Leptin	0.89(0.52-1.54)	0.6825
SCF	0.79(0.24-2.56)	0.6922
NGF	0.95(0.66-1.35)	0.7590
GCSF	0.97(0.76-1.22)	0.7707
IFN γ	0.91(0.42-1.94)	0.8004
GMCSF	0.94(0.58-1.52)	0.8046
IFN α	0.97(0.76-1.24)	0.8058
IL-17	0.96(0.67-1.38)	0.8354
IL12p70	0.96(0.61-1.51)	0.8535
IL-10	0.96(0.61-1.53)	0.8775
FGF	0.95(0.43-2.08)	0.8945
IL-17F	0.97(0.64-1.47)	0.8965
sTRAIL	1.02(0.73-1.43)	0.9009
Resistin	0.99(0.74-1.31)	0.9191
sVCAM	1.01(0.77-1.33)	0.9269
TGF α	0.98(0.59-1.64)	0.9486
IL-13	0.99(0.55-1.78)	0.9744
IL-15	0.99(0.66-1.49)	0.9750
TGF β	1(0.57-1.76)	0.9917
IFN β	1(0.7-1.43)	0.9928

Note: EDSS non-responders were defined as having an increase of at least 1 Expanded Disability Status Scale (EDSS) point from baseline to 2 years post initiation of therapy. Baseline cytokine values were 2-log transformed odds ratios (OR), confidence intervals (CI) and p-values were assessed using logistic regression.

Table e-8: Serum cytokine concentrations with statistically significant changes from baseline to 3 months in EDSS responders and non-responders.

Responders (n=114)						
Cytokine	Baseline		3 Month		Δ from BL to 3M	
	Mean	SD	Mean	SD	P-value	Direction
CXCL10/IP10	67.38	17.64	244.32	177.31	< 0.0001	up
CCL2/MCP1	74.54	130.55	154.52	249.97	0.0007	up
IL-1α	35.42	31.77	46.80	23.28	0.0010	up
IFNβ	6.47	12.84	11.68	25.89	0.0029	up
PAI	3003.00	1400.61	2722.56	621.82	0.0121	down
CD40L	7666.54	8047.95	9529.21	11399.68	0.0161	up
IL-8	646.04	1392.37	383.25	1068.58	0.0190	down
IL-17A	3.10	1.49	3.37	1.77	0.0277	up
ENA	1342.11	576.62	1233.78	569.99	0.0406	down
NGF	35.20	14.75	37.83	17.62	0.0426	up
HGF	85.95	68.25	74.27	40.10	0.0435	down

Non Responders (N=39)						
Cytokine	Baseline		3 Month		Δ from BL to 3M	
	Mean	SD	Mean	SD	pvalue	Direction
CXCL10/IP10	65.88	18.10	269.81	224.20	< 0.0001	up
IL-1α	32.26	13.83	47.60	26.99	0.0001	up
VCAM	10718.00	4749.01	12535.83	5338.01	0.0015	up
CCL2/MCP1	45.45	35.28	112.96	140.75	0.0041	up
IFNβ	7.28	11.82	9.43	9.76	0.0136	up

Note: SD = standard deviation, EDSS = Expanded Disability Status Scale, BL= baseline, 3M = 3 months, Up = increase in concentration, Down = decrease in concentration. P-values were determined using a paired t-test.

Table e-9: Variability in serum cytokines in all RRMS samples.

Cytokine	Mean	SD	CV
IL-1β	15.18178	85.38205	562.398
IFNα	92.82164	282.0426	303.8543
IL1RA	1592.452	4373.452	274.6364
CXCL1/Groα	28.53919	73.52668	257.6341
IL-8	466.6038	1201.103	257.414
MIP1α	87.7992	183.8879	209.4415
IFNβ	8.79136	18.32557	208.4497
IL-17F	3.439355	7.149955	207.8865
GCSF	4.995596	9.486231	189.8919
CCL2/MCP1	105.3178	182.0219	172.8311
LIF	9.168905	12.11207	132.0995
CD40L	8152.059	9357.037	114.7813
IL-6	161.4753	182.7868	113.198
CXCL10/IP10	158.9792	162.0083	101.9054
TGF α	28.04252	23.93896	85.36666
Rantes	1196.324	913.6358	76.37026
MIG	66.54243	50.791	76.32874
ICAM	24096.02	18070.9	74.99537
VEGF	74.90045	52.87619	70.59529
HGF	77.903	53.22889	68.32714
IL-1 α	40.76071	26.71024	65.52938
IFN γ	4.28972	2.719828	63.40339
TNF β	19.93169	12.5423	62.92644
sTRAIL	62.2846	38.80343	62.3002
Resistin	2605.451	1590.732	61.054
VCAM	12264.53	6971.499	56.84279
IL12p70	121.1801	67.3262	55.5588
IL-17	32.58402	18.0982	55.54318
GMCSF	54.67159	29.89452	54.68017
MCP3	41.24495	22.38827	54.28123
IL-2	50.35949	26.59118	52.80272
IL-10	24.61486	12.78802	51.95244
IL-15	26.51929	13.51781	50.97352
IL-7	38.44577	19.30628	50.21693
Leptin	2344.315	1169.727	49.89632
IL-5	171.7358	84.972	49.47832
TGF β	22.64879	10.8607	47.95269
Eotaxin	38.60524	18.50225	47.92678
IL12p40	74.96423	35.52513	47.38945
NGF	36.62356	17.24343	47.08289
PDGF	2479.453	1158.717	46.73277
ENA	1273.79	573.886	45.05344
IL-4	17.65607	7.584387	42.95625
IL-13	28.74356	12.29113	42.76136
MIP1 β	1325.875	546.8478	41.2443
PAI	2813.971	1068.451	37.9695
MCSF	53.84071	18.41836	34.20899
FGF	69.67874	23.74226	34.07389
sFasL	49.45654	16.76712	33.90274
TNF α	222.9109	74.15677	33.26745
SCF	552.0407	116.3982	21.08507

Note: SD = Standard deviation, CV = Co-efficient of variation, RRMS = relapsing remitting multiple sclerosis.

Table e-10: Baseline clinical and demographic data of patients grouped by cytokine clusters.

Baseline Characteristics	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6	P-values
n	23	53	20	37	16	8	
Diagnosis [RRMS/CIS (%RRMS)]	15/8 (65.2)	43/10 (81.1)	13/7 (65.0)	26/11 (70.2)	12/4 (75.0)	5/3 (62.5)	0.5920 ^a
age, yrs (SD)	37.4 (6.8)	38.0 (8.7)	33.5 (9.3)	35.0 (9.0)	36.1 (10.1)	38.1 (7.6)	0.4256 ^b
Disease duration, yrs (SD)	4.3 (5.0)	6.6 (7.8)	3.5 (4.3)	4.1 (5.1)	3.4 (3.3)	3.0 (3.7)	0.3060 ^b
Sex F/M (% F)	15/8 (65.2)	37/16 (68.8)	13/7 (65.0)	29/8 (78.4)	9/7 (56.3)	5/3 (62.5)	0.6506 ^a
Baseline EDSS (SD)	1.3 (1.4)	1.9 (1.5)	1.8 (1.4)	1.3 (1.0)	1.5 (1.1)	1.2 (1.4)	0.1790 ^b
Number of relapses 2 yrs before BL (SD)	1.3 (0.7)	1.5 (0.7)	1.6 (0.7)	1.3 (0.7)	1.4 (0.7)	1.9 (0.8)	0.2647 ^b
Mean time between HDMP and BL, months (SD)	8.6 (8.2)	11.5 (9.7)	6.1 (6.0)	8.9 (8.5)	13.2 (9.5)	9.0 (6.9)	0.2105 ^b
Previous DMT use before BL [n(%)]	3 (13.0)	3 (5.7)	2 (10.0)	3 (8.1)	2 (12.5)	2 (25)	0.3496 ^a
IFN Preparation [n (%)]							
IM IFNβ-1a	11 (47.8)	30 (50.8)	10 (50.0)	15 (40.5)	8 (50.0)	4 (50.0)	0.2754 ^a
SC IFNβ-1b	5 (21.7)	6 (11.3)	6 (30.0)	16 (43.2)	1 (6.3)	2 (25.0)	
SC IFNβ-1a	7 (30.4)	17 (28.8)	4 (20.0)	6 (16.2)	7 (43.8)	2 (25.0)	

Notes: n = number, RRMS = relapsing remitting multiple sclerosis; CIS = clinically isolated syndrome, SD = standard deviation, F = Female, M = Male, EDSS = Expanded Disability Status Scale, IM = intramuscular, SC = subcutaneous, Resp = Responders, Non-Resp = Non-responders. HDMP = High dose methylprednisolone, DMT = Disease modifying therapy, BL = Baseline, Yrs = years. P-values were evaluated using ^aChi square tests or ^bKruskal Wallis tests with Dunn's multiple comparisons.

Table e-11. Previous Treatments of in the patients grouped by cytokine clusters.

Previous Treatment	Grp1	Grp2	Grp3	Grp4	Grp5	Grp6
	n	n	n	n	n	n
GLAT	1	2	1	0	2	1
IVIg	0	0	0	2	0	0
Azathioprin	0	0	0	1	0	0
Investigational medication	2	1	1	0	0	1
No previous treatment	20	50	18	34	14	6

Notes: GLAT = glatiramer acetate, Ivig = intravenous immunoglobulins.

Table e-12. Frequency of patients with relapses at 12 and 24 months in groups defined by baseline cytokine profiles.

	Group 1	Group 5	Not 1 and 5	P-value
12 months				
Relapse/No Relapse	2/21	1/15	48/70	0.0007
(% Relapse)	8.70%	6.25%	40.68%	
24 months				
Relapse/No Relapse	5/18	1/15	61/57	0.0002
(% Relapse)	21.74%	6.25%	51.69%	
	Group 3	Group 6	Not 3 and 6	P-value
12 months				
Relapse/No Relapse	10/10	5/3	36/93	0.0258
(% Relapse)	50.00%	62.50%	27.90%	
24 months				
Relapse/No Relapse	13/7	5/3	49/80	0.0384
(% Relapse)	65.00%	62.50%	37.98%	

Note: P-values were evaluated using Chi-square tests.

Table e-13: Patients that switch off IFN- β or develop neutralizing antibodies to IFN- β by 24 months post initiation of therapy.

	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6	P-values
n	23	53	20	37	16	8	
Switching off IFNβ [IFNβ off/on (%off)]	6/17 (26.1)	9/44 (17.0)	4/16 (20.0)	10/27 (27.0)	2/14 (12.5)	1/7 (12.5)	0.7359
NAbs [pos/neg (% pos)]	4/19 (17.4)	5/48 (9.4)	3/17 (15.0)	4/33 (10.8)	0/16 (0)	0/8 (0)	0.4692

Notes: n = number, pos = positive, neg = negative, NAbs = neutralizing antibodies to IFN- β . P-values were evaluated using Chi square tests.

Table e-14: Serum cytokine concentrations with statistically significant changes from baseline to 3 months in the six groups of MS patients.

Group 1 (N=23)						
Cytokine (pg/ml)	Baseline		3 Month		Δ from BL to 3M	
	Mean	SD	Mean	SD	P-value	Direction*
CXCL10/IP10	61.09	6.73	222.07	154.71	< 0.0001	up
IFNβ	3.11	1.66	6.35	3.40	< 0.0001	up
sTRAIL	45.93	20.29	57.93	26.06	0.0003	up
IL1RA	371.10	335.23	1048.03	1273.95	0.0039	up
IL-1α	27.27	4.97	42.69	27.37	0.0082	up
sVCAM	11478.68	4664.73	13090.41	4468.74	0.0103	up
IFNα	30.41	28.81	54.82	58.47	0.0198	up
CD40L	9658.91	4370.82	15522.04	14217.97	0.0336	up
IL-17F	1.63	0.81	1.93	1.01	0.0422	up
MIG	45.97	32.49	61.63	38.68	0.0486	up
CCL2/MCP1	34.97	17.09	100.42	163.13	0.0518	up
Group 2 (N=53)						
Cytokine (pg/ml)	Baseline		3 Month		Δ from BL to 3M	
	Mean	SD	Mean	SD	P-value	Direction
CXCL10/IP10	51.95	9.51	242.71	208.15	< 0.0001	up
CCL2/MCP1	30.44	17.21	98.54	108.29	< 0.0001	up
IL-1α	21.30	7.61	37.15	18.63	< 0.0001	up
IFNβ	3.16	2.21	5.59	2.99	< 0.0001	up
IFNα	30.83	23.08	74.39	63.03	< 0.0001	up
IL12p40	42.54967	21.0874	53.64724	27.13676	0.0002	up
NGF	21.49	10.68	26.92	13.38	0.0004	up
MIG	33.62	27.33	59.85	57.69	0.0007	up
IL-10	14.87	6.60	17.75	8.37	0.0010	up
IL-15	15.40	7.74	18.80	10.29	0.0012	up
Eotaxin	24.61	14.80	29.99	16.32	0.0014	up
sVCAM	8987.17	3694.95	10477.14	3481.67	0.0016	up
IL-1β	0.87	0.07	0.91	0.13	0.0017	up
CXCL1/Groα	10.29	3.99	13.42	7.61	0.0020	up
VEGF	38.85	19.16	47.36	25.25	0.0026	up
MIP1α	29.21	19.79	41.32	30.34	0.0027	up
IL1RA	166.13	78.16	792.29	1473.91	0.0029	up
IL17	2.39	1.23	2.81	1.62	0.0036	up
GMCSF	32.75	13.71	38.95	17.20	0.0045	up
LIF	1.72	2.60	3.41	4.63	0.0047	up
MIP1β	997.83	249.42	1140.55	405.55	0.0062	up
IL12p70	71.57	29.42	85.66	41.91	0.0064	up
GCSF	0.85	2.28	2.24	4.24	0.0071	up
MCSF	46.23	16.43	51.63	20.14	0.0081	up
TNFα	167.88	40.26	183.48	48.18	0.0083	up
sTRAIL	34.86	17.14	45.38	24.13	0.0107	up
IL-5	104.52	37.85	122.31	53.26	0.0119	up
IL-4	11.97	3.55	13.50	4.88	0.0142	up
IL-13	19.44	6.91	22.17	9.51	0.0160	up
IFNγ	2.86	0.77	3.24	1.31	0.0186	up
FGF	55.54	16.03	60.44	21.69	0.0215	up
IL-2	33.73	11.52	38.72	14.96	0.0258	up
TNFβ	16.35	5.84	18.20	7.48	0.0291	up
MCP3	25.78	10.49	30.41	14.06	0.0299	up
ICAM	19161.95	17723.52	21168.40	18077.20	0.0302	up
CD40L	805.79	1150.26	2037.74	4193.96	0.0342	up
TGFα	17.24	6.09	18.91	8.73	0.0404	up
SCF	466.70	82.14	490.58	99.25	0.0427	up

Group 3 (N=20)						
Cytokine (pg/ml)	Baseline		3 Month		Δ from BL to 3M	
	Mean	SD	Mean	SD	P-value	Direction
IL-8	3953.84	590.38	1644.19	1951.21	< 0.0001	down
CXCL10/IP10	80.99	18.34	253.77	205.29	0.0013	up
IL-17	4.14	1.36	3.30	1.49	0.0013	down
VEGF	145.44	47.72	101.10	59.68	0.0032	down
Resistin	5395.36	654.51	4429.60	1430.42	0.0041	down
MIG	121.62	35.44	85.88	42.49	0.0049	down
sTRAIL	135.17	29.54	98.04	54.05	0.0054	down
sFasL	57.18	10.27	48.57	16.45	0.0079	down
IL12p40	117.88	30.16	98.63	34.92	0.0117	down
Eotaxin	59.66	15.15	49.13	20.28	0.0164	down
PAI	4766.31	2615.43	3549.39	1575.25	0.0223	down
ICAM	29370.96	19904.16	25185.90	15075.81	0.0233	down
TNFβ	21.72	4.04	18.94	6.50	0.0336	down
IL-1α	44.02	13.80	55.70	27.75	0.0390	up
HGF	182.84	105.93	122.53	63.69	0.0445	down

Group 4 (N=37)						
Cytokine (pg/ml)	Baseline		3 Month		Δ from BL to 3M	
	Mean	SD	Mean	SD	P-value	Direction
CXCL10/IP10	75.76	10.14	244.37	153.75	< 0.0001	up
IFNβ	5.42	3.90	7.59	4.14	< 0.0001	up
PDGF	2695.36	863.03	2233.09	743.72	0.0007	down
HGF	80.82	28.46	70.59	25.86	0.0061	down
CCL2/MCP1	44.89	18.30	111.59	145.80	0.0086	up
VEGF	93.12	20.87	80.78	29.27	0.0112	down
Eotaxin	49.39	16.41	43.41	15.80	0.0264	down
ENA	1519.56	478.04	1306.46	614.84	0.0303	down
TGFα	31.02	15.01	25.14	8.95	0.0316	down
IL-7	44.31	9.74	39.72	12.60	0.0395	down
IL-5	213.05	41.22	191.29	70.63	0.0457	down
IL-4	21.37	4.58	19.49	5.54	0.0499	down

Group 5 (N=16)						
Cytokine (pg/ml)	Baseline		3 Month		Δ from BL to 3M	
	Mean	SD	Mean	SD	P-value	Direction
CXCL10/IP10	85.23	17.58	315.69	209.72	0.0004	up
IL-1α	42.58	8.04	56.85	24.04	0.0106	up
IL-2	66.73	15.30	57.90	18.18	0.0235	down
PDGF	3056.70	853.83	2650.72	747.37	0.0244	down
IL-7	49.00	6.07	43.43	10.63	0.0273	down
IL-5	249.96	56.09	214.26	70.63	0.0371	down
CCL2/MCP1	35.28	14.65	154.60	210.91	0.0394	up

Group 6 (N=8)						
Cytokine (pg/ml)	Baseline		3 Month		Δ from BL to 3M	
	Mean	SD	Mean	SD	P-value	Direction
IL1RA	641.91	723.71	1076.50	1024.35	0.0182	up
CXCL10/IP10	72.78	19.68	281.60	214.98	0.0259	up
IL-1α	39.48	13.08	57.12	17.08	0.0369	up
TGFβ	23.01	12.68	29.42	15.33	0.0382	up

Note: BL = baseline, 3M = 3 month, SD = standard deviation. P-values were determined using a paired t-test. *Up = increase in concentration; Down = decrease in concentration.