

Supplementary figure S1. Median (error bars = interquartile range) levels of interleukin 6 in 12 patients (8.5%) starting with tocilizumab at baseline. * $p < 0.05$, ** $p < 0.01$ rise from baseline

Supplementary table S1. Spearman's rank correlation coefficients (r_s) between biomarkers and sum US scores and clinical parameters during follow-up

	Sum GS score	Sum PD score	Assessor's global VAS	DAS28	Swollen joints (of 32)	Tender joints (of 32)	Patient's global VAS	Joint pain VAS
One month								
Calprotectin	0.51**	0.53**	0.51**	0.44**	0.42**	0.21*	0.23*	0.32**
S100A12	0.30**	0.38**	0.35**	0.29**	0.28**	0.13	0.08	0.11
IL-6	0.39**	0.42**	0.43**	0.38**	0.36**	0.20*	0.15	0.24*
VEGF	0.18*	0.17*	-0.03	0.08	-0.01	0.05	0.08	0.17*
ESR	0.04	0.14	0.28**	0.56**	0.10	0.08	0.09	0.12
CRP	0.21*	0.23*	0.29**	0.30**	0.17*	-0.02	0.05	0.08
Two months								
Calprotectin	0.50**	0.53**	0.50**	0.45**	0.46**	0.24*	0.20*	0.25*
S100A12	0.26*	0.36**	0.39**	0.32**	0.30**	0.16*	0.19*	0.20*
IL-6	0.51**	0.49**	0.55**	0.43**	0.50**	0.25*	0.16	0.20*
VEGF	0.21*	0.19*	0.17*	0.11	0.10	0.03	0.09	0.17*
ESR	0.06	0.15	0.22*	0.57**	0.09	0.13	0.22*	0.25*
CRP	0.30**	0.33**	0.34**	0.30**	0.28**	0.03	0.13	0.13
Three months								
Calprotectin	0.37**	0.46**	0.48**	0.44**	0.41**	0.21*	0.29**	0.27**
S100A12	0.32**	0.36**	0.36**	0.30**	0.31**	0.18*	0.14	0.12
IL-6	0.43**	0.47**	0.53**	0.35**	0.53**	0.18*	0.24*	0.29**
VEGF	0.19*	0.16	0.17*	0.03	0.13	-0.07	0.16	0.16
ESR	0.01	0.12	0.21*	0.57**	0.05	0.07	0.22*	0.18*
CRP	0.18*	0.26*	0.33**	0.44**	0.26**	0.05	0.20*	0.20*
Six months								
Calprotectin	0.48**	0.47**	0.44**	0.37**	0.45**	0.12	0.23*	0.20*

S100A12	0.26*	0.24*	0.33**	0.27**	0.23*	0.09	0.14	0.18*
IL-6	0.40**	0.49**	0.36**	0.36**	0.40**	0.15	0.17*	0.22*
VEGF	0.18*	0.12	0.17*	0.04	0.10	0.01	0.14	0.16
ESR	0.19*	0.21*	0.22*	0.53**	0.09	0.09	0.09	0.09
CRP	0.33**	0.35**	0.35**	0.41**	0.28**	0.07	0.22*	0.17*

Twelve months

Calprotectin	0.25*	0.31**	0.20*	0.25*	0.24*	0.12	0.22*	0.23*
S100A12	0.07	0.17*	0.03	0.09	-0.00	-0.04	0.04	0.04
IL-6	0.43**	0.43**	0.33**	0.24*	0.37**	0.13	0.11	0.20*
VEGF	0.07	0.01	0.02	-0.08	-0.03	-0.08	0.09	0.07
ESR	0.01	0.15	0.25*	0.60**	0.11	0.14	0.17*	0.09
CRP	0.20*	0.30**	0.27**	0.34**	0.26*	0.14	0.13	0.12

Sum GS score = sum of grey scale scores on a 0-3 scale of 36 joints and four tendon sheaths, sum PD score= sum power Doppler scores on a 0-3 scale of 36 joints and four tendon sheaths, VAS = visual analogue scale, DAS28 = disease activity score of 28 joints (including ESR), VEGF = vascular endothelial growth factor, IL-6 = interleukin 6, ESR = erythrocyte sedimentation rate, CRP = C-reactive protein, *p<0.05, **p≤0.001

Supplementary table S2. Spearman's rank correlation coefficients (r_s) between calprotectin and sum US and sum Lansbury US scores

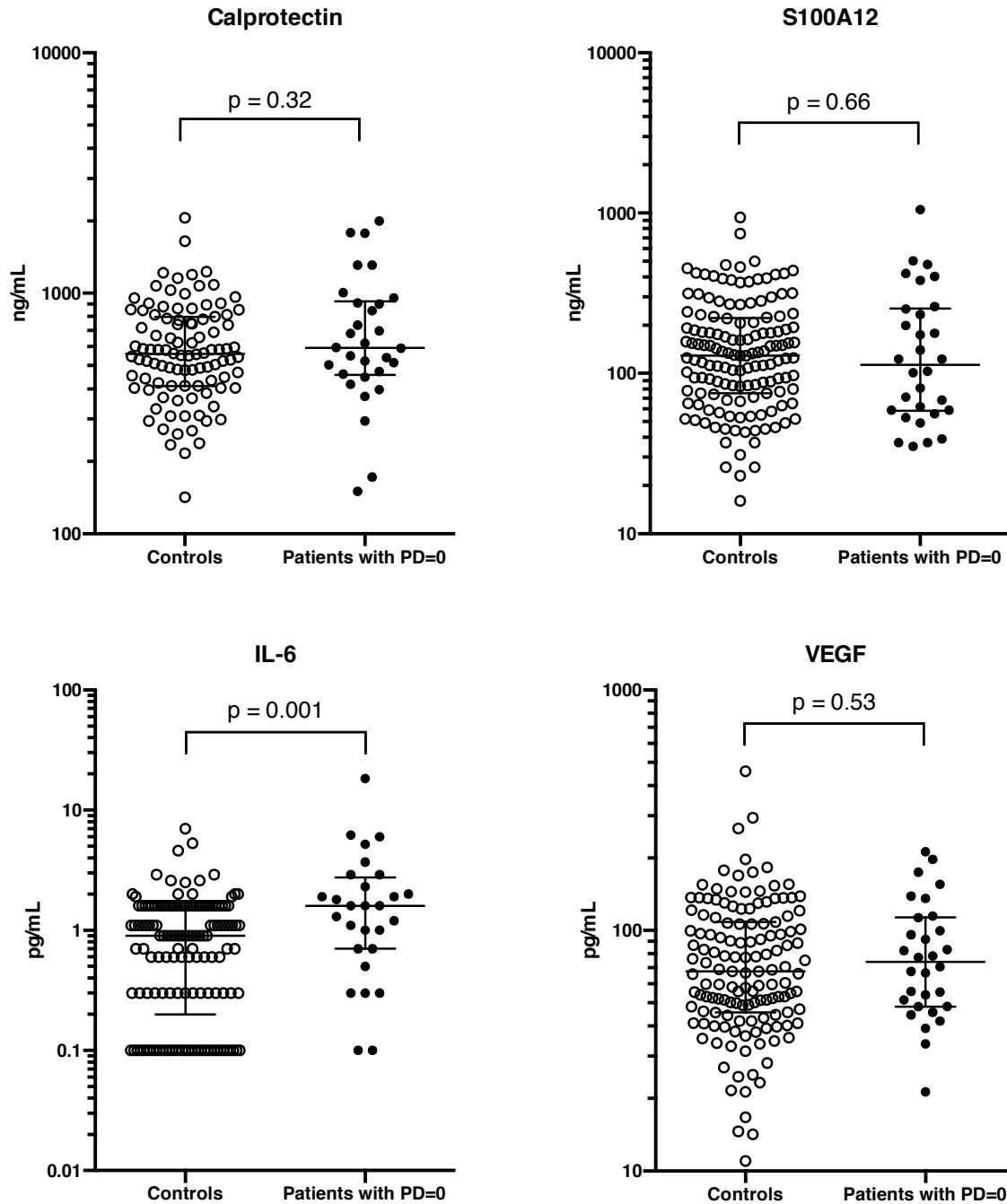
	Sum GS score	Sum LGS score	Sum PD score	Sum LPD score
Calprotectin				
Baseline	0.59**	0.62**	0.62**	0.63**
1 month	0.51**	0.47**	0.53**	0.57**
2 months	0.50**	0.43**	0.53**	0.52**
3 months	0.37**	0.41**	0.46**	0.47**
6 months	0.48**	0.47**	0.47**	0.50**
12 months	0.25*	0.29**	0.31**	0.29**

GS=grey scale, LGS=Lansbury grey scale, PD=power Doppler, LPD=Lansbury power Doppler, * $p < 0.01$, ** $p \leq 0.001$

Supplementary table S3. Spearman's rank correlation coefficients (r_s) between calprotectin/conventional inflammatory markers and sum ultrasound scores in patients using tocilizumab (n=12)

	Sum GS score						Sum PD score					
	Baseline	1 month	2 months	3 months	6 months	12 months	Baseline	1 month	2 months	3 months	6 months	12 months
Calprotectin	0.66*	0.45	0.53	0.30	0.64*	0.54	0.50	0.27	0.83**	0.67*	0.57	0.57
ESR	-0.007	-0.26	-0.38	-0.27	0.07	0.36	0.21	-0.22	-0.24	0.09	-0.07	0.49
CRP	0.41	0.43	-0.04	-0.11	0.43	0.64*	0.36	0.26	0.22	0.54	0.23	0.72**

Sum GS score = sum of grey scale scores on a 0-3 scale of 36 joints and four tendon sheaths, sum PD score= sum power Doppler scores on a 0-3 scale of 36 joints and four tendon sheaths, ESR =erythrocyte sedimentation rate, CRP = C-reactive protein, * $p < 0.05$, ** $p \leq 0.001$



Supplementary figure S2. Median levels with range of inflammatory markers in controls (n=100 for calprotectin, n=141 for S100A12, IL-6 and VEGF) and patients with no PD activity at 12 months (n=30 for calprotectin, S100A12 and VEGF, n=28 for IL-6 (patients on tocilizumab omitted))

Supplementary table S4. Spearman's rank correlation coefficients (r_s) between changes in inflammatory markers and sum US scores/DAS28 from baseline to one, two, three, six and 12 months

Baseline to one month	ΔSum GS score	ΔSum PD score	ΔDAS28
ΔCalprotectin	0.29**	0.35**	0.47**
ΔS100A12	0.22*	0.17*	0.22*
ΔIL-6	0.10	0.23*	0.15
ΔVEGF	0.14	0.11	0.32**
ΔESR	0.14	0.20*	0.65**
ΔCRP	0.14	0.24*	0.41*
Baseline to two months	ΔSum GS score	ΔSum PD score	ΔDAS28
ΔCalprotectin	0.39**	0.43**	0.55**
ΔS100A12	0.17*	0.18*	0.35**
ΔIL-6	0.30**	0.33**	0.31**
ΔVEGF	0.12	0.18*	0.26*
ΔESR	0.21*	0.30**	0.60**
ΔCRP	0.32**	0.33**	0.42**
Baseline to three months	ΔSum GS score	ΔSum PD score	ΔDAS28
ΔCalprotectin	0.42**	0.46**	0.50**
ΔS100A12	0.22*	0.21*	0.31**
ΔIL-6	0.25*	0.25*	0.21*
ΔVEGF	0.07	0.10	0.22*
ΔESR	0.14	0.22*	0.55**
ΔCRP	0.20*	0.27**	0.39**
Baseline to six months	ΔSum GS score	ΔSum PD score	ΔDAS28
ΔCalprotectin	0.43**	0.45**	0.43**
ΔS100A12	0.21*	0.23*	0.24*
ΔIL-6	0.36**	0.48**	0.28**
ΔVEGF	0.07	0.11	0.17*
ΔESR	0.24*	0.22*	0.49**
ΔCRP	0.34**	0.35**	0.37**
Baseline to 12 months	ΔSum GS score	ΔSum PD score	ΔDAS28
ΔCalprotectin	0.46**	0.51**	0.46**
ΔS100A12	0.27**	0.36**	0.26*
ΔIL-6	0.32**	0.38**	0.25*
ΔVEGF	0.17*	0.22*	0.25*
ΔESR	0.36**	0.42**	0.56**
ΔCRP	0.42**	0.50**	0.47**

US = ultrasound scores, DAS28 = disease activity score of 28 joints, GS = grey scale, PD = power Doppler, VEGF = vascular endothelial growth factor, IL-6 = interleukin 6, ESR = erythrocyte sedimentation rate, CRP = C-reactive protein, * $p < 0.05$, ** $p \leq 0.001$

Supplementary table S5. Median (interquartile range) levels of biomarkers in EULAR good, moderate and non responders at three, six and 12 months

	Good responders	Moderate responders	Non responders	p-value 1	p-value 2	p-value 3	p-value 4
Three months	n=44	n=40	n=57				
Calprotectin (ng/mL)	546 (460)	691 (705)	748 (812)	0.04	0.02	0.73	0.11
S100A12 (ng/mL)	110 (248)	192 (234)	154 (216)	0.14	0.08	0.85	0.24
IL-6 (pg/mL)	2.2 (21.1)	3.1 (9.3)	4.5 (8.7)	0.77	0.20	0.36	0.19
VEGF (pg/mL)	78.6 (129.6)	46.6 (97.4)	76.4 (82.9)	0.18	0.87	0.17	0.49
ESR (mm/h)	7 (16)	20 (20)	19 (15)	0.000	0.000	0.87	0.02
CRP (mg/L)	1 (1)	2 (4)	2 (6)	0.02	0.002	0.62	0.03
Six months	n=53	n=43	n=45				
Calprotectin (ng/mL)	579 (350)	718 (557)	780 (867)	0.08	0.02	0.34	0.05
S100A12 (ng/mL)	103 (143)	137 (203)	152 (219)	0.17	0.07	0.57	0.15
IL-6 (pg/mL)	1.9 (3.6)	2.4 (4.3)	3.3 (8.5)	0.29	0.02	0.12	0.02
VEGF (pg/mL)	71.9 (90.4)	62.3 (93.7)	76.2 (82.1)	0.98	0.57	0.58	0.52
ESR (mm/h)	10 (12)	18 (16)	12 (14)	0.003	0.03	0.43	0.36
CRP (mg/L)	1 (2)	2 (5)	2 (6)	0.002	0.001	0.71	0.03
12 months	n=57	n=41	n=43				
Calprotectin (ng/mL)	619 (486)	641 (502)	666 (834)	0.58	0.22	0.50	0.26
S100A12 (ng/mL)	140 (275)	133 (128)	135 (327)	0.69	0.52	0.29	0.35
IL-6 (pg/mL)	1.9 (3.5)	2.1 (4.0)	2.9 (9.6)	0.82	0.16	0.22	0.13
VEGF (pg/mL)	79.9 (122.8)	68.0 (74.6)	64 (66.8)	0.76	0.58	0.84	0.65
ESR (mm/h)	10 (13)	15 (14)	17 (14)	0.03	0.000	0.25	0.004
CRP (mg/L)	1 (1)	2 (3)	3 (7)	0.23	0.001	0.03	0.001

IL-6 = interleukin 6, VEGF = vascular endothelial growth factor, ESR = erythrocyte sedimentation rate, CRP = C-reactive protein

p-value 1: difference between good and moderate responders, p-value 2: difference between good and non-responders, p-value 3: difference between moderate and non- responders, p-value 4: difference between good/moderate and non-responders